Ce–M–M–

Research Center for Molecular Medicine
of the Austrian Academy of Sciences

Research Report 2018

Ce–M–M–

Research Center for Molecular Medicine
of the Austrian Academy of Sciences

Research Report 2018

ÖAW AUSTRIAN ACADEMY OF SCIENCES

The Mission of CeMM

is to achieve maximum scientific innovation in molecular medicine to improve healthcare.
At CeMM, an international and creative team of scientists and medical doctors pursues free-minded basic life science research in a large and vibrant hospital environment characterized by outstanding medical tradition and practice. CeMM's research is based on post-genomic technologies and focuses on societally important diseases, such as immune disorders and infections, cancer and metabolic disorders. CeMM operates in a unique mode of super-cooperation, connecting biology with medicine, experiments with computation, discovery with translation, and science with society and the arts. CeMM trains modern biomedical scientists to make great contributions. The goal of CeMM is to pioneer the science that nurtures the precise, personalized, predictive and preventive medicine of the future.

Introduction Research Report 2018

CeMM Directors
Anita Ender and
Giulio Superti-Furga

The year 2018 has seen an important turn in the development of CeMM. For the first time in many years, we have experienced an injection of new ideas and energy through the much-needed and welcomed expansion of faculty. Despite our success, measurable by many parameters and benchmarking operated within the EU-LIFE group of institutes, CeMM core funding has remained more or less the same for the last ten years, equating to a decrease in purchasing power. We are grateful for the financial support provided by our mother institution, the Austrian Academy of Sciences, which is key to keeping the infrastructure running. But for too long, we have allowed this to affect our operation, watching, as institutes and institutions have entered the precision medicine field that we helped to pioneer, with new funds and resources and pretty much our slogans. In 2018, we identified a strategy to move forward nonetheless, building on the trust and reputation we have earned within the scientific community. This manifested itself in a call, put out jointly with our sister institute, the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases, for adjunct faculty members: adjunct faculty are essentially expert volunteers who want to participate in our PhD training and research program and CeMM's faculty life, counterpointed by our weekly science meetings and speckled with brain-storming discussions. In a competitive call, we obtained dozens of applications and, with the help of an international scientific hiring committee, settled on five new colleagues: two chemists, Miriam Unterlass and Nuno Maulide, and three medical doctors, Georg Stary, Andreas Villunger and Thomas Reiberger. We welcome them wholeheartedly and thank their mother institutions for their trust and friendship. We are confident that these new colleagues will greatly enrich our medical, technical, scientific and human horizons, forming the basis for CeMM's success in the future decade.

We also would like to acknowledge a past member of faculty: Denise P. Barlow. On commemorating the first anniversary of her passing, we decided, in consultation with the other Viennese life science institutions with which she was associated in various ways and with the approval of her family, to launch an award in her name. The Denise P. Barlow Award, sponsored by IMP, IMBA, MFPL and CeMM, will be a yearly recognition for the best thesis on molecular mechanisms emerging from any of these four institutes, and will go specifically toward supporting scientists in the delicate transition to postdoc life, often made additionally difficult by financial bottlenecks associated with moving, childcare, trainings and the like. The award celebration will be a good occasion to welcome back past awardees and to celebrate the deep impact that Denise P. Barlow has had on molecular biology and in particular genetic imprinting and long non-coding RNAs.

Remaining on the topic of inspirational colleagues, 2018 has seen a fundamental step in the recognition of the person whose contributions have certainly been the single most decisive in turning Vienna from a rather peripheral research locality for molecular biology to the internationally visible buzzing hub that it is now: Max L. Birnstiel. One of us (GSF) was a PhD student in Zurich and part of the IMP founding team, and had the privilege to follow Max, the professor, and Meinrad Busslinger, the direct supervisor, from Zurich to Vienna and to participate in the amazing adventure that ensued. The conversation with Margaret and Kirsty Birnstiel, Max's wife and daughter, about possible ways to honor Max Birnstiel's memory and fundamental contributions, that started in 2015, flowed naturally. As a result, CeMM and IMP had the extraordinary privilege of being involved in the creation of the Max Birnstiel Foundation. This will also allow CeMM to participate in the VBC Summer School for the first time in the coming year: an inspiring initiative dedicated to introducing young people to molecular biology. How wonderful to have all of this made possible by the foundation honoring the very person that kickstarted our community's entire molecular biology journey!

In terms of empowering forces, 2018 also saw the kickoff of an exciting project that is immense in terms of size and potential impact. RESOLUTE (Research Empowerment on Solute Carriers) is one of the largest grants CeMM has coordinated so far, financed with almost €24 million by the Innovative Medicines Initiative of the European Union and EFPIA. Chemical matter, such as nutrients, vitamins and drugs do not enter biological systems, like the human body or the cells in a human body, simply by diffusion. Instead, these molecules require proteins called transporters to permeate the various membranes that delineate biological systems. There are hundreds of these transporters encoded in the human genome, but their specificity, i.e. exactly what they individually transport, and their function has been elusive. However, as all chemical matter requires them to access biosystems, they are of fundamental biological, medical and pharmacological relevance. The RESOLUTE consortium, consisting of six academic laboratories, one biotech and six pharmaceutical companies, has a detailed and multidisciplinary plan on how to "decode" the specificity of all these transporters (what they transport) over a period of five years and, better still, how they function together in an integrated manner. For CeMM, this is a transformative experience, both in terms of the intellectual and the logistical challenge as well as in terms of the social know-how of coordinating a group of scientists with and from such diverse backgrounds and environments. For once, the "scientific chapter", drafted under our responsibility in this postgenomic book of knowledge for precision medicine, is really extensive. A true upgrade.

But also CeMM's interface with the arts has made important advances. The empty Western wall of the 8th floor seminar room has become home to a sculpture of lacquered wood and metal by Klaus Pamminger, who had already contributed to the CeMM Brain Lounge. Called "Stiegenhaus, 11 Square Albin Cachot, 75013 Paris-13E RC01-BDJ", it is inspired by the staircase and landing ascended in a fateful manner by actress Catherine Deneuve in a famous Luis Buñuel movie. A video that illustrates the link to the geometry involved accompanies the sculpture. A liaison between mathematical precision, light, color and one's personal biographical decisions capturing a precise motion. We really feel an overwhelming gratitude to the artist for this generous donation. But also, because he spent an incredible amount of time hanging and repairing the sculpture after repetitive physical attacks caused by the clumsiness of scientists, who are, among other things, slowly being trained at CeMM to live in harmony with art without resorting to physical force. Through this process we were also lucky enough to meet and befriend artist Jonas Feferle, who agreed to "do" the 12th chair of the Brain Lounge carousel. Jonas gave the backrest a silver translucent, ultra-elegant and discrete shroud that both reflects objects outside and offers an entry into another dimension beyond its surface. It has the quality of traditional silvered relics or wooden statues, or an ancient chocolate bar. Certainly evoking a yearning for something sublime. Thank you, Jonas. Now there are only two chairs to go. Artists of the world, your ideas are welcome!

This year's Research Report revolves around the most quintessential of Viennese institutions and the stage for multicultural communication "par excellence": the Kaffeehaus. No other place represents ease of conversation and exchange of ideas better. A "neutral" place, where everybody armed with the coins required to purchase a coffee feels equally at home. A place that provides warmth and comfort in the long winters and discrete, non-invasive company to even the loneliest of souls. Throughout the centuries, the very fabric of Vienna's cultural life has notoriously been sewn from the thread of the different coffeehouses in the first and many other city districts. Love affairs, inventions, job offers, companies, poems, novels, marriages, intrigues, crusades and campaigns of all sorts were born there. We staged discussions on what 2018 meant for CeMM in some of the Kaffeehäuser that indeed make up much of CeMM's extramural life. You have to imagine them not as something artificial, but truly as an extended CeMM living room and at the same time, a real interface with civil society. It's virtually impossible not to meet someone you know, even in a city of nearly 2 million. We hope you enjoy the tour and the accompanying discussions. We thank everyone who participated, photographers Lukas Beck and Franzi Kreis for the wonderful pictures, and as usual, our visual identity partners Lichtwitz Leinfellner visuelle Kultur KG for accompanying us throughout the journey. Even if some may not be aware of it, corporate identity for CeMM is not a necessity or a choice, it is a fundamental part of our DNA, a vital thread that runs through all our activities. If you attempt to disentwine it from CeMM's research and training activities or from our building, you may as well kill the cultural institution CeMM. We would like to thank Eva Schweng, overall editor and master of the book. This year we pay tribute to your work by putting you on the cover of the Research Report, where you belong.

We end by thanking the Board of the Austrian Academy of Sciences for the steady and discrete support, without which we would collapse and, last but not least, all CeMMies, novices as well as veterans and alumni. It is your hard work and your fabulous research that this is all about and the rest of this book tells of your success.

Giulio Superti-Furga and Anita Ender

CeMM and its Kaffeehäuser

In this CeMM Research Report, we take our discussion outside of CeMM and into the city. An immediate extension to the physical perimeter of our headquarters are the Kaffeehäuser/coffeehouses. Each one was chosen for specific reasons. Enjoy the tour and imagine sipping a "Melange".

Café Weimar on Währinger Strasse is just 500 meters or seven walking minutes away from CeMM. It has traditionally been home to many strategic meetings with the management of the Medical University and many MedUni faculty members. It was family run until recently and is a very 9th-district place, with few tourists and a solid cuisine. Conveniently, it is also a place where you can meet Anton Zeilinger, the President of the Austrian Academy of Sciences, our "boss", as his university institute is on Boltzmanngasse. The whole neighborhood has left an indelible imprint on world literature because of the wonderful novel by Heimito von Doderer *Die Strudlhofstiege (Strudlhof steps)*. Our discussion on chemical biology is conveniently set there, as this is where other talks on the same topic have already taken place.

Café Landtmann on Universitätsring is a quarter of an hour away from CeMM by public transport which corresponds to a walk of just over 20 minutes to cover the 2-kilometer distance. It is the most venerable of all Wiener Kaffeehäuser and an extended living room to many ministerial offices. At Café Landtmann, you might rub shoulders with senior officials of the nearby Ministries or the University of Vienna, or you might go there to be seen by them. At certain times of the week, everyone knows everyone else, at least from "looking away", as an old Viennese saying goes ("Ich kenn' Sie vom Wegschau'n"). Leading bankers, politicians, architects, and business people meet there, and many momentous events have come to pass in Vienna as a result of casual encounters across the tables of leading Kaffeehäuser. Located across from the main building of the University of Vienna and the Town Hall and in very close proximity to the offices of the Ministry of Education, Science and Research, Café Landtmann has, over the years, been the venue of many key discussions impinging on CeMM's fate and budget. The joint press conference with the Medical University of Vienna, announcing the discovery, by Robert Kralovics and Heinz Gisslinger, of the calreticulin gene as a missing gene in the genetic landscape of myeloproliferative neoplasms was held there. Symbolically speaking, it was appropriate to hold the directors' discussion on CeMM's strategy in Café Landtmann. No other Kaffeehaus could confer as much prestige. And the food is excellent.

Café Prückel is a CeMM outstation near the headquarters of the Austrian Academy of Sciences. Together with Café Engländer and Café Diglas, it is where one hangs out between the large Academy meetings, typically between a *"Klassensitzung"* (meeting of the mathematical/natural sciences class) and the *"Gesamtsitzung"* (plenary meeting). But one also meets there to prepare for individual meetings at the Academy, for scientific or administrative reasons. Finally, one goes there to "recover" after particularly stressful meetings, typically related to budget. Only 250 meters away from the beautiful Academy building, which was built in the mid-18th century and has been the seat of the Academy since the mid-19th century, Café Prückel is where you can meet Academy members and officials having lunch. While located on the "other side of the 1st district" from a CeMM perspective, Café Prückel is easy to reach from CeMM using the U3 subway (Stubentor station), the *"Ringwagen"* tram or the compact 3A bus that cuts across the 1st district from Schottentor to Stubentor (two former city gates). Historically, many meetings important to CeMM have taken place in Café Prückel which is why we decided to pay symbolical tribute to our mother organization by setting our meeting related to the subject of inflammation there.

Café Eiles is only a 20-minute walk from CeMM, nearer to the city center and right by subway stops. It is also close to the hotels where CeMM usually puts up its guests. Drawing a slightly younger crowd and generally less formal than Landtmann, Weimar and Prückel, it is also quite a large coffeehouse, making it not all too hard to find a table. It is also slightly less likely to meet "important people" there and thus slightly more discreet than the ones mentioned above (though a Viennese Kaffeehaus is never anonymous!) A café very often frequented by CeMMies for small meetings dealing with future activities, career and strategy, it is also the place where key discussions and hiring for one of CeMM's spin-off companies, Haplogen, occurred. Sitting at one of its window tables, it is fun to watch the busy *"Zweierlinie"* traffic (road named after its former "No. 2" tram route, parallel to and outside of the *"Ring"* road) or the various pedestrians on Josefstädter Strasse. The genomic discussion took place at this venue, also to acknowledge the growing diversity of the people who make up modern Vienna today.

Coffee Pirates on Spitalgasse in front of *"Altes AKH"* (old hospital), 5 walking minutes away from CeMM, is the nearest Kaffeehaus and also the most recently established, dating from about the same year CeMM took up residence in the new building. From those starting years, CeMMies colonized the place due to their appreciation for its dedication to high-quality coffee, freshly roasted and ground, and the English language skills of the super-friendly and competent baristas. Meant to evoke a private living room, all the chairs are uniquely different, music is often played on a vintage vinyl record player and there is tap water, free for the taking. Before coming to work, many CeMMies arriving from the Alser Strasse tramway stops or, living nearby, drop in to grab a take-away coffee. This is essentially where the CeMM spin-off company Allcyte was incubated and also where it threw its "coming out" party. Symbolically, we thought that it would be appropriate for the most novel addition to CeMM faculty to discuss their views in this most modern of the CeMM Kaffeehäuser.

We hope you enjoy our little tour of the Kaffeehäuser, rather than thinking of researchers as being confined to an ivory tower, can relate to them as members of civic society, sitting next to you, drinking coffee, exchanging ideas and discussing how the future may look.

One of our Viennese coffeehouses from the inside.

Coffeehouses

Café Weimar
Währinger Straße 68
1090 Vienna

Coffee Pirates
Spitalgasse 17
1090 Vienna

Café Eiles
Josefstädter Straße 2
1080 Vienna

Café Landtmann
Universitätsring 4
1010 Vienna

Café Prückel
Stubenring 24
1010 Vienna

Points of Interest

CeMM Research Center for Molecular Medicine of the ÖAW
Lazarettgasse 14
1090 Vienna

Vienna General Hospital
Währinger Straße 18–20
1090 Vienna

Medical University of Vienna
Spitalgasse 23
1090 Vienna

University of Vienna
Universitätsring 1
1010 Vienna

Vienna City Hall
Friedrich-Schmidt-Platz 1
1010 Vienna

Ministry of Education, Science and Research
Minoritenplatz 5
1010 Vienna

Vienna University of Technology
Karlsplatz 13
1040 Vienna

St. Stephen's Cathedral
Stephansplatz 3
1010 Vienna

Austrian Academy of Sciences
Dr. Ignaz Seipel-Platz 2
1010 Vienna

Science at CeMM

Science

1st Talk at Café Landtmann

Strategy and Directions

Giulio Superti-Furga
and Anita Ender

Strategy and Directions

Discussion on the 2018 challenges, decisions taken, trends for the future, EU-Life

What is new about 2018 in terms of directions, governance, organization?

Ender: The most important thing was the search for the new Adjunct PIs, the real success story of the year. I am happy that we found five wonderful candidates out of 100 applications that are a perfect fit for CeMM in terms of collaboration, compatibility, spirit and scientific outreach.

Superti-Furga: I agree, I think that the strategic decision to include Adjunct PIs was a very important one. In one go, we are expanding our intellectual brain pool and we have great expectations that it will yield yet other bridges to medicine, to the Medical University but also to patients and patient needs, an area which is likely to become more and more important. But I am also very happy about the development towards chemistry in terms of our empowerment. Maybe we can also say that in 2018, our attempts to be more inclusive, in a general sense, and to sort of have as much diversity as possible, have improved, and that we have implemented more actively some of the principles we set out, for example in the LIBRA protocol.

Ender: I am also grateful to the universities who immediately allowed us to bring in these new people. From the Medical Universities in Vienna and Innsbruck, to the Vienna University of Technology and the University of Vienna.

Superti-Furga: I think it's a great sign of the support and, let's say, solidarity that we are experiencing with these universities, that they are so willing to collaborate with us.

Ender: Maybe it's also important to mention that with this search, we saw there is much interest in collaborating with us, and we are now thinking about how to involve the applicants who did not get a chance to have an adjunct appointment with CeMM, to open other doors for collaboration.

Which other institutes have impressed/inspired you most in 2018?

Superti-Furga: I think two institutions rather than institutes, have shown to us the importance of being very serious about excellence and never to compromise about it: EU-LIFE and the ERC. I think in both cases, we learn to avoid "elite remorse", or the embarrassment of being very good, and at the same time saying, "We are not that good, really, and we can include other people by lowering the standards". I think that is always a mistake and it happens all the time. I think it is important that we are very, very certain about the fact that the best way to help our community and society is to be very clear and unapologetic about why our duty is to aspire to be as good as possible and to inspire people by the effect this creates. If I may, I would like to mention other cases we have found motivating, I would like to mention the Gulbenkian Institute with its phenomenal new leadership. Monica Bettencourt-Dias has created, in a very short time, an incredible momentum for her institute. I think that is a wonderful example of how positive leadership can move people.

Science is not providing all the answers, but it is a sure way to address certain problems or to meet certain challenges.

Have you maximized the amount of third-party funds that can contribute to your goals?

Ender: For me, it is yes and no. We are becoming better in the success rate of grants, but in total, I think we can never have enough funds because we always have more ideas than we can actually support. We have some great examples, the Innovative Medicines Initiative grant, the ERC grants, which show that we are good at acquiring third-party funds, but CeMM has not reached maximum potential yet.

Superti-Furga: I agree that we have improved very much. It was a very important year and this Innovative Medicines Initiative Grant, RESOLUTE on solute carriers, is a game changer. It is certainly a new kind of grant. The great thing about diversifying the support base, is that from each grant we learn something new and different. It is clear that the ERC has taught us to think in very bold terms and to try to be razor-sharp in the line of argumentation of why it is interesting. For IMI, I think what we are learning is really how to coordinate different interests, whether this is a common, global and important goal, and how nice it is to see a lot of collaborative spirit in such a variety of organizations including several pharmaceutical companies.

What do you think is currently limiting CeMM's potential success and impact?

Superti-Furga: I believe that the access to chemistry has so far been limiting, and in a way, I think it is good to keep being challenged to obtain third-party funds, but I do believe that being constantly strapped by a rather stagnant core budget has not been too helpful in being generous with regard to being creative. I mean, you've been thinking twice about every cent before spending, which not all scientists may be affected by, but in the end, it is a distraction for a lot of people, including us, and that could go into being more creative. So I think, if we had something of a regular increase in budget that sort of matched the real costs we incur, this would be something we would be very grateful for. Also, the space we have is very limited. We are currently exposed to changes that arise when someone leaves. Something like 30% more space would give us a modicum of ability to remain this 'critical mass' group of people, even if there is some fluctuation.

Ender: I agree, there are certain constraints in funds and space, but to be honest, I don't think that's our biggest threat. It has always been down to our own ambition, and it is about our own motivation to be successful and to find solutions. So, one of our core values is to be persistent and to achieve the goals we really want to achieve, and I believe this is the only limitation we have in our organization.

Superti-Furga: Is there something that you would consider having reached? The success you are looking for? Is there something where you can say, "If we do this, then we'll be successful?"

Ender: That's the point when I would leave CeMM, if you think you have reached everything, or that you can plan and predict everything. Never to stop dreaming about new activities and new ideas is our intrinsic CeMM value, right? It's difficult to say where we will be in a few of years from now. We certainly have goals and objectives, but there are so many things coming up around us that we cannot foresee. I hope we will remain flexible and also curious to address these new challenges.

How important is Europe and the European Union for CeMM?

Ender: You should start because, with your function at the ERC, you certainly stand for the European Union.

Superti-Furga: I would like to say that the European horizon for us, is the natural horizon. I mean our thinking is planetary, we think globally, but "global" is a bit too large to swallow and a little too pretentious.

Ender: And by "us" you mean the scientists?

Superti-Furga: By "us" I mean the CeMM perspective and community. CeMM as it aspires to be, and you know best who our natural partners are. I think there is a European dimension. And what I associate with this is that the national, domestic dimension is just too small. The national dimension is probably just too small for any European country, but most certainly so for a country as small as Austria. So for us – and I think that is very important to say – Europe represents our playground, our home turf. We are proud and happy to be in Austria and we are also proud and happy to be in Vienna, but our home turf is Europe. Europe is our home. Then, of course, there are strategic collaborations, but there is also friendly competition with groups and institutions in America and with Asia. In science, the national dimension simply does not exist.

Ender: And I think, for the profession of scientist, it is very important not to have to worry about visa issues or working permits. You need to be able to go where the interesting questions are and where you can get a good job offer with suitable working conditions. We have 46 nationalities at CeMM. We see it's difficult for some of our employees to settle down, to bring their families, to focus on their scientific goals. There is a lot of bureaucratic distraction. So I agree, in science, in collaborating and competing with each other, you don't have these kinds of borders. The European Union provides a great opportunity in this regard.

What are the biggest threats around the corner?

Ender: For me, it is this transition of the institute from the start-up phase to a more sophisticated, structured institute. There was a lot of can-do-attitude at the beginning, people were motivated, wanted to achieve, put in a lot of effort in building up the institute and its reputation. Now, in the second phase of our existence, we need to become increasingly more organized and process-oriented. Being disciplined and fulfilling all these guidelines, for example in human resources or data management, but still not losing the original kind of motivation is a challenge for the entire scientific and admin staff, as well as for our collaborators. I think this is something we have to address and that we are currently facing. But I also think we will manage, as overall, identification with the institute and its culture is still strong.

Superti-Furga: Yeah, I think this also comes with success. I mean, people take success for granted, and do not invest anymore in what is, let's say, the emotional link, the emotional effort of keeping the institute as interesting as in the beginning. I think I agree with this. Another major challenge I perceive is society's reduced faith and investment in science. Science is not providing all the answers, but it is a sure way to address certain problems or to meet certain challenges. You do see society appreciating this very much. People are forgetting the scientific achievements of humanity and romanticizing the idea of a technology-free world. Think about how some people say vaccination is an individual choice. Smoking is a very good example of the fact that we all know how smoking really is affecting a lot of different health situations. Nevertheless, we are constantly in a situation where young people in Austria, for example, keep smoking like crazy, right? As if they didn't know the science behind it. Let's go back to understanding the relationship between science, progress and the well-being of humanity and the planet. We are running out of time!

If you had one big wish or a few big wishes regarding CeMM, what would these wishes be?

Ender: It would be a wish directed at our stakeholders and strategic partners, something about transparency and fact-based decisions. A lot of decisions in Austria are made behind closed doors, particularly those involving the planning of new initiatives. It is necessary to have a different discussion culture.

Superti-Furga: Allow me to have rather pragmatic wishes. I am dreaming about the possibility of enlarging our social encounter space at CeMM for the winter. You know, we have these fantastic terraces in the summer, where we engage in many important interactions among people, but now it would be great if we also had a "Wintergarten". The second wish regards the space to do more drug screening and drug discovery, but we have plans with the Medical University of Vienna regarding that, in the new Center for Translational Medicine and Therapeutics.

Ender: Hasn't the city of Vienna already promised us this kind of winter sunspace?

Superti-Furga: They've promised us several times, and I think now we are getting closer. I think it would be a beautiful recognition of what we have done for the municipality, for the city, and so I have high hopes that this is something that will indeed happen.

Ender: So let's not call it a wish anymore, but an achievable goal. Maybe we will be able to celebrate at the end of 2019.

2nd Talk at Café Prückel

Flame Out

Andreas Bergthaler, Robert Kralovics,
Christoph Binder, Sylvia Knapp

Flame Out

Resolution, memory effect and organ crosstalk in inflammatory processes resulting from environmental, metabolic, infection-, pain- or cancer-based stress

Is there a scientific discovery that impressed you in the last year regarding this area of research? Any leading laboratory that inspires you?

Knapp: What impressed me most this year was probably all this single-cell RNA-seq data that came out of multiple labs, among which some prominent labs, especially in Israel. It is also impressive that they found cell types that were not known before and that play a role not only in inflammation but also in homeostasis. The lab that inspires us is, of course, Ido Amit and his whole gang at the Weizmann Institute that publishes five *Cell* papers a year, in addition to those in *Nature, Science* and so on. I think that is really top, top, top. And the second person that impressed me was Yasmine Belkaid. Our Landsteiner Lecturer investigates, among other things, how commensal bacteria shape the immune system in a way that immune cells – in her case in the skin, really commensal-specific immune cells – are required to initiate repair. I think these are quite revealing and impressive findings.

Binder: I agree with Sylvia. I think this single-cell sequencing data has been really very insightful. It tells us how heterogeneous the inflammatory processes in different tissues are, and I think that it will be the basis for many studies to come. I am sure Robert will likely comment about the interface between clonal hematopoiesis and inflammation, which is something that excites me a lot. How much cellular metabolism can actually control and direct the inflammatory response has been an evolving picture in the last years. So when cells are acting and operating during resolution, there is a different metabolic program that is turned on. There is a number of papers that have contributed to the better understanding of this, particularly in the context of sterile inflammation, how for example accumulation of lipids can actually change the response to the same ligands. I think that is something that teaches us a lot and that we will spend a lot of work on in the next years.

Kralovics: As Christoph mentioned, I am coming from a different angle. I am a cancer geneticist and last year was quite remarkable in linking clonal hematopoiesis and leukemia evolution to major changes in inflammatory signaling: two papers from mouse modeling, one from Abdel Wahab's lab at the Memorial Sloan Kettering Cancer Center that was published in *Cancer Cell*, show mutation in splicing factors. Splicing factor mutations are a huge class of very interesting, mutually exclusive mutations that occur across all the myeloid malignancies but also in solid tumors. And nobody knew how the gene defects that are downstream of these splicing aberrations can converge and exert the same kind of phenotype. It turns out that the phenotype somehow funnels into activation of NF-kappaB signaling. And one gene in particular, MAP3K7, which was found in SF3B1-mutated mouse models. It also turns out that, when the investigators looked into patients, they found the same inflammatory signature, and again on the other type of mutation, the SRSF2 mutations, both in mouse models and in patients. The paper shows that CASP9, which is also a negative regulator of NF-kappaB signaling is somehow abrogated. That was in August last year, and right after that, there was another paper from Steven Lane's group, published in *Blood,* about DNMT3A, which is again a very common aberration. A loss of DNMT3 or some point mutation, again linked to NF-kappaB signaling. So, NF-kappaB signaling now becomes a center of attention for all these chronic myeloid malignancies. And this is a common theme that adds a little bit of additional

data to the story that came out several years back on TET2 deficiencies. So, essentially, TET2, the splicing factor mutations, DNMT3A, all somehow converge on inflammatory signaling. And the beauty of these studies is that these defects are not only found in cancer patients, but as Christoph said, they are some of the earliest aberrations that turn polyclonal hematopoiesis into monoclonal, and that you know, is a very frequent phenotype in the elderly population. So, apparently, in the population of people aged about 70, between 5–10% of these supposedly healthy individuals are already clonal and have an increased risk of thrombosis. This was published in the New *England Journal of Medicine* by Benjamin Ebert's group and is now the major focus in the hemato oncology field. This is how we are somehow converging with all the groups that study very basic processes of inflammation. The trigger of inflammation is not oxidation of lipids, it's not a pathogen, but a somatic mutation. You actually have some intrinsic trigger of inflammatory signaling, just by loss of epigenetic regulators or presence of an oncogene.

Binder: Well, we don't know that. It's the response that may be altered, but in fact, when you think about it, TET2 and DNMT3, they do opposite things, but both converge. So, maybe what they do here has nothing to do with their original function.

Kralovics: You are right, because inflammatory signals are so broad and so highly regulated.

Binder: And maybe that's one explanation for why some individuals are more susceptible to, say, oxidized lipids or other triggers of inflammation. What I think is so interesting about this is, when considering personalized treatment or personalized medicine, clonal hematopoiesis, or the status of clonal hematopoiesis, may be one of the ways to stratify patients, to decide whether or not they should receive anti-inflammatory therapy. I think that is a major advance, at least when considering chronic inflammation.

Bergthaler: What excited me the most? I think it kind of dovetails with what has been said: our better appreciation of tissue complexity. Basically, how different cell types interact with each other through different means and how non-immune cells contribute to the immune system – so, the role of parenchymal cells wherever there are fibroblasts in the skin or hepatocytes in the liver – and how all of these cells interact and communicate with one another. I often think of the technological advances that have been made. Single-cell sequencing is one of them. But I think there are other approaches as well that are very exciting, including imaging approaches. In terms of labs that inspire us, there are researchers, such as Ruslan Medzhitov, who really are conceptual thinkers at the forefront, attempting to identify the evolutionary basis for what's happening in inflammatory responses. I think that is very inspiring. Sometimes what is needed then, is actual experimental data to prove or to back this up, but I think it allows us to think beyond and out of our box. What I am also excited about – at least I came across this twice in two papers – are weird cellular memory effects. In this case, T cells that you take out of a mouse, then you expose them to a drug – which is done, for example, in a paper by Erica Pearce – and then you put these cells back into a mouse. So the drug has been washed out, and yet, if you look months later, you can clearly distinguish those cells that have been treated with a drug compared to the control. I wonder whether this is classical epigenetics or maybe there is more going on and this is potentially connected to trained immunity.

What are the scientific hypotheses that we should all try to tackle together?

Kralovics: Well, our mouse models are centered around modeling hematological malignancies. And here we have two mouse models, where the JAK2-V617F mutation and the CALR mutations are knocked in. In one of these models, in a longer follow-up of mice, fibrosis develops. And of course, fibrosis is a rather severe complication in these patients, and it is a consequence of inflammatory processes. According to one of our hypotheses we formulated during our faculty recess in the summer, this may be a much broader phenomenon, because oftentimes inflammation is rather systemic. So, it's not a completely crazy idea to believe that you have inflammation induced by an oncogenic mutation., So, this is something we started to formulate into project concepts. We ordered the mouse models, we added two additional mouse models, the SF_3B1 knock-in and the TET2 knock-out, and these could then be read against the background of this oncogene. So, I would say, we essentially model these processes in a very realistic genetic model. And, of course, we look for some high-penetrance, early onset myelofibrosis. And in these mice, we would like to see what other organs are affected by fibrotic damage. This would be something our groups could tackle together.

Bergthaler: So, where do you see concrete links to labs at CeMM to help you tackle this question of fibrosis?

Kralovics: Well, of course, Sylvia and you directly. Of course, the two organs that might be affected are the lung and the liver.

Bergthaler: What I find particularly exciting as an opportunity, is when we think about the human patient. There probably isn't a single patient with just one disease. They are always present in co-morbidities. So what is, I guess, one of CeMM's strengths and what our Strategic Collaborative Program "Flame Out" is all about, is basically trying to integrate and combine different diseases and to see how they influence each other, sometimes not even driven by a hypothesis, but just simply doing it because we can, and because those labs are available at CeMM. And fibrosis could be such an umbrella to look at different options.

Kralovics: Another aspect is, that our hypothesis is more about trying to generalize things, but maybe, such a general hypothesis is not applicable to all patient groups. We might find those particular cases, perhaps 1–5% of the patients, that develop particular complications, where that hypothesis actually fits. We know that the diseases are inherently heterogenous and complex. So, I think these are opportunities to understand individual patient groups stratified by molecular or other markers and to see what the underlying disease mechanisms are.

Binder: If you consider inflammation that could feed into and even promote clonal hematopoiesis, what we are interested in looking at is how diet could contribute to these TET2 mutations and other mutations associated with clonal hematopoiesis and whether this feeds into that vicious cycle, preventing resolution of inflammation.

Kralovics: And one quite interesting additional aspect that is emerging, is patients that don't have a particular molecular mutational landscape but are receiving a specific treatment like JAK inhibitors. It turns out that the cancer patients only benefit by suppressing inflammation. But these bring along a completely new set of clinical problems, like, you know, immunodeficiency or emergence of viral infections. JAK inhibitor treatment now generates a whole lot of problems, including the emergence of mutant cancer cells that are normally kept in check by the immune system. You want to treat myelofibrosis, and a new cancer emerges, that was already there. It has been shown that the burden prior to therapy was low.

Knapp: Of course, if you suppress some inflammation.

Bergthaler: How long do you administer these JAK2 inhibitors?

Kralovics: Usually the patients benefit for up to three years, but then there is some sort of resistance to them, and you need to take a break. The drug is withdrawn and then re-introduced. The problem is that this drug was approved for myelofibrosis with splenomegaly and patients benefit miraculously. Splenomegaly resolves within weeks of JAK inhibitor therapy. This is primarily when the spleen is not actually infiltrated by the tumor cells. And if you suppress inflammation, the splenic architecture changes to a certain degree, but the content of tumor cells does not. So it is truly some sort of response by the spleen to certain cytokine stimulation that changes its structure making it no longer penetrable to the cells, and it just grows large, which is a major problem. With splenomegaly, the life quality of the patient drops. Extramedullary hematopoiesis is usually at the pinnacle of inflammation. In high-grade inflammation, you have fibrosis, so the fibrosis causes extramedullary hematopoiesis. It's just more progenitors in the periphery, but at that stage, you have such massive cytokine dysregulation that the spleen responds and actually becomes impenetrable or less penetrable and just grows to a massive size. So it is an inflammatory phenotype, not an infiltration of tumor cells. Of course, there is a certain turnover of clonal cells in the spleen as well. And in many other mouse models it was shown to be enough to inhibit the JAK2.

Bergthaler: What is actually the definition of inflammation? Because in the end, you say that may be something that is simply a stress response. Christoph, what are the hypotheses connected to this inflammation, deflammation theme that your lab is tackling?

One should always consider that inflammation is something good, that we have a mechanism to fight infections and to protect us.

Binder: Where I see a lot of potential for interaction is in understanding what position my lab or your lab has in this vicious cycle of non-resolving inflammation. That can teach us a lot. More specifically, I actually sent Sylvia a paper a couple of days ago which reported very strong clinical evidence for patients with pneumococcal pneumonia having a worse outcome after myocardial infarction, which is most likely associated with dysregulated resolution of inflammation. And, very specifically, that is something Sylvia and I would like to look into in more detail, because we have the expertise on both sides. And again, this leads back to the theme of chronic and acute inflammation, like bacterial and sterile inflammation: Where do they meet? How do they cross talk and what is really happening there?

Bergthaler: Do you have mouse models set up for myocardial infarctions?

Binder: We have now started to set up these mouse models for myocardial infarctions actually. A postdoc in my lab, Dimitris Tsiantoulas, learned about this in Cambridge. We also have a very good collaborator here at the Medical University of Vienna and that's the perfect setup. You ligate the coronary artery, you induce a heart attack and then you look at the healing of the infarct tissue.

Knapp: Very much in line with what Robert and Christoph said, I think what interests us – and is also linked to others – is inflammation, injury or insult at different tissue sites, that affect, for instance, the immune response in the lung, heart, liver or bone marrow. So the interconnection between these organs, not seeing everything at an organ level but at a system level, is what we call tissue memory. These effects, we are getting more and more of a glimpse into, are where I see us linked. And the coolness of CeMM, I would say, is also that we are working on these different aspects that allow us to tackle a challenge more easily.

Bergthaler: And maybe to add to this from my lab: I think, what we are increasingly trying with different projects is to have these infection models, but we really approach inflammatory changes in a rather abstract way that is basically also applicable to non-infectious diseases. In that sense, I think this could at least be a mental bridge to cancer, and to autoinflammation, although of course, the signaling pathways are not exactly identical. There are different cell types involved, but the general framework is not that different. And whether you are stressed by a virus or bacteria, or by high cholesterol, may not be that different at the end of the day. At least it is good exercise, because we don't know anything about cancer, and yet we are immersed in an institute where at least half of the groups are working on cancer. So I think this is also a synergistic opportunity for us, being at CeMM.

How would you paraphrase this in really lay terms?

Binder: I think in lay terms, I would say one should always consider that inflammation is something good, that we have a mechanism to fight infections and to protect us. But the problem is that in certain situations it can go wrong, and it can harm us. And we would like to understand why and under what conditions this protective response of inflammation – which is basically intended to kill whatever causes the injury, like a bacterial or viral infection – can become harmful in certain situations. Which means, I believe, when it sort of becomes chronic. That can also interfere with other disease entities such as clonal hematopoiesis and hematological malignancies.

Knapp: I would add that, let's say, cells of the immune system are primarily or notoriously known to fight infections and cause diseases, but in fact they are incredibly important in preventing inflammation. So, when it comes to keeping tissue healthy or maintaining homeostasis, immune cells are basically the key to healthy tissue in real life. I mean, luckily, we are not constantly infected, and this is also due to the fact that we have an immune system. But most of the time, our immune system is probably busy keeping inflammation from happening. And in the end, we die from some chronic type of inflammation. Aging is a trigger for inflammation, and immune cells are probably as important in preventing as they are in fighting infections.

Bergthaler: I guess one key word in this regard is context, because inflammation really depends on the tissue context, on the environment, on the timing, also the phase of infection of another disease. It may be harmful, it may be beneficial. Inflammation always has a bit of a negative connotation, doesn't it? But it really depends on the given disease whether the net outcome for the host is thumbs up or thumbs down in the end. That's why it is important to gather as much information as possible. I think another idea for this strategic program is for us to take our existing models, where we focus on one primary organ – the lung in the case of pneumonia, or the liver in the case of high-fat diets – but then to actually look beyond at other organs and to see how maybe this connects. And maybe people have missed parts of the puzzle simply because they looked at the obvious place, under the street lamp at night. I think that is also something where we can cross-fertilize and benefit from each other.

Binder: Evolutionarily, obviously, you are selected for certain genes or variants of genes, that protect you from bacterial infections. But now these are the same individuals that are more likely to respond to a sterile trigger and develop chronic inflammation – and this is sort of the price we pay for having a very protective genotype. I think, in addition to the germline variants that could predefine our responsiveness, the somatic mutations that have been identified now will also be more and more interesting in terms of understanding individual and personal responsiveness to both bacterial, viral, but also sterile triggers of inflammation. I think that is something we will always have to keep in mind when we study humans – the fact there is such a great variation of responses.

Knapp: It's incredibly exciting that there is this one paper that studied the different immune responses in humans in a simplified manner. And the one thing that determines most is, whether they have CMV infection, whether they are carriers of CMV or not. It's not genetics, it's CMV or some unknown viral infection that basically determines whether they respond in one way or another. There are a lot of things, we have no clue about.

Bergthaler: It's amazing how the wiring of this whole response system works and how resilient it is at the end of the day, because I think, overall, we are all pretty healthy, at least in the developed countries. We have antibiotics and so on. But it's built into our genes, yet we still don't understand how the genes interact, how the cells interact, how the organs communicate with each other, and how in most cases, evolution has selected for this to work. That's maybe not surprising, but I think we still don't understand how this is actually happening, and a better understanding will help us interfere therapeutically.

Kralovics: To explain inflammation in blood cancers in lay terms also pretty much relates to the same topic. The immune cells, you know, are generated by hematopoiesis. All the changes happening, the cancer happening in this particular tissue compartment, have or has an immediate impact on all the immune functions in these patients. And, of course, inflammation now has been recognized as a sort of major modifier of the outcome in these patients. How to intervene in this inflammation is also a major problem. You cannot just use brute force suppression, because you'll have an infection coming up or other cancers emerging. So, I think it is also about knowing how to intervene in a way that ensures preservation of the immune function to a certain degree, but eliminates, for example, morbidity resulting from fibrosis. All these issues have to be fine-tuned and we have to find ways to suppress this activation, because inflammation is hyperactivation to some stimuli, and somehow find ways to gradually intervene or intervene in a very focused manner, to get a good therapeutic effect in these patients and not to have consequences of therapy that would result in a worsening of the disease, right?

Bergthaler: Or also harnessing these evolutionary conserved mechanisms for vaccination, for example, and really exploiting what's already there.

Is there anything regarding this area that was achieved in your laboratory/at CeMM that you think is worth mentioning?

Binder: What we found was in a way exciting and added to some of our previous papers. We demonstrated that antibodies, so-called natural antibodies that protect from bacterial infections, also seem to protect us from developing venous thrombosis. So we did clinical studies in humans, where we actually found that the recurrence of thromboembolic events is associated with the titers of the same antibodies that also protect from infection. So again, that really supports the dual role of our immune system. Another thing I found very exciting was the fact that we found – which takes us back to what you pointed out, Andreas – that it's so important to integrate all tissues and all cells when we try to understand the immune system. We found that one very specific cytokine or mediator that controls B-cell development also plays an important role in controlling the inflammatory response of macrophages. So, other cells called BAFF, or B-cell activating factor, that have not been implicated in responding to that molecule before. And we found that this is very important in a way, because it is a molecule that is already therapeutically targeted by biologicals, by monoclonal antibodies.

Bergthaler: That's macrophage-intrinsic?

Binder: And we discovered this effect of BAFF on macrophages. It controls inflammation in macrophages. But so far, in the whole of literature and previously, it has only been implicated to play a role in B-cell biology, and this is why it is therapeutically targeted with monoclonal antibodies that are already given to patients with lupus to deplete B cells and get rid of autoantibodies. But what we found out is that if you deplete BAFF, you also affect the inflammatory response of macrophages and theoretically this could be harmful. So it is very important to integrate all of this, and I think that was an important piece of evidence, again demonstrating that it is very important to look at all of the effects in an integrative way and not to focus on one part of the pathway that has been implicated before.

Kralovics: So, in my lab, we participated in a large clinical trial in this particular regard. It was a phase III, where interferon was applied to the patient group that we are studying in the lab, in particular polycythemia vera. And very interestingly, you have interferons which are one of the mediators of inflammation. Essentially, if you apply interferons systemically, the stem cells mutated with this JAK2 kinase mutation disappear during the course of treatment and essentially you restore polyclonal hematopoiesis in these patients. This data is hopefully going to be published soon. In the meantime, the European regulatory agencies have approved interferon treatment as a first-line therapy for polycythemia vera, based on this trial. So this is actually one of the major developments, and it is already public, for we reported on it at the ASH (American Society of Hematology) Meeting.

Bergthaler: So what was your role in getting this approved?

Kralovics: My lab conducted the entire molecular characterization of about 300 patients on the genetic side and we looked at baseline samples and end-of-treatment samples. We also quantified the molecular response in these patients. Essentially, we showed a very global response rate, regardless of what mutations the patients carried. They all pretty much universally went into molecular remission and that was our part in the study.

Knapp: I think what we contributed last year was basically that we looked at the interplay between different immune cells acting in the maturation of the lung at or after birth. What we found is that when the lungs develop and the immune system takes over or migrates or establishes itself in a tissue, there is a very complex interplay between different immune cells. Surprisingly, we discovered cells that have been known for years, for example eosinophils or basophils, that play an important role in actually shaping the tissue environment in the lung and that there are also tissue-resident types of basophils, which were thought to be only a rare blood cell type involved in allergies. What I find exciting is that it is becoming more and more clear that these ancient or old cells we have known for years have multiple other functions we didn't know about, and that we can find them now, even in developing lungs in mice.

We not only want to find treatments, we want to understand inflammatory pathways to eventually come up with smarter therapies.

Bergthaler: We've built a lot of resources and gained a better understanding, so while we haven't published any of these things yet, I think we have a better understanding of how little we actually know when we infect a mouse with a virus, for example, and then try to see how the metabolism changes, both in the liver and in the serum. And maybe it's not surprising, but there is still very little out there for every body compartment that you try to measure these changes for; it's often different and does not correspond. And I think that's biology for you, where, of course, the same changes don't occur in the liver or in the spleen. Trying to bring the things together and trying to mechanistically understand them is difficult, but we are getting there. We also have several advanced projects in this regard, where we implicate either a connection between, for example, the liver and T cells or between inflammation and adipose fat tissue and study how this rearrangement might then modulate and fine-tune the immune response in the course of infection. So, work in progress.

Do you have the necessary tools? Anything that needs to be further developed?

Bergthaler: CeMM is very much a technology-driven place, we have – I think – great core facilities that distinguish us from other, maybe bigger institutions. I think we are effective in this regard, but do we need more tools or specific tools for the future for your projects, something you can think of that is either in development anyway or that you would like to get for the institute?

Binder: In my opinion, what we really need – and we have discussed this with Robert several times – is not some innovative technology, but a monoclonal antibody facility.

Binder: It's such an elegant way to interfere with pathways, where you introduce more subtle phenotypes and do not genetically disrupt anything, and it would be amazing if we could have some sort of facility that fast-track develops monoclonal antibodies.

Bergthaler: Because if you want to target something in the cell, you need to have monoclonal antibodies.

Kralovics: For large mammals, you need large housing facilities, which is a bit beyond CeMM's scope and ability. I talked to a couple of places, such as the Veterinary Research Institute. They even have horses, and they were thinking about camels before, and if there was some incentive for them, they would be on it. But in the meantime, I've found something much easier: rabbit facilities. My former colleague runs a rabbit-breeding facility. She supplies laboratory rabbits to more or less all of the Czech Republic. The red tape on getting protocols approved in the Czech Republic is very straightforward. It's a simple protocol, you have about two months' turnover on these applications and we could just really have antigens shipped, immunized, and get the serum and the spleens back.

Binder: What we need is a facility where we can grow these hybridomas and make a lot of these antibodies.

Kralovics: And of course, around it, the phage display or mammalian cell display technologies, because they already somehow functionally evaluate the antibodies prior to cloning. So you select clones that already come with certain binding properties. And then you have a – how shall I say – functional antibody repertoire that is basically much easier to screen. You don't need super high-throughput anymore.

Bergthaler: OK, so that was antibodies. What other technologies are you thinking of?

Binder: What do you think about CyTOF? We have been discussing this for such a long time, but in the meantime, so many papers have been published, simply doing CyTOF analysis of cells, all published in high-ranking journals. I think this is a technology that will stay around for some time, and it was probably a mistake not to invest in it.

Bergthaler: One technology I am very excited about, and that we've started to use, is metabolite tracing in vivo, so where you administer heavy isotope-labelled metabolites of your interest into a mouse and then, at a given point in time, you harvest organs, or you sort cells, and you use mass spec to see where these heavy-labelled metabolites go and how they were converted into the next metabolites of a given cycle. We've done only a few experiments so far, but I think it looks very promising. What's clear is that we will need some full-time bioinformaticians to dig deeper, but even the very first experiments show the potential. Actually those heavy-labelled metabolites are surprisingly cheap. That is not the bottleneck we initially thought it would be.

Bergthaler: We've tried a few things. At the moment glucose and arginine. And it works. So what we've done, together with the Metabolomics Facility, and where I think Kristaps has done a marvelous job in the last two years, is to set up all these new metabolite read-outs. I foresee this as one way of investigating the crosstalk between organs and in vivo, and I think that's where our expertise of proteomics, mass spectrometry, and metabolomics will come in very handy.

Knapp: Do you sort cells? How many cells do you have to sort?

Bergthaler: So far, we have done mostly bulk tissue, but we have already sorted cells. We haven't yet done the tracing mass spec on this, but ideally, you need at least 106 cells, that's why we didn't bother with sorting and used chunks of tissue instead. And that is already complex enough, if you're trying to figure out what's going on.

Binder: I think that's a very important thing and, in the context of resolution, that is when cells ingest dying cells and you want to know where the metabolites come from, it will be interesting to find out which metabolites influence the phagocyte. Is the influence coming from the dying cell?

By when, do you think, will we see this research have an impact on medical practice?

Bergthaler: I think we've already heard one example where there is a drug actually being re-purposed for a given malignancy. Robert, when do you think Interferon will be used on polycythemia vera?

Kralovics: It is already being used off-label, but now it is becoming a first-line therapy and the decision on this drug's market authorization will already be made this year, earlier this year. So this is already going to be produced and will be released for general practices and hospitals and clinicians. So it is already happening, but now it will happen on a much greater scale.

Binder: I think to some extent we are already working on translating these efforts into international collaborations, where we start smaller clinical trials to see if we can interfere with the outcome after myocardial infarction with patients by using approved immune-modulatory therapies. But that's obviously a collaborative effort – as these things always are. But what will really impact medical practice, I cannot say. It depends on the outcomes, but I think an important step we are taking, is that we are now thinking more and more of translating our findings into real, small clinical trials.

Knapp: I think we are learning a lot from many anti-inflammatory therapies that are in place, like JAK2 inhibitors. So, we can deduce and even try to figure out why something is happening, or what happens if you block a certain pathway in humans. Even though, in our case, we want not only to find treatments, we also want to understand inflammatory pathways in order to come up with smarter therapies eventually.

Binder: But we could influence the stratification of patients sooner because our insights could help identify sub-groups of patients.

Kralovics: Or whether or not stratification makes sense.

Binder: Yeah.

Kralovics: Because sometimes it doesn't.

Bergthaler: I agree, my lab does basic research, and if there is to be any direct impact, it's probably 5 to 10 years away. I think that's the reality. But better understanding of the mechanisms could indirectly influence the decisions of other programs that are maybe closer to clinical developments and patient care. So in that sense, at least for me, we do basic research and we do not claim to revolutionize clinical medicine or anything.

Binder: It depends on what you mean by "impact" on medical practice, because in a way, medical practice is being impacted all the time, because people become interested in certain findings and then they start looking at their patients differently. In a way, this is an early impact. Real impact, so whether a new drug or treatment is introduced, is obviously not so predictable.

3rd Talk at Café Weimar

Drug In

Stefan Kubicek, Joanna Loizou,
Georg Winter, Giulio Superti-Furga

Drug In

Uncover the mechanism of action of known and new chemical entities to modulate cellular function, identity, differentiation and growth to ameliorate disease, increase precision and avoid resistance to therapy

What are the chemical entities that you are using? Where do they come from? Do you design them?

Kubicek: We have a CeMM library which has around 90,000 compounds, for 2,500 of which we have an idea of what their molecular target is. These are approved drugs, compounds that are currently being tested in the clinic, but these are also so-called chemical probes for certain classes of enzymes that we have, a CeMM-wide interest, including kinases and chromatin-modifying enzymes. Then, we have a large set of compounds that we selected for their chemical diversity, and so these are structures we know very little about, except for their performance in the screens that we have running at CeMM. They are selected to cover as broad a chemical space as possible.

Loizou: Do you have in your collection any FDA-approved drugs and are there any examples of repurposing these from your studies?

Kubicek: Yes, we have. We have purposely tried to cover the FDA-approved and generally approved drugs as widely as possible. In this context, we made a specific collection that we named the *CeMM Library of Unique Drugs or CLOUD*, in which we attempted to keep all the diversity there is in these approved drugs but fitting it to the format that we like to use in drug screens which is a 384-well plate. What we do a bit differently than all the other screening approaches, is that for all these drugs we have annotated them very well with the plasma concentration that is achievable in the clinic.

Superti-Furga: In 2018, what we have started using more intensively is this library of metabolic drugs. They have been assembled by my laboratory together with PLACEBO in the Kubicek laboratory, as a collection that covers enzymes and transporters that affect intermediate metabolism. We use them to probe the effect that interfering with metabolism creates on some of the interesting assays we have. Typically, we also look at the expression of transporters in response to that. The other group of chemical agents we are using we could call "tool compounds" that affect cell biological properties, typically affecting proteostasis and ER homeostasis. Lastly, in 2018, we started to design some new kinds of PROTACs together with Georg Winter and we are looking forward to testing them.

Winter: This is one of the things we are most interested in. Typically, we get these compounds either from collaborative efforts with laboratories in Boston with which I worked during my postdoc years. We also design them ourselves and the gist of these small molecules is really that, as opposed to most other molecules that bind and inhibit a particular protein, these bind and degrade them. So, we can eliminate entire proteins out of the cellular environment. We are particularly interested in applying this technology to probe and understand gene control to be able to potentially drug proteins so far considered undruggable.

Is it difficult to plan or to predict drug action?

Loizou: Technologies such as machine learning have been instrumental within the last 2 to 3 years in helping us predict and design more efficient ways of utilizing drugs. I think this is going to be a tool and a way to push forward by which we can plan and predict drug action in a cheaper, more efficient, faster and more precise manner.

Superti-Furga: So, when comparing profiles, using artificial intelligence makes sense …

Loizou: To design, to predict and to speed up the drug discovery purpose.

Winter: I think, based on the protein class, it's sometimes straightforward to predict or design them to achieve a certain on-target effect. So, we know that they inhibit a particular enzyme. I think what is always interesting to investigate is what else these molecules might do. Traditionally, we have been thinking about small molecules as something that competes off endogenous ligands or metabolites, but more and more we realize that small molecules can do much more. They can change the properties of proteins, they can change stability, they can change interaction partners within cells by just contributing a certain type of binding energy and, all of a sudden, one protein is able to talk to another protein inside a cell. I think this is something that we'll see much more of in the years to come and I believe this will be what is hardest to predict as opposed to target effects inside the same protein family.

Kubicek: I also feel that the proteins and domains for which we have structural resolution, particularly for the structurally guided large-scale efforts to predict targets, still only represent a very limited fraction of all the possible proteins and protein interaction sites that are out there. So, finding targets from compounds that are active in phenotypic screens – and a large proportion of the screens that we do are cell-based and phenotypic – is still a major challenge. Certainly, some technologies that have also been developed at CeMM allow us, in a global picture, to ask the question, "What are all the proteins that are potential interaction partners for certain drugs?", in a cellular context. They are very valuable, both for finding a relevant target but then, of course, also for cases where a drug is designed to have a certain action and mechanism, and is optimized for that, and then for figuring out what else it is doing in terms of off-targets.

Superti-Furga: I think this is probably the area where CeMM is most highly competitive at the international level. I think collectively, the different groups have a good set of approaches and capabilities to figure out the mechanism of action of chemical agents, but I think it is still very, very difficult. I think this is for several reasons. It starts with the identity of cell lines, that often needs to be determined first, the purity and the conformation of the individual chemical agents is sometimes unclear. Many agents may have cell-type- or even cell-state-specific effects and often they are composite effects or compound effects of hitting multiple targets. Sometimes they are of the same class and sometimes of different classes. So, true chemical probes that hit a few very well-characterized targets are not many.

Loizou: And how has CeMM contributed to experimental approaches aiming at nailing down a specific target that a drug may have?

Superti-Furga: Traditionally, the ability to look at proteins engaged by drugs through proteomics has been a very powerful approach, despite all its limitations that have to do with concentration of the target and the affinity. But also, in recent times, I think that has been very nicely complemented by genetics, where we have an increasingly versatile tool box to interrogate by genetic modifiers of drug action what is going on. Then, as you mentioned, the sophistication in the phenotypic characterization of cellular effects leads to the ability to compare and parse and cluster effects so that you can also try to do it that way. All those things together, you know, the molecular and the phenotypic profiling, are becoming more and more powerful.

Is it not presumptuous to do in academia what pharmaceutical companies can clearly do much better?

Superti-Furga: For sure, yet we consider our activities complementary to the activities of pharmaceutical companies. We can do crazier things, for example we have developed this technology that looks at mononucleated cells of the blood for changes in viability and interaction, something that perhaps would not have been done in pharma. We don't believe we can be drug developers. In terms of drug discovery, we are limited by the diversity of the compounds that we have, but we have the freedom of engaging in crazier kinds of assays and doing things that most industry scientists could never do, but that we do. And by so doing, we identify interesting effects that are worth following up.

Loizou: I would also agree that I think drug development is very complementary between what academic research institutes do and big pharma does. As Giulio said, research institutes can be more exploratory, whereas pharmaceutical companies tend to go for a low risk and short-term gain in terms of time invested in developing products. And indeed, we have seen that a collaboration between industry and academia is very fruitful and there are several examples of very efficient pharmaceuticals, including chemotherapeutics, which have been developed by a close collaboration between academic exploratory work and big pharma developing the drugs.

Kubicek: I would also agree, right, that what pharma is particularly good at is developing a candidate or a target to further an approved drug. But what academia can do much better and much more freely is to really understand targets and come up with ideas. That's what it is also doing to bring good rationale related to why it is important to target or not to target a particular pathway, and on the other hand, to really bring novel, overwhelming concepts that would really turn the whole concept of drug ability upside down by finding new, entirely new mechanisms, by which proteins can be targeted, degraded and so on.

Winter: I also think that some of these fundamentally new aspects of how drugs can be made, they really need to stem from a deep understanding of underlying biology. Particularly interesting cases are when drugs or drug ideas emerge from laboratories that have been devoting years of research to really understanding one particular pathway, one particular protein. I think this is also something that academia can contribute and is already contributing to the entire drug development and drug discovery process, simply because this is time- and curiosity-driven research that pharma can't afford, where they would typically take something that seems like a sure theme and then spend a lot of efforts in hit and lead generation, come up with a metabolically stable molecule that is tested in every type of stability assay to then be able to really test it first in animals and then in patients eventually.

Kubicek: I dug out a recent PNAS paper that tried to analyze what is actually academia's contribution to new drug approvals by analyzing how many novel chemical entities were approved from 2010 to 2016, and then, for each of them, trying to analyze what are the old publications on the target of that drug – if it was a drug for a new target – or on the drug itself. They came up with a number of more than 800 million in public spending for each novel one.

Are there any breakthroughs or new trends we can associate with 2018?

Loizou: For me, what was striking about 2018 was that it was a record year for the number of FDA-approved drugs. In fact, in 2018, there were 61 drugs approved by the USFDA, which is the US Food and Drug Administration. But the striking thing is actually what type of drugs were approved to treat which diseases, because 51% of those drugs were actually released in order to treat rare or orphan diseases. I thought that was really quite surprising and interesting because this is normally a group of diseases for which, in each individual disease, there are very few patients, but when taken as a whole, of course, they affect a large majority of the population. These patients tend to have very few treatment options. So, moving towards a more beneficial therapeutic avenue for them is, I think, really important.

Kubicek: I think also, when you look at the structures of these newly approved drugs, you can really see that they cover a wide spectrum, from RNA-based therapeutics to very small, rather small molecules, larger small molecules. This really highlights that there is a broad spectrum of agents that are approved in the clinic and certainly, yes, also shows clear contributions of academic research, which has highlighted that all of these were druggable pathways.

Winter: I think from a chemical biology perspective or chemistry perspective, it's pleasing to see that the majority of all newly approved drugs are still small molecule therapeutics as opposed to cellular therapies or biologicals like antibodies. So, I think there is still reason to be excited about chemistry and biology for drug discovery.

Superti-Furga: I think what really has changed is the appreciation that drugs may have these additional mechanisms of action where they modulate and create interactions. So, it's really like a gain-of-function kind of situation. Contributions that we probably would not have anticipated. It is not clear how generally this is applicable and how often it occurs, but conceptually, we can say in 2018, we all became more aware of that very, very important, additional perspective, which is that drugs may just manage the interaction among the existing molecules more often than we imagine.

Kubicek: Maybe also very fragment-based discovery. It's a trend that has been around for some years, but now really, the concept that using not only crystallography and NMR-based methods on an isolated target but really that also very, very small molecules, so to put fragments in a cellular context, can be used to elucidate targets and potentially new targeting mechanisms.

What really has changed is the appreciation that drugs may have these additional mechanisms of action where they modulate and create interactions.

Is there anything regarding this area that was achieved in your laboratory or at CeMM that you think is worth mentioning?

Winter: One thing in this field that we now have learned, if we stick with PROTACs for a minute, is that the idea that everything that these molecules would bind, they would also degrade, is not correct. So, you could make a multi-functional binder that would bind to many different kinases and a PROTAC-derived form that degrades different, but not all, kinases. You need particular steric requirements to be able to recruit the protein to the E3 ligase. These steric requirements really dictate the selectivity space of degradation. It turns out that you can take an inhibitor that binds to multiple proteins and by, for instance, systematically altering the linker region, tune these ligands in a way that they can degrade particularly interesting subsets of the kinases. This is an incredibly powerful tool to engineer selectivity in a molecular scaffold, or a chemical scaffold, that is otherwise unspecific.

Superti-Furga: Let me ask you, is it just steric properties, or are there also properties of the targets themselves that make them more or less accessible to degradation?

Winter: I think this hasn't been addressed in sufficient detail. Limitations could for instance be the particular cellular compartment a target resides in. I think what has been clear, what has been surprising, is that just the affinity per se is not that relevant, so you can degrade proteins even though the kinase only binds in the single-digit, two-digit micromolar range.

Superti-Furga: What was interesting is to see that by studying the genetics of drug resistance in vitro, which is in a petri dish with cell culture, you may not only learn something about the drug in question, but you may also discover entirely new, regulatory properties of the target itself. This was the case for the protein called LZTR1 that clearly regulates a pathway that is centered around RAS.

Loizou: Well, in my lab we are interested in understanding and studying diseases that occur due to defects in DNA repair genes. One of the diseases we were focusing on is Fanconi anemia that consists of an inability to remove cross links from DNA. The way that we were asking this question was to basically question how we can rewire cells which are deficient in DNA repair to now become DNA-repair-proficient. Through genetic approaches, we identified a novel deubiquitylating enzyme called USP48. What we identified is that USP48 has the ability to restore DNA repair in the cell lines defective for Fanconi anemia in an error-free manner. We are exploring ways of how to inhibit USP48 as a potential therapeutic avenue.

Kubicek: We are excited about the fraction of small molecules in the nucleus of a cell and their contribution to gene expression and control of transcription. This is based on a project where we were interested in regulators of BRD4-mediated transcriptions and where we found a folate metabolic enzyme, MTHFD1, to be physically recruited to certain regions in the genome where BRD4 acts as an enhancer of transcription, and it has just been accepted, so we are happy! We are excited about that and it's hopefully also what we are going to solve in the next five years. In my ERC project, we really want to ask the question: What are all the endogenous metabolites contributing to the regulation of gene expression in the nucleus? And we develop methods that would specifically target these metabolic enzymes in the nucleus while leaving them intact and functional outside in the mitochondria and in the cytoplasm.

Do you have the necessary tools? Is there anything that needs to be developed further?

Kubicek: Understanding small molecules and where in a cell they travel, where exactly which metabolite is, and so on, is an immensely challenging question, because diffusion is very fast, on the millisecond scale. We don't have a single published nuclear metabolome, so a description of all the metabolites in a cell's nucleus versus the cytoplasm.

Superti-Furga: Are you able to do that?

Kubicek: I mean we have it in the paper that is now accepted. We use a fast protocol of nuclear isolation where it takes us just three minutes to kind of get the nuclei out and then compare to cytoplasm. The metabolite composition is very, very different, but then still, on a free-flowing time scale, it would take milliseconds for a metabolite to cross the cells… so three minutes is an enormous time scale. We are also thinking of, say, finding methods to somehow block the nuclei, a pause that would give us a longer time scale. We've done some very preliminary experiments where we would just incubate nuclei at buffers for different times.

Winter: What we want to implement next year maybe, is to also integrate synthetic DNA approaches, so basically to be able to synthesize drug-resistant alleles at scale. Or synthesize parts of proteins that might determine whether a particular protein is degraded by a certain drug or not. And therefore, have a more rapid method to assess different drug candidates, how easy it might be to degrade a protein, what are general rules that make a protein degradable, and so on.

Superti-Furga: I think it is my obligation as Scientific Director to be constantly mindful of what kind of technologies are limiting our approaches. I think the difficulty everyone has, is to have enough access to medicinal chemistry or generally, organic synthesis, to the point that we can experiment with things more and play around with them. Just as Georg mentioned, the ability of doing this at the protein level from the target is fantastically powerful. The enlargement of our faculty, to include two new faculty members who are chemists, will represent – certainly a cultural enrichment – and also a practical enrichment of the tool box. But in the medium-long run, we need to further build the internal capacity. Clearly, these are some of the things we are planning to do in 2019: proceed with the plans around chemical biology and create a center that is competent in identifying new chemical entities that have not been seen yet.

Loizou: From my perspective, it is important to remember that useful cellular assays are very important tools also. So, with my lab being interested in understanding DNA repair and how DNA repair pathways are rewired, we traditionally do that by assessing how DNA damage will impact on cell survival, but of course that's not a very accurate measure of how DNA damage is dealt with. So now we are setting up more relevant tools which will directly allow us to measure effects of drugs, compounds or chemotherapeutic agents on DNA repair rather than on cell survival.

Kubicek: We've been doing most of our chemistry so far, following up on a hit from a screen in collaboration and with chemists outside of CeMM or at contract research organizations, where we designed the molecules, but we have them synthesized elsewhere. That is working well, but clearly there is a benefit of doing it in-house. We are very happy that now we have a chemist in the lab, Marton Siklos, who has already – in the last month – made 20 new molecules.

Superti-Furga: Wow.

By when do you think will we see impact of this research in medical practice?

Winter: In the targeted protein community, 2019 will be a very interesting year because this is the year where these specifically designed heterobifunctional molecules will be first tested in clinical trials. So, these are the first programs that will likely be targeting the androgen receptor specifically in a therapy-resistant subpopulation of patients. To the best of my knowledge, these clinical trials are to start at the beginning of 2019. Interestingly, there are already drugs in the clinic that act as degraders, most notably the so-called immunomodulatory agents, or IMiDs, such as the drug Revlidmid, which is a blockbuster drug for the treatment of multiple myeloma and 5q- myelodysplastic syndromes. It took the scientific community sixty years or more to understand that IMiDs follow this unique mechanism of action of changing the function of the ubiquitin E3 ligase CRBN, but there will be plenty of opportunities to try to copy this particular drug's mechanism of action. One example similar to the IMiDs are the sulfonamides that work via a mechanism that is very similar. They lead to degradation of the particular splicing factor which otherwise would also be undruggable and those molecules were tested in phase II clinical trials, but again, at this point, with a wrong understanding of their actual mechanism of action and thus likely following a suboptimal trial design that lacked relevant and informative biomarkers.

Superti-Furga: I just would like to say that, from my perspective, I think this is really a wonderful challenge for CeMM. It may take years, but I think the entire organization is now reaching a certain level of maturity that may set – as future goals – the ambition to try to see some of the, let's say, chemical biological or, in a bold sense, drug discovery projects, coming from a lab at CeMM eventually entering a clinical program. I think it's a reasonable goal. It will take, I assume, let's say, five years, typically, to come to that point, but that should not let us shy away from that goal. That is sort of my perspective.

Kubicek: Yes, certainly. Following up a bit on what Georg said, I was recently trying to see, whether anyone had done global proteomics of approved drugs at early time points. We also concur with Giulio that, yes, our ambition should be to move some of the findings forward to the clinic. For the folic pathway, of course, it is also a pathway that is already in the clinic, so we hope that understanding the contributions of the pathway in the cytoplasm, in the mitochondria and in the nucleus, will also have a clinical impact through better patient stratification and better drugs.

Loizou: Well, the development of inhibitors for DNA repair enzymes has received a lot of attention in recent years, not only for the treatment of cancer but also for other diseases associated with DNA repair defects. Indeed, it was a synthetic lethal interaction between BRCA and PARP-1 which led to the development of PARP inhibitors in the clinic, which was the first example of a specific synthetic lethality in the treatment of cancer. So, I think, considering the interest not only from academic labs but also from pharmaceutical companies in developing such inhibitors as a way to treat diseases, this will become a reality in the coming few years.

Superti-Furga: Joanna, did pharmaceutical or biotech companies become interested in your research based on your chemical, biological findings and identification of new effects of known compounds and so on and so forth?

Loizou: We've certainly been contacted by both academic groups and also pharma companies for several of our projects. More recently, on the project we just published this year, so in 2019, on understanding how kinases, which are enzymes that phosphorylate substrates, are involved in the DNA damage response and DNA repair. Because kinases are enzymes, firstly, but also because they are frequently deregulated in many cancers, they are a group of proteins that received a large amount of attention from pharma-ceutical companies.

Superti-Furga: And druggable …

Loizou: Yes, they are druggable as enzymes. Recently we were contacted by a pharmaceutical company that wanted us to advise them on developing a program they have on targeting an enzyme with inhibitors as a novel therapeutic, chemotherapeutic approach.

Superti-Furga: I think this is something that, maybe to wrap up, the organization is learning to do better and will need to do yet more efficiently, namely to partner with dedicated companies that are professional in the ability of taking some of these projects along, particularly in those situations, where we still would be involved somehow, by contributing some of the understanding on the target or the mechanism of action of the drug. That is something we have already seen, we have multiplied our relationships, and we are trying to do that, eye to eye, without losing, let's say, control of the projects, but at the same time being adults and partners and acknowledging contributions fairly.

4th Talk at Café Eiles

Gene Over

Kaan Boztug, Jörg Menche,
Christoph Bock, Vanja Nagy

Gene Over

Investigate the genetic and epigenetic basis of human pathophysiological manifestations and phenotypes, from rare to common, from individuals to large cohorts, taking into account single-cell contribution, cell lineage, mosaicism and clonality and including network-based meta-analysis and disease modeling

Of how many people do you think you have analyzed some sort of genetic/genome information in the last ten years and how do you ensure data protection?

Bock: I wouldn't like to break down genomic impact into pure numbers, but in terms of our lab's focus, which has been on epigenetics over the last six years, samples have added up to something in the order of 10,000 – of which the vast majority is DNA methylation, but there is also a significant amount of chromatin accessibility data. This data helps us understand not only the genetic basis of a disease but oftentimes also provides insight into cancerous processes, which are also signs of immune dysregulation.

Menche: Is ensuring data protection a major issue in your group?

Bock: All genetic information and by extension epigenetic and transcriptional information is kept to very high standards of data protection. Nevertheless, it is important to recognize that data of this diverse nature can convey extensive private information, not only personal identity as used for forensic fingerprinting, but also DNA methylation information. You can accurately reconstruct for example smoking status and the number of smoking years from DNA methylation data. An American company is now even using DNA methylation-based age prediction to adjust life insurance premiums. So, this obviously means that we have to be very careful in terms of avoiding unauthorized access, while at the same time supporting international data exchange for research purposes as much as possible.

Menche: Let's turn to one of your best customers, I imagine that is Kaan's group. How many people have you analyzed over the last ten years?

Boztug: Just like Christoph, we don't care to define success so much by numbers because, as you know, our lab is majorly focused on solving individual patient cases, oftentimes theses are unique cases, rare disease patients that have a unique genetic defect. So even an n=1 can be the very significant start to a major discovery. That being said – just like Christoph's lab for epigenetics – we have certainly looked at a couple of thousand patients with different undiagnosed medical histories that we try to pinpoint down to a genetic etiology, mostly focusing on DNA sequencing to identify causative mutations for these patients.

Menche: And this trend is increasing, I imagine, if we wanted to pinpoint some sort of development.

Boztug: Absolutely. Our lab, like other labs, has seen a dramatic increase in the numbers of genetic samples that we are being referred to, which is because people are recognizing more and more how important this sort of deep genetic investigation is. And the other trend that we are seeing is that, obviously, with the costs of next-generation sequencing decreasing, people are moving more and more from panel sequencing towards exome sequencing, towards genome sequencing, because all of a sudden it is becoming affordable. So, genetic investigation is probing into increasingly deeper levels while the costs are decreasing on a per-base level.

Menche: What about data protection? The doctor of course has the highest obligations in this matter.

Getting a diagnosis has a major positive impact on the diagnostic odyssey of rare disease patients.

Boztug: Absolutely. Of course, protecting data is a very important endeavor and again, we are very happy to be part of a larger organization that has genetic and genomic medicine as one of its major hallmarks and thematic focuses. On the other hand, in my clinical practice, almost on a day-to-day basis, I experience that patients that are truly sick – or their parents in many cases because oftentimes small children are affected – are very interested in having people investigate them, even at the potential risk of genetic information being identifiable sometimes. In other words, there is an ethical debate that needs to consider the potential benefit of patients being included in a study, compared to the relatively low risk of information really being identified.

Boztug: I am, let's say, on the opposite end of the scale in terms of numbers. My team comes from a basic neurobiology point of view where we would like to take a particular gene and really study it in a lot of detail, especially using animal models. So, we spend a lot of time on each gene. That being said, we have started collecting and recruiting patients that are suffering from neurodevelopmental disorders and this is in the order of dozens and we hope to increase this to a much greater scale in the coming year. We have had some early level of success that is encouraging us to continue doing this. And of course, as everyone has mentioned, particularly because of the new data protection laws that have come out across Europe, we are incredibly aware and careful that all the data is protected appropriately and by European standards and the standards of the hospital that we are part of. I think Kaan touched upon this – especially in the rare disease community there is a lot of drive and there is a lot of push for data sharing and for certain information to be shared, not only between researchers themselves but within Europe and also outside of Europe. Because in order to confirm novel genes, you need to find patients that are suffering from similar clinical symptoms and we have to share these clinical details with other researchers and clinicians in order to confirm our findings and significantly shorten the diagnostic odyssey of each rare disease patient. And this poses a certain number of challenges – in order to find a balance to and preserve patient privacy, and for their data to be protected, to the best of our abilities, but at the same time not preventing us from actually being able to help them.

Menche: Much of the work we do in my group relies heavily on publicly available data, which Vanja also mentioned. If you consider, let's say, GWAS data that we have been using for many years and continue to use, I have used data on hundreds of thousands of patients. In a narrower sense, through actual collaborations with clinical partners and with physicians, this would be in the order of a few hundred at best, but it's also a trend that is increasing and certainly intensifying. What I can add on top of that is that we rely very much on the strict regulations of our collaboration partners that provide us with de-identified or anonymized data.

What has changed more recently? What is the limiting step in terms of analysis?

Menche: Clearly, at least according to my observations, the information that is being collected – I imagine also by our clinical cooperation partners – is becoming more and more high dimensional and diverse. So, there are more profiling expeditions where not only the genome is collected, but maybe also a proteome or transcriptome or metabolome. And a challenge related to this is, perhaps not so much computationally but really conceptually, how to integrate these diverse datasets that may span an entire range, from the molecular level to the cellular or organ level all the way to clinical phenotypes of entire cohorts. How to extract information and make something useful out of these data expeditions?

Boztug: Well, a number of things have changed. I think people are certainly becoming more aware that the multidimensional consideration of individual patient cases is what has the highest likelihood of succeeding in terms of pinpointing the genetic or even epigenetic etiology of a disease. In this regard, actually, our workflow has also changed. If I look back at the last couple of years, we are now trying much more to integrate not just genetics but also epigenetics, RNA sequencing, and a systems biology/network medicine perspective into our ways of characterizing patients, individual patients, but also diseases. The other trend that we see for immune diseases is that there is a greater need for medical doctors, alongside with researchers, to connect with different institutions, countries, the globe. It is still not unlikely that for some of the gene defects that we are working on in the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases, there may be patients in India, China and Japan that we just don't know about because there is no standardized database.

Nagy: So for neurological disorders, the challenge is obviously to functionally validate any novel genes that we find in a neurological disorder. Nervous tissue from humans required for genetic and molecular validation and research is not really accessible, so this is a major challenge in the field itself. And historically there has been a heavy reliance on animal models, but animal models have their limitations. Certain diseases, such as certain microcephalies for example, cannot be modelled in mice to the extent that would reflect the human condition. So, induced pluripotent stem cells have really taken over in laboratories. Transdifferentiated fibroblasts that are made into neurons and 3D organoid systems mimic early development of the brain. As a matter of fact, cerebral organoids, or mini-brains were developed right here in Vienna at IMBA and have created a very exciting boost and revolutionized the ways we can validate novel genes, understand neuropathologies and even search for patient-specific therapeutics. So this would certainly be something that is changing for the better in our field.

Bock: To me, 2018 has really been the year that artificial intelligence made it into the headlines, into common perception everywhere. That has tremendous potential, because obviously, artificial intelligence and machine learning, can consider extremely large datasets and make sense of them not only for prediction, but also increasingly in terms of understanding. But we are also hitting major roadblocks in this regard. Artificial intelligence experts are very difficult to get, we are educating far too few of them, so clearly there is the need for a lot more education, an outreach initiative to build a new generation of bioinformaticians, computer scientists, artificial intelligence technologists that can drive this change.

Any breakthroughs or new trends we can associate with 2018?

Bock: I think we have seen two dramatic breakthroughs in 2018. Perhaps the most visible – although I wouldn't want to call it a "breakthrough" – is the birth of the first CRISPR babies, the first gene-edited human beings. This was met with much deserved outrage in the scientific community, because in many ways it was done in direct violation of and contradiction to well-established standards enshrined in the scientific community's laws and regulations. Nevertheless, technologically, it was not entirely unexpected, because the methods have been there and available, so it was a matter of time before this was going to happen. I wish it had happened in a much more ethically sound and systematic, open, and regulated endeavor. CeMM has had a discussion on this, and issued a public statement, emphasizing not only the ethical limitations, but also the broader relevance of CRISPR technology. This was also picked up on by the Austrian Academy of Sciences. More generally, we are seeing a perhaps premature, but very clear push toward CRISPR genome editing technology with a real impact for human beings in general, and for medicine in particular. The other major breakthrough has been single-cell technology that is now everywhere. Single-cell sequencing but also increasingly high-resolution imaging technology coming together in initiatives like the Human Cell Atlas will provide great reference maps and a kind of starting point for dissecting diseases in full appreciation of their complexity.

Nagy: From a neuroscience perspective, to continue along the lines of what Christoph mentioned, the single-cell technologies that map out cell types in the brain are also a highlight for me. For instance the Allen Brain Atlas. They created a 3D model of total brain cell content, in incredibly comprehensive 3D imagery, available to researchers, and importantly, it is also updateable. This is really going to change the way the new and the young community of neuroscientists will be able to view the mouse brain. And eventually this will also happen for the human brain as well. On the other hand, to point out how little we still know about the brain, George Paxinos, who is one of the best-known cartographers of the human brain, or brain in general as we know it, has actually just discovered a new brain region or the connection between the spinal cord and the brain. So while we have all of this technology in front of us and we can do all these amazing things, we are still discovering different regions of the brain that can have huge implications. Particularly, this newly discovered region that is involved in motor processing and peripheral sensory input can have huge implications for diseases like Parkinson's.

Menche: I will also piggyback on something Christoph has already mentioned, which is artificial intelligence. For instance, Google's DeepMind team that came up with a program that taught itself to play chess, Go and shogi, and that can beat any human player. It has also found the first applications into medicine for certain specific applications where computer algorithms are now able to classify and diagnose – at least in laboratory experiments – at the level of an expert physician. Technically, most of these rely on huge amounts of imaging data, which is an area we are also exploring, for instance in terms of how to use imaging and classification and characterization of large-scale imaging experiments to improve our understanding of how drugs work.

Boztug: I am not sure if I can pinpoint one specific or two specific breakthroughs in 2018. In times where there is a lot of disagreement on political grounds, scientists have managed to actually collaborate quite well and maybe even better than before. This is true for people that work in biomedical research but also in more basic fields of research. And I think this is maybe another important message that we as scientists can send, namely regarding the significance of transnational and international collaboration for the betterment of humankind. This is not a breakthrough, but I think this is an important role that we as scientists have, particularly in times when some debates become particularly irrational in other fields, let's say, in politics.

Is there anything regarding this area that was achieved in your laboratory/at CeMM that you think is worth mentioning?

Bock: I think my two personal highlights of the last year were the following: first, we had a paper in *Nature Medicine* in the summer that described the disease progression in glioblastoma, the deadliest of brain tumors, based on a comprehensive Austrian cohort. This was the largest study that we have yet done in close collaboration with the Medical University of Vienna, involving several departments, including neuropathology, neuro-oncology, neurosurgery, radiology, etc. This study pulls together a massive dataset that combines not only epigenetic information but also brain imaging, digital pathology and several other layers into an integrative analysis. And it follows how these brain tumors first emerge and then, after surgery, chemotherapy, and radiation therapies, are initially cut back, but then reemerge as drug resistant tumors that ultimately kill the patient. The other point is that, over the last year, we have seen the wide adoption of our CRISPR single-cell sequencing technology, CROP-seq. Not only have we used it quite effectively in our lab, but it has also become a widely used technology, essentially as a new paradigm for CRISPR screening with many different labs already having published first results and showing the power of this technology that was originally developed at CeMM.

Boztug: Well, for us, 2018 has also been exciting in several regards. At the end of last year we were granted an ERC Consolidator Grant, which is important to motivate us to keep going and to keep our momentum and the focus on these rare gene defects which teach us so much about nature and the physiological functioning of molecules, cells and pathways and how they are important in a whole-body and in a disease perspective.

Menche: My team took part in two art exhibitions that I am very proud of, one here in Vienna and one in Munich. And we took our virtual reality holodeck on a road show to Ghent in Belgium, which was also really nice. That is definitely something I enjoy doing and that I would like to pursue further.

How important is it to be embedded in the MedUni/General Hospital setting?

Boztug: I cannot live in one world without the other, in practice. In reality, I am very happy both about the physical proximity of CeMM and the Medical University of Vienna and also the St. Anna Children's Hospital. I am really grateful that I have actually seen open doors in both directions from the research world to the clinics and vice versa. I think when we do research, we have an obligation, especially as medical doctors and physician scientists, to do something meaningful for humankind and for sick patients. And we are trying to use this opportunity to the best of our abilities for the betterment of these sick patients. So yes, I think it is crucially important for an institution that focuses on molecular medicine with a relevance to diseases to be embedded in such a setting and I am really happy about this specific setting that we have entered into. That is very fruitful and that is why we are here.

Bock: The close collaboration with groups and clinics of the Medical University of Vienna and the General Hospital is a major driving force in our research. I have already mentioned the collaboration on glioblastomas. We also have very strong collaboration in the area of hematology, studying leukemias, with several papers in the pipeline. And beyond that, we are working closely with the St. Anna Children's Hospital and the Children's Cancer Institute which gives rise to exciting endeavors combining clinical cohorts and clinical insights with high-throughput technologies in pediatric cancer research. Through the Biomedical Sequencing Facility of CeMM and the Medical University of Vienna, our technology platform for next-generation sequencing, we have also supported a large amount of collaborations, interactions and individual projects with sequencing services and have increasingly contributed to making the vision of "whole genome medicine" a reality in many fields of clinical and experimental medicine.

Nagy: It is absolutely critical that research labs involved in basic science are in direct contact and in the direct vicinity of the clinics, because we can provide the kind of assays that would be able to dig into patient sequencing databases and to prioritize genes that can aid in some of the diagnostic and therapeutic decisions that clinicians can make. Our work together with systems biologists for example, can utilize known gene networks in any particular group of disorders. I think psychiatric disorders are a perfect example and can even help redefine the disease. We are beginning to understand that clinical findings are simply not enough. Cognitive symptoms can be very tricky, and it is necessary to actually find the biological underlying cause of the disease in question. So it is absolutely critical that labs like ours that are involved in basic science are actually embedded within the clinical community.

Menche: In my own team, many people do not have a very strong biomedical background. So we, have physicists, mathematicians, and some people with a more chemical background or an artist, and to us it is absolutely critical to be immersed in this environment, in order to keep on track in our very interdisciplinary endeavors. To ensure that we ask the right questions.

By when do you think will we see impact of this research in medical practice?

Bock: In terms of therapy development, the path from target discovery to approved medicine has been traditionally very long. 10 years is often given as a realistic estimate. However, we do see a whole new generation of academic labs that are now involved in the development of new small-molecule drugs. There are other treatments, too, which can be developed quite efficiently in a university setting. CRISPR gene therapy is one, cell-based therapy such as CAR T cell therapies another, mRNA-based therapies might be yet another, or antisense oligo nucleotide-based therapies.

Menche: The research part in my group that is by far closest to medical practice, is done together with Kaan and Vanja. One thing that I am dreaming about or that I am being delusional about is that, perhaps within the next 5 years, I would love to see some of our virtual reality in a clinical research setting. Kaan and Vanja, when is it that our methods are going to be useful in that sense?

Nagy: I was really just going to say for a rare disease patient, whose case is solved, the impact is right now. Getting a diagnosis has a major positive impact on the diagnostic odyssey of rare disease patients. We try to, intelligently, with your help, pick the certain genes that we would screen for, that we would functionally validate, and then go back to the undiagnosed patient files of our clinical partners and see if we can help them identify causative genes already prioritized by standard sequencing techniques.

Boztug: I fully agree. We have seen tremendous impact. The mere fact of having a diagnosis often changes a lot for patients in terms of their psychological well-being. And in some selected cases, this has a direct implication for treatment, because we know some treatments that are efficient for certain diseases. Or actually, we have showcased that in some cases, we can repurpose existing drugs, in a sort of precision medicine type of approach, and use them for specific individual patients given their specific genetic background. That being said, I think the major challenge in the field, for us and also for many other people, remains to be more efficient, to really make that step into targeted therapies for these patients. This will be a major effort that will require a combined effort of treating physicians, researchers and chemical biologists, but that also needs support and collaboration with the pharma industry. All together in an alliance to best serve patients and their individual needs.

5th Talk at Coffee Pirates

Adjunct Principal Investigators

Thomas Reiberger, Georg Stary,
Thijn Brummelkamp, Nuno Maulide,
Miriam Unterlass, Andreas Villunger

Adjunct Principal Investigators

Discussion on 2018 scientific findings/breakthroughs, expectations for 2019 and the future, views on CeMM

What in your view is the hottest scientific finding of 2018?

Villunger: What's hot always lies in the eye of the beholder. But, scientifically speaking, I found some recent publications linking chromosome missegregation to innate immunity sensing and activation of the immune system. Very hot. I think that's something that was unexpected for me. How this system actually senses, how our body senses errors in mitosis and communicates them to the immune system, in order to stop cells from transforming.

Reiberger: For me, it was the fact that, in patients with liver failure who often develop extrahepatic organ failure, repetitive plasma exchange worked to improve the outcome. There have been reports on very promising outcomes in patients with acute liver failure in intensive care, using plasma exchange in patients, even resulting in improved mortality. So, why is that so surprising? Because we don't know yet what it is, in the plasma, that mediates this. But in the future, the technologies that we have available, proteomics and metabolomics, will probably tell us why plasma exchange worked for this condition.

Stary: For me, the hottest scientific finding is the implementation of new immunotherapies in different fields of medicine, such as for example melanoma, where there are a lot of new options available now. To me, that's the breakthrough of last year.

Brummelkamp: And for me, the hottest scientific breakthrough having the biggest impact on my type of research is not from last year, but from a little longer ago, and that's CRISPR/Cas9, which last year also influenced almost every experiment we did. For the coming years, I expect that this technological breakthrough will remain most influential for our research.

Maulide: As our colleague Andreas so nicely and so eloquently put it, this lies in the eye of the beholder. In my case, the hottest scientific finding is not directly connected to my research but is actually something I think is of importance to us as humankind, namely the discovery of water and organic compounds on Mars. Because I think that is kind of earth-shattering – which is a nice word to use when you talk about Mars – it's Mars-shattering in the way we conceive the building blocks that are required for life, and how on earth – again a nice word – they can be found in Mars in such a conclusive way.

Villunger: It opens a new real estate market.

Maulide: It's true...

Unterlass: That, too.

Maulide: Because of the water, real estate agents all over the country will be ...

Villunger: ... lining up for the space odyssey.

Unterlass: What I found last year's most and actually coolest publication, and that's chemistry, was a Nature paper by Lee Cronin from Glasgow, who basically used an AI robot to discover new reactions. So it's really chemical synthesis fully done by a robot, but the robot is fed artificial intelligence algorithms and it learns and discovers new reactions that no one even knew existed before. And I think they published like 10 new reactions the robot found.

What was an impressive medical/clinical or technological breakthrough last year?

Villunger: Well, for me, again maybe not last year, but in the last couple of years, also biased by the type of research I was doing as a postdoc, it was great to see that molecules I've worked on (BH3-only proteins) and helped to discover, are now also, for the first time, real drug targets, and that drugs that target protein-protein interaction and interfaces, which was deemed impossible twenty years ago, are now basically entering the clinics. So, I think that is pretty cool, and also holds high potential for similar drugs to be developed, for example, targeting key pathways in cancer.

Reiberger: So for me, in terms of medical advances, it's clearly antiviral treatment for hepatitis C, which has really cured a lot of patients, and we have already seen the positive consequences for the liver transplant waiting list. And the second impressive medical breakthrough I would like to highlight here is the benefit of immunotherapy in different types of advanced cancer.

Brummelkamp: I'm especially fascinated to see the diversity of impactful therapeutic modalities expand. There are not only small-molecule enzyme inhibitors, growth factors or antibodies but also PROTACs to hit molecules that were previously undruggable, RNA-based therapies, gene therapy, gene editing and cell-based therapies are beginning to take off. That excites me.

Maulide: In my case, there are actually two: one of them has already been alluded to, which is the use of artificial intelligence in chemistry. I was more impressed by another paper where a lot of data about a specific transformation was fed into an algorithm and then the algorithm was able to predict the outcome of reactions that had not already been done, with a precision of 1%, which is quite impressive. The other one I found really amazing – we all know how Cryo-EM changed the way protein structure is determined – is that Cryo-EM can also be used to determine the structure of small molecules. This was described in two papers, and it was so simple. We were surprised at the simplicity and the rapidity of this method. Just taking something off the shelf, a powder, putting it there, three minutes, bam – you've got the structure with one ångström resolution. So, if we can get beyond the need to get a single crystal for proper x-ray diffraction, even for small molecules, I think this is gonna be quite a bomb.

Unterlass: I absolutely agree. I think, technologically speaking, in chemistry, the coolest thing for me last year was micro electron diffraction, which was used to determine absolute configurations of small molecules in an electron microscope. And the funny thing is, it sounds boring because this was already known for proteins, and you find yourself thinking: OK, a protein is big, so congratulations, you can do it with a small molecule now, hooray. But what is new, I would say, is really that the crystallites are much, much smaller than for proteins, so the crystals that were used to determine molecular structures in micro electron diffraction, they are like, I think a factor of 1,000 smaller than what you need in order to do single-crystal diffraction of a small molecule. So it's really, what Nuno said, you take some random powder that does not even look like a crystal and you put it into an electron microscope and ta-da! You can do that with mixtures of powders, right, because you would have different particles in the TEM. It's like, quite cool.

Maulide: Very cool. My question was: could we actually take a solution and let it evaporate on the plate and then directly use the powder?

Unterlass: Yes. I think, yeah.

Unterlass: Wonderful!

What do you expect CeMM will provide for you in this beautiful year of 2019?

Villunger: That's fairly simple: a fun environment to do research in with lots of interactions and new faces and friends. To discuss scientific problems, and beyond, that also matters, but I think that's my expectation. And building on that, some fruitful collaborations that will also take my science to the next level. Because together, we are better.

Reiberger: For me, I think what I can expect from CeMM is a lot of methodological and intellectual input, which is essential for a translational, clinical researcher. I think it's not only the methodology but also the people connected to the methodology that will actually make the difference, as opposed to other institutions, where you have core facilities doing analyses without providing the scientific framework. And on the other hand, also the environment itself that makes me think of methods and methodology that I can use and that I hadn't thought of before. So I expect my scientific horizon to be broadened and deepened by CeMM.

Stary: Yeah, so for me, it's the perfect research environment that you cannot have at a clinical department, where you can't have the creativity and the input present at CeMM. And lots of interactions, this hypercollaborative environment that is really happening at CeMM. That's what I am looking forward to for this year.

Brummelkamp: I like to be exposed to a scientific community that is really different and very energetic. And I enjoy that very much. I hope, of course, to get new ideas, collaborations and fun out of this.

Maulide: So, I had written a pre-canned answer which read "a fruitful and inspiring space for collaborations, a place to advance fundamental chemistry into asking and answering questions about biology". Then I had the non-official answer which is "caspase inhibitors, immunosuppressant drugs and cancer therapies". That's the non-official.

Villunger: All new chemicals based?

Maulide: All new chemicals based. But caspase inhibitors, in any case.

Villunger: Of course, of course.

Maulide: And immunosuppressants … that'll give us something to talk about.

Unterlass: I would hope for CeMM to allow me to learn much, much more about biology and medicine, which I totally need and want to do, and I think this is the right place to really learn a lot and get exposed to all kinds of different aspects. That's number one, and number two, would be really to have and enter into many cool, intriguing collaborations that are possible if people are different enough in what they do, but also have kind of a common goal. And I totally see that, yeah, CeMM is a place where you can do this kind of stuff. Cool.

Villunger: Cool. Halfway through, time for a coffee break.

Unterlass: Now come the fun questions, the even more fun questions. So, the second part will be a lot more entertaining.

What would you like the CeMM community to associate you with/recognize you for?

Villunger: What I want them to think of me? Well, I think I would be pleased, if at the end of the year, people would say recruiting Andi to CeMM was a good idea and that he is an asset because he is outgoing, outspoken and open-minded and it's always fun to discuss with him and he occasionally even has a smart idea that helped them move to the next level.

Reiberger: I would like CeMMies to see me as a physician-scientist who can put experimental molecular findings into clinical context. On the other hand, I would like them to see me as a partner who can provide patient data and primary human material to translate some exciting basic research findings into human medicine. I am happy to answer any questions related mostly to clinical medicine. That's what I can offer and that's what I want to offer. And obviously, if there are any questions in regard to liver and hepatology, I would love to be the "go-to person".

Stary: So, I would like to be recognized by CeMMies as one of the clinicians that not only sees patients but can also ask more in-depth scientific questions in order to do some meaningful science that is not too superficial, I would say. And, of course, to then also be helpful with different projects that need some translational spin, some clinical application.

Brummelkamp: I hope to be seen as a pleasant colleague by the CeMM people. Somebody who's interested in a broad area of science and willing to collaborate. That would be my goal.

Maulide: It's the chemists' turn now. I would hope to be seen as a magician chemist who can make incredible modifications in molecules and open up chemical space to help address whatever biological question they have.

Villunger: Like the caspase story.

Maulide: Exactly, for example a caspase. Just as an example.

I think every city in the world needs a CeMM because that would move things forward.

Unterlass: I would hope CeMMies associate my team and myself with synthetic creativity and problem solving in chemistry, so that they come to us if they need some, you know, problem-solving in chemistry. I would hope they associate us with consistent high quality in what we do, with a collaborative spirit, like Thijn said. I also think that's very important. And finally, I would hope they associate us with – that they see us as people who have their hearts in the right place. Wonderful!

Maulide: Sure, beautiful.

If CeMM expanded in size and scope, what would you add?

Villunger: In size and scope? Actually, I have been thinking about this a fair bit and – whatever I say now is based on my ignorance of not knowing what else is around in Vienna – but I was actually thinking that for me, tissue engineering in the context of regenerative medicine is something that is the future.

Unterlass: OK.

Villunger: And actually, I think this could fit quite nicely into the overall concept of CeMM. You have drug development, drug screening, drug purposing and I think I would move a bit away from the molecule, from the molecular side, to the biology of creating 3D structures that can replace human tissue.

Unterlass: But that's very material-style stuff.

Villunger: Well, if you think of stem cell biology and all the potential it holds, I think this could be something that is an add-on.

Reiberger: I would also like a program on regenerative medicine, maybe artificial organs. You know, the idea of growing organs in a dish is probably something that could solve our lack of donor organs. For example, for patients waiting for life-saving liver transplants, but also in other fields of organ transplantation. And another thing I would suggest is to have a team of biologists, molecular biologists, immunol-ogists on some of the clinical boards, tumor boards, whatever, so they understand that both the clinical problems and the things that are observed in biology can also be found in the clinics, while biologists might see the patterns that clinicians don't see. So, you know, we might have more joint meetings on clinical boards that can benefit both "sides".

Brummelkamp: Well, if CeMM expanded in size, I would hope that the expansion would also lead to an increase in research facilities, because I think shared facilities for microscopy and DNA sequencing make for a good research institute, where projects and new research groups can flourish. So, that is very important. And beyond that, I would think there would also be a place for some basic, fundamental research in the area of cell biology. Because many students are trained at CeMM, it could be healthy to incorporate a little bit more of this into the institute.

Maulide: I'm sorry for stealing from you, Miriam, but I think CeMM should expand into chemistry. And I think you may have a similar idea, because it is kind of obvious. Either some-thing on the border between medicinal chemistry and synthetic chemistry, or why not really go into chemical biology, for which I still think there is no proper space in the Viennese land-scape. I think CeMM could be the ideal location for chemical biology, in a modern sense.

Unterlass: Ah, Nuno.

Maulide: And caspase inhibitors.

Unterlass: We cannot always say the same thing, but you also have an overlap in the physician's corner.

Villunger: I think this is not mutually exclusive, because exploring chemical space and drug medicinal chemistry and biology is great. Because maybe you can define chemical compounds that may help you to design and develop tissues. You know, maybe you can substitute natural ligands with synthetic ones, and then these might be much more efficient, much cheaper, much safer or more specific. So, I think there could even be an overlap, if they ever decide to go in this direction, which I think would be convenient, because the hospital is right there, so … think about human organoids.

Maulide: Next door.

Villunger: Next door. So the source is there, and from that perspective, maybe this is something to consider. Giulio will decide.

Unterlass: Yeah, I would also add some medicinal-chemistry-type drug discovery facility. I guess that's what companies do and maybe it's boring, but I would think it should be half computational and half synthetic, where you do chemoinformatics and make stuff efficient from a computational point of view and then synthesize it, highly efficiently.






When I think of CeMM I think of people that are creative, energetic,inspiring, ambitious and proud, so I think of *Chef's Table*.

Villunger: Very efficiently.

Unterlass: High-throughput – many molecules – new molecules.

Villunger: What's your target? Or what's your favorite target then, aside from synthesizing all these molecules?

Unterlass: When you say "target", you mean what for?

Villunger: Yeah.

Villunger: You want to test it on something – a certain disease, or a certain …

Unterlass: This sounds harsh, but the target doesn't matter so much to me. What is personally interesting to me is scaffolds that you can diversify into all kinds of applications, so you can make materials on the one hand, but you can also use them for biological applications. There are, for example, some funny scaffolds that are good at inhibiting kinases and that really, molecularly, are ideal for making materials, if you look at the chemical functions they have. By this, I don't mean that I am particularly interested in inhibiting kinases, but I find it beautiful to identify molecules or fragments that can do lots of things by diversification.

Andi, if you were to build a second CeMM, in which city of the world would you do it and why?

Villunger: I won't say Innsbruck, although it would be great because we could go skiing after coffee breaks.

Stary: So, is it Innsbruck?

Villunger: No, I have been thinking about it, and one thing is that I come from the snow, which is why I like the beach and warm weather. I've also spent a lot of time in Australia, so I thought Sydney would be a nice place for different reasons. Because there is actually an EMBL initiative in Australia which I think basically funds groups all over the country, meaning huge distances, of course. And I think it would be great if this could be united in one physical building next to the Harbour Bridge. And you could think about a CeMM-EMBL joint venture to bring great science to the 5th continent. I know it's a drag to get there, but once you're there, it's really nice.

Unterlass: OK.

Reiberger: So personally, I think every city in the world needs a CeMM because that would move things forward.

Reiberger: And if you could build a flying CeMM, that would also be nice, because you could go from one city to another and spend as much time there as you needed. But on a very subjective note, I would intuitively go with Singapore, just because I've visited the city and it's a very lively, very colorful, very bright, very dynamic city. So, when I take into account the goals and the mission of CeMM, I think it fits nicely.

Villunger: I had that on my list too, as an alternative.

Reiberger: Apart from Innsbruck.

Villunger: Apart from Innsbruck. Halfway to Sydney.

Reiberger: As a stopover, more or less.

Stary: So, I fell in love with Boston and I think CeMM would go really well with the city. There are a lot of institutes in the same league I would say. A lot of collaboration partners and biotech companies and so on, so I think that's an environment that would be very positive.

Brummelkamp: Personally, I would favor Amsterdam. I'm not leaving Amsterdam, but it would be great if CeMM would move.

Maulide: To follow along these lines, I think Lisbon would be a great place for a CeMM, but for many reasons. It is a very livable city, it has a very lively biomedical scene, there is already an institute there with a mission very similar to CeMM, the Champalimaud Foundation, which is more into the neuroscience aspect of things, but they are also very high level. And I actually think Lisbon would be a great place for an institute like CeMM.

Villunger: Would be a compromise regarding Sydney. 'Cause you have the beach, the surf, the nice scenery, and nice food.

Maulide: And only three and a half hours' flight, so it's …

Villunger: So, I … agreed!

Unterlass: And very good coffee, in Lisbon.

Maulide: You like the coffee there?

Unterlass: Yeah, very, very much so. I would build my second CeMM in Montréal, because first of all, it's also a very livable city. I think it ranks No. 20 or 21 on the Mercer list. Yeah, and then, it's bilingual, which is really cool because it's also super multicultural and very culturally active and that's all very important for scientists to be creative, right? We need an environment that opens our minds and I think bilingualism is actually a good thing for that. And really, the most important is the internationality in Canada, which we totally lack in Austria, I think. I mean CeMM is a very international place, but in general, it's still too difficult for researchers and scientists from abroad to come here. The whole visa process, all this stuff is complicated, not super welcoming for other cultures. And I mean in Montréal, it's just like you can find any kind of food, you can find any kind of religion or language and people are very open-minded about that. I think that would be an awesome place. And I think it's very nice that all of us chose cities that are very livable.

Maulide: Yeah, of course.

Unterlass: Because it's also very important for your co-workers to be happy where they live, right?

If you think of CeMM and CeMM life, what popular TV series does it best compare to?

Villunger: It should be *The Sopranos* according to Giulio, of course, although I personally favor *Friends* over *The Sopranos*. That's it.

Reiberger: I like the idea of *MacGyver* because this guy always finds his way out. However, since he's just one guy, I think he has to team up with *The A-Team*. So, it would be a combination of *The A-Team* and *MacGyver*.

Villunger: That's pretty cool.

Stary: I think that's the hardest question. I'm not really into many TV series but, yeah, something like a mixture of *Friends* and not taking things too seriously. *Simpsons* is also a good choice, of course, yeah, but I think the perfect TV series has yet to be created, with some special characters that would be in place then.

Villunger: You should have said *South Park*.

Reiberger: Yes, absolutely.

Brummelkamp: When I think of CeMM, I think of people that are creative, energetic, inspiring, ambitious and proud, so I think of *Chef's Table*. You know *Chef's Table?* You don't know it? *Chef's Table* is a documentary about top chefs all over the world and their restaurants. The difference is that CeMM is more collaborative and much less individualistic. However, I think the creativity and ambition fits in well with CeMM.

Maulide: I haven't watched TV in ages. I associated inspiring, ambitious, unique solutions. And then I would say *Dr. House's* mind is the meanest.

Unterlass: Nuno, I hate you for answering the same things.

Maulide: Really?

Unterlass: No. The first part, I do not watch TV, I have not watched TV in forever, I do not know any series and I just fake laughed at all of your series because I don't know this *Dr. House*.

Maulide: Come on. Really?

Unterlass: But I think I have something that comes to my mind directly. When asked to compare CeMM to something, that would be the Bauhaus School. I think CeMM is totally like Bauhaus in terms of …

Villunger: Yeah, its architecture …

Unterlass: Yeah, the Bauhaus state school, in terms of being radically different. And I think that's a wonderful thing to do, being, yeah, radically different in a high-quality, experimental, innovative way. Yeah, Bauhaus, totally.

Maulide: You can combine it with *Mr. Bean*.

Unterlass: I don't know.

Stary: Who is *Mr. Bean*?

Unterlass: But if you think about it, I mean, there are other high-level institutes in the world, yeah, but CeMM is different – is really different. And for example, doing such a thing like hiring five Adjunct PIs all at once to add to Thijn and Kate. That's quite a radical thing to do, and that's, you know, radically different, it's cool. Love it.

Maulide: I think, whenever all of us attend something at CeMM, when there is a speech or something, we always think: boy, I wish some of these things could be replicated at my home institution – and then you think, yeah, yeah, ok never mind – not gonna happen. But I wish.

CeMM 2018 Highlights

With the aim to shape the precision medicine of the future, CeMM is committed to tackling biomedical challenges with a focus on cancer, immune disorders, and infectious diseases.

A New Player in Regulation of Cell Proliferation in Leukemia

The team used a gene-trap screen to discover that the protein LZTR1 is a signaling factor that restrains RAS signaling (and thus cell proliferation). Its inactivation makes chronic myeloid leukemia cells resistant to the drug imatinib.

The disease: Chronic myeloid leukemia, a disease characterized by the uncontrolled growth of white blood cells; specifically of the *myeloid* cells (granulocytes: neutrophils, eosinophils and basophils) as opposed to the *lymphocytic* cells. The initial phase may last for years with relatively minor symptoms, hence the name chronic. However, progression to a more aggressive state frequently occurs if untreated.

The medicine: The disease can often be controlled for a long time with tyrosine kinase inhibitors such as imatinib, that dampen down the signaling pathway in the cells that leads to cell proliferation and survival. Eventually, resistant cells may emerge over time.

The aim: To better understand the signaling pathways and mechanisms that can enhance cell survival and make them drug-resistant.

The news: LZTR1 had been identified some time ago, but not very much was known about its physiological function. Now it is known to be involved in attaching ubiquitin modifications to RAS proteins, which reduces RAS/MAP kinase pathway activity. Most likely as a 'substrate adaptor protein' for the CUL3 E3 ubiquitin ligase. So now, for the first time, LZTR1 has a specific mechanistic role, also explaining several rare human diseases involving RAS deregulation (e.g. Noonan syndrome).

This work was done by postdoctoral fellow and medical doctor Johannes Bigenzahn and colleagues in the Superti-Furga group, together with the laboratories of Marek Mlodzik in New York, Adjunct PI Thijn Brummelkamp in Amsterdam as well as Robert Kralovics and Georg Winter at CeMM. Published in *Science*.

Bigenzahn JW, et al. **LZTR1 is a regulator of RAS ubiquitination and signaling.** *Science.* 2018 Nov 15. pii: eaap8210. doi: 10.1126/science.aap8210. [Epub ahead of print]

Mapping Cell Types in Lung Development: Immune Cells Asserting their Identity

The researchers made the first single-cell resolution map of the structural and immune cell repertoires of the lungs through late embryonic and early postnatal development. They discovered a tightly intertwined cellular interaction network and some unexpected findings on basophils that shape early developmental stages of alveolar macrophages.

The challenge: The lungs are subjected to substantial adaptations at birth, when they are required to provide oxygen to the body for the first time. In this important time window, the lung's immune cell repertoire develops and matures, to be prepared for a life exposed to outside challenges such as pathogens and environmental threats.

The system: The lungs are a very special organ, in that they are exposed to the outside world like no other part of the body. They have a huge surface area where air from the outside exchanges gases with the blood across delicate membranes. Therefore, immune cells such as macrophages have very special tasks to do there.

The aim: To understand the development of the immune system in the lungs and, ultimately, how to intervene to correct inappropriate responses.

The news: A high-resolution map of all cell types and subsets, including the stages in their development and their interactions. A searchable data resource for other researchers. Rare cells that might have been overlooked have important roles in shaping the immune system in the lungs.

This work was done by Merav Cohen and Amir Giladi at the Weizmann Institute of Science in Israel, led by Ido Amit, together with Anna-Dorothea Gorki from the Sylvia Knapp group at CeMM and the Medical University of Vienna. Published in *Cell*.

Cohen M, Giladi A, Gorki AD, et al. **Lung Single-Cell Signaling Interaction Map Reveals Basophil Role in Macrophage Imprinting.** *Cell.* 2018 Nov 1;175(4):1031-1044. e18. doi: 10.1016/j.cell.2018.09.009. Epub 2018 Oct 11.

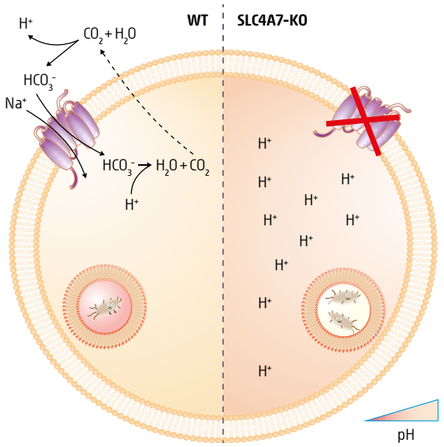


Fig. 1 SLC4A7 and bicarbonate-driven cytoplasmic pH homeostasis identified as an important element of phagocytosis and the associated microbicidal functions in macrophages.

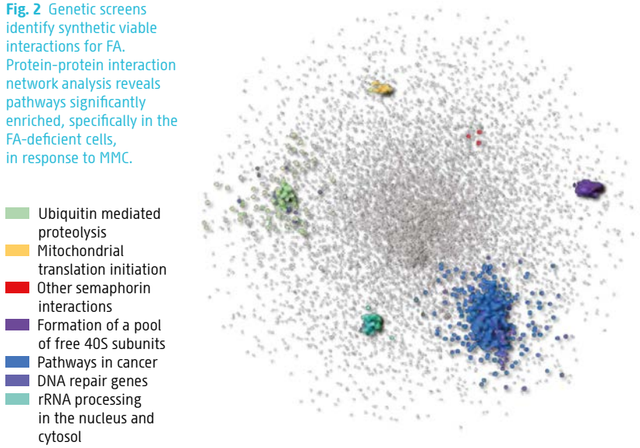


Fig. 2 Genetic screens identify synthetic viable interactions for FA. Protein-protein interaction network analysis reveals pathways significantly enriched, specifically in the FA-deficient cells, in response to MMC.

A Zinc Transporter with a Surprising Role in Programmed Cell Death

A gene-trap screening strategy led to the unexpected discovery that SLC39A7, a protein that transports zinc across the membranes of the endoplasmic reticulum, was necessary for the programmed cell death process called necroptosis. Necroptosis can be induced by a signal activating the TNFR1 receptor present at the cell plasma membrane, but if the zinc metabolism in the endoplasmic reticulum is disturbed, the receptor protein is not processed properly and is absent from the cell surface.

The system: Necroptosis is a form of programmed cell death, important to eliminate damaged or infected cells. It results in the cell bursting and releasing its contents, which contributes to the induction of inflammatory and immune responses. The process has been discovered quite recently and already linked to several pathologies, but its basic mechanisms are still only partially understood.

The surprise: We tend to think of signaling processes in cells – receptors, hormones, kinases, G proteins etc. – as separate from basic metabolism – the ordinary things any cell has to do in order to survive, such as regulating its pH or ion concentrations, or producing new proteins. But in fact they are connected, as illustrated here with altered levels of zinc in the endoplasmic reticulum affecting the trafficking of TNFR1 receptors to the cell surface and, consequently, its ability to signal.

The technique: Gene trapping is a way of casting the net wider. It allows to disrupt genes one by one in individual cells, while at the same time inserting a DNA tag so that each gene can be identified afterwards by sequencing. By applying a selection method that monitors the process of interest – in this case, a signal that triggers cell death-relevant genes can be identified. Surviving cells have a genetic modification that impairs necroptosis, and the study of the targeted genes revealed novel mechanisms important for this process.

This work was done by Astrid Fauster, Manuele Rebsamen and colleagues from the Superti-Furga group in collaboration with the laboratory of Kaan Boztug at the Ludwig-Boltzmann Institute for Rare and Undiagnosed Diseases and the St. Anna Children's Hospital in Vienna. Published in *Cell Death and Differentiation.*

Fauster A, et al. **Systematic genetic mapping of necroptosis identifies SLC39A7 as modulator of death receptor trafficking.** *Cell Death Differ.* 2018 Sep 20. doi: 10.1038/s41418-018-0192-6. [Epub ahead of print]

Epigenetic Analysis of Aggressive Brain Tumors

Glioblastoma is a brain cancer with devastating prognosis. A collaborative project led by a CeMM team – together with scientists from MedUni Vienna, the Austrian Brain Tumor Registry and clinicians from all over Austria – demonstrated how epigenetic analysis of tumor samples collected in routine clinical practice could be used to better classify and treat the disease.

The disease: Glioblastoma is an aggressive brain cancer with a high degree of molecular heterogeneity among the cancer cells. This results in the evolutionary selection of those cells that can withstand drug treatment. In order to develop better therapies for glioblastoma, detailed knowledge of the tumor cells' molecular heterogeneity will be crucial, given that this heterogeneity provides the substrate from which drug resistance evolves.

The project: Whether and how epigenetic regulation changes when a glioblastoma becomes therapy-resistant has been a largely unsolved question. To investigate the role of epigenetics in glioblastoma disease progression, DNA methylation was analyzed in more than 200 such patients, focusing on the epigenetic changes that occur during disease progression.

The results: Combining epigenetic data with brain imaging and digital pathology, the study established important links between glioblastoma at the level of molecules, cells and organs. These associations can be exploited to improve disease classification. Moreover, this study provides a rich resource for understanding the role of epigenetics in glioblastoma and a new set of tools with broad relevance for personalized medicine.

This work was done by Johanna Klughammer in the group of Christoph Bock, in close collaboration with scientists at the Medical University of Vienna and clinicians at eight hospitals throughout Austria. Published in *Nature Medicine.*

Klughammer J, et al. **The DNA methylation landscape of glioblastoma disease progression shows extensive heterogeneity in time and space.** *Nat Med.* 2018 Oct;24(10): 1611-1624. doi: 10.1038/s41591-018-0156-x. Epub 2018 Aug 27.

Covering the Bases (while Pumping Acid)

Phagocytosis, defined as uptake of solid particles by phagocytic cells such as macrophages, is a crucial part of the innate immune system. Using a human macrophage-like cell line model, the researchers performed focused genetic screens to identify solute carriers (SLCs) relevant to the process of phagocytosis. A multidisciplinary team led by CeMM scientists discovered that the bicarbonate transporter SLC4A7 was necessary for acidification of the phagosomes. Located at the cell surface, SLC4A7 balances the cytoplasmic pH, which is a prerequisite of successful phagosomal acidification.

The system: Phagocytosis is a stepwise process from sensing and ingesting a potential pathogen to acidification and digestion. These steps are associated with transient and rapid changes in cellular metabolism.

The project: SLCs are responsible for the exchange of various metabolites and ions between a cell and its environment. To investigate how SLCs impact phagocytosis, an SLC-wide CRISPR/Cas9 knockout library was used for genetic screens in macrophage-like cells using pH-sensitive reporter particles allowing to distinguish the different steps of phagocytosis.

The surprise: The study identified SLC4A7, a transporter known to balance cytoplasmic pH by bicarbonate import, as essential for efficient phagosomal acidification. Hence, a protein that has a basic metabolic function was found to be crucial for specialized cellular function. The process of phagocytosis – ingesting and digesting another cell or other matter – is a huge metabolic effort for the macrophage and the process of acidifying the inside of the phagosome puts stress on the acid/base balance of the whole cell.

The point: Whether macrophages are able to carry out phagocytosis or not is relevant to disease processes. Modulation of macrophage activity to be either more aggressive (towards pathogens or cancer cells) or less active (in autoimmune diseases) is therefore of therapeutic interest.

This work was done by Vitaly Sedlyarov and Ruth Eichner of the Superti-Furga group, in collaboration with colleagues at the University of Geneva, the University of Vienna and the Medical University of Vienna. Published in *Cell Host & Microbe.*

Sedlyarov V, Eichner R, et al. **The Bicarbonate Transporter SLC4A7 Plays a Key Role in Macrophage Phagosome Acidification.** *Cell Host Microbe.* 2018 Jun 13;23(6):766-774.e5. doi: 10.1016/j.chom.2018.04.013. Epub 2018 May 17.

Inflammatory Signals in Atherosclerosis: The Bad, the Good and the Unexpected

Unexpectedly, treating mice with an antibody against the B-cell activating factor, BAFF, promoted the development of atherosclerosis, the formation of fatty plaques on the walls of blood vessels that cause heart disease. The team discovered a new effect of BAFF that is independent of its main receptor BAFFR. They found evidence that BAFF suppresses inflammatory signals in M1 macrophages, the type that is found in atherosclerotic plaques.

The expectation: Anti-BAFF antibodies block the action of BAFF and reduce the number of B cells, which are part of the problematic inflammatory process in atherosclerosis.

The surprise: The anti-BAFF antibodies made the atherosclerosis worse, even though they reduced the number of B cells.

The explanation: The stimulating effect of BAFF on B cells via the BAFFR receptor is not its only action. It also acts via the TACI receptor to restrain inflammatory signaling of the TLR9 in macrophages. Once again, immune regulation is more nuanced than we expected.

The note of warning: Anti-BAFF antibodies are approved as a treatment for systemic lupus erythematosus. This possibly should be done with increased care and vigilance to detect and limit any negative effects in the form of atherosclerosis or cardiovascular disease.

This work was done by Dimitrios Tsiantoulas and colleagues in the group of Christoph J. Binder, in collaboration with colleagues at the Medical University of Vienna, the University of Cambridge, UK, the University of Utrecht, the University of Lausanne and INSERM, Paris. Published in *Circulation.*

Tsiantoulas D, et al. **BAFF Neutralization Aggravates Atherosclerosis.** *Circulation.* 2018 Jun 1. pii: CIRCULATIONAHA.117.032790. doi: 10.1161/CIRCULATIONAHA.117.032790. [Epub ahead of print]

More than One Way to Repair DNA

The genetic disease Fanconi anaemia is caused by defects in a set of proteins responsible for repairing crosslinks in DNA. The team implemented a global genetic screening strategy to identify genes whose loss compensates for mutations in the Fanconi anaemia pathway. One of the genes discovered was USP48, an enzyme that removes ubiquitin units from proteins. Knocking out USP48 improved the ability of cells with the Fanconi mutations to repair their DNA and suppress genomic instability. This rescue interaction is dependent on the 'tumor suppressor' protein BRCA1 and depends on regulating the ubiquitination of H2A histones, proteins that are involved in packaging and unpackaging DNA in chromosomes.

The context: DNA repair depends on a fundamental set of processes in cells and the crosstalk between these pathways is not yet fully understood. DNA damage and the accuracy of repair mechanisms determine the rate at which mutations are introduced, which can contribute to cell death but also to the development of cancer. Germline mutations in DNA repair genes can give rise to rare diseases that are characterised by a range of pathophysiological phenomena. One such disease is Fanconi anaemia that occurs when DNA crosslinks cannot be removed from DNA. These patients develop bone marrow failure due to cell death and are also susceptible to cancer development. This disease has no curative therapies.

The discovery: To identify potential therapeutic possibilities for Fanconi anaemia, the group took an unbiased genetic screening approach using gene trapping. This approach revealed that loss of USP48 could alleviate phenotypes associated with Fanconi anaemia hence identifying this enzyme as a potential therapeutic target for this disease.

This work was done by Georgia Velimezi, Lydia Robinson-Garcia and colleagues in the group of Joanna Loizou, in collaboration with colleagues at the University of Cambridge, UK, the University of Leiden, Netherlands, the University of California in San Diego and the University of Toronto. Published in *Nature Communications.*

Velimezi G, Robinson-Garcia L, et al. **Map of synthetic rescue interactions for the Fanconi anemia DNA repair pathway identifies USP48.** *Nat Commun.* 2018 Jun 11;9(1):2280. doi: 10.1038/s41467-018-04649-z.

RESOLUTE – Research Empowerment on Solute Carriers

Cells, like the organs and organisms they belong to, require energy to fuel their activities and molecular building blocks to grow, divide and specialize their function. How do cells gain access to energy and building blocks? It needs to come from the environment, blood, interstitial fluid or other cells. And, ultimately, from food.

We have learned a lot in the last 30 years of molecular biology on how cells complete many complex tasks, such as DNA replication, gene transcription, formation of organelles, control of protein folding, protein secretion and hundreds of other activities. But how the uptake of nutrients, vitamins, microelements, xenobiotics and drugs from the environment occurs and how this chemical matter is differentially distributed within the cells, is not fully understood. In particular, the activity of the various transporters suspected to be responsible must be coordinated and well orchestrated in terms of metabolic needs and cellular functions. A large proportion of the thousands of membrane proteins encoded in the human genome that are thought to be transporters are still considered "orphans" in terms of "cargo specificity" (what they actually transport) and function (what they are actually needed for). Some years ago, we publicized the need for a large and coordinated research effort in the scientific community (César-Razquin A, et al. A Call for Systematic Research on Solute Carriers. Cell. 2015). Now there is an initiative, addressing exactly that.

The RESOLUTE (Research Empowerment on Solute Carriers) consortium is a public-private research partnership supported by the Innovative Medicines Initiative (IMI) with 13 partners from academia and the pharmaceutical industry. Starting on July 1, 2018 and with a duration of 5 years, the mission of RESOLUTE is to intensify worldwide research on solute carrier transporters (SLCs), and to establish them as a novel target class for medical research.

SLCs are integral membrane proteins that control essential physiological functions, including nutrient uptake, ion transport and waste removal. SLCs can be regarded as gatekeepers of the cell and, counting more than 400 members, they constitute the second-largest group of membrane proteins in the human genome and the largest group of transporters. SLCs are vital for maintaining homeostasis in the human body, and genetic polymorphisms in SLCs are associated with diabetes, several types of cancer and neurological diseases, such as amyotrophic lateral sclerosis (ALS), Alzheimer's disease or schizophrenia. There are also several rare diseases and inborn errors of metabolism, such as defects in thiamine and folate uptake, that can be ascribed to SLCs. Importantly, SLCs can function as drug targets as well as constitute paths for drug absorption into specific organs. Despite their key physiological and medical relevance, SLCs still remain a relatively understudied or *locked* class of proteins and potential targets.

The RESOLUTE consortium, which includes universities and other public research institutes, a biotech company and several companies that are members of the European Federation of Pharmaceutical Industries and Associations (EFPIA), was formed to systematically unlock SLC function, specificity and regulation. Project coordination is shared between Giulio Superti-Furga (CeMM) as the academic coordinator, and the EFPIA project lead, Claire Steppan (Pfizer Inc.). Other partner organizations within the consortium include the University of Oxford, the University of Liverpool, AXXAM Spa, Leiden University, the Max Planck Society, the University of Vienna, Novartis Pharma AG, Boehringer Ingelheim, VIFOR Pharma Group, Sanofi-Aventis Recherche & Développement (SARD), and Bayer AG. Aside from the core members, RESOLUTE also incorporates a variety of *Academic Expert Laboratories*, the *Structural Biology Alliance* and the *Antibody Partners*, which supply specific resources and methodologies.

RESOLUTE

efpia

imi innovative medicines initiative

Disclaimer The RESOLUTE project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777372. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA. This communication reflects only the authors' views and neither IMI nor the European Union or EFPIA are responsible for any use that may be made of the information contained therein.

By combining an open-access *ethos* to the techniques and resources, with the highest-possible quality of research output, RESOLUTE expects to accelerate SLC knowledge to the global benefit of both basic academic and applied research. RESOLUTE will approach this ambitious endeavor by (i) generating reliable and validated biological tools and reagents, such as engineered cell lines and plasmids, which will be freely available to the scientific community, (ii) employing a systematic investigation on SLCs that combines the power of the genomic engineering and omics approaches, (iii) developing functional assays for SLCs, and (iv) making the data and resources generated publicly accessible in a novel data and knowledge base.

The RESOLUTE consortium was awarded an Innovative Medicines Initiative grant in the context of the H2020 Programme of the European Union. The project costs are covered by a €12 million grant under the auspices of the IMI joint undertaking as well as by in-kind contributions from industry partners for €11.85 million. The IMI *(www.imi.europa.eu)* is a partnership between the European Union and the European pharmaceutical industry. Since 2008, IMI has facilitated open collaboration in research to advance the development of personalized medicines for general health and well-being, especially in areas of unmet medical needs.

The RESOLUTE consortium is expected to accelerate the pace of research of the solute carrier class of transporters by providing the scientific community with research output and techniques openly and pre-competitively. This will lead to a considerable gain in knowledge and is anticipated to have a large impact on medicine and drug discovery, as well as on our general understanding of the interface between biological systems and the environment.

RESOLUTE builds partially on previous insights on SLC transporters generated through the "Game of Gates" ERC Advanced Grant in the Giulio Superti-Furga laboratory as well as other projects on transporters funded by individual fellowships and the FWF "Vitra" grant. At CeMM, we cherish the opportunity to become a worldwide hub for SLC research and knowledge and to learn from a formidable group of industry and academic partners. Students and postdocs in the RESOLUTE team are trained on how to manage projects across several sites, identify and characterize suitable drug targets as well as how to formulate assays for drug discovery campaigns. The RESOLUTE community is having a lot of fun working together and changing for good the way SLC transporters are appreciated by the wider scientific community.

For more information visit the web portal *www.re-solute.eu* and follow RESOLUTE on twitter *@RESOLUTE_IMI*.

César-Razquin A, *et al.* **A Call for Systematic Research on Solute Carriers.** *Cell.* 2015 Jul 30;162(3):478-87.

RESOLUTE members at consortium meeting at CeMM in Vienna.

Facilities at CeMM

Three research facilities with cutting-edge technologies and expertise are dedicated to supporting scientists at CeMM, the Medical University of Vienna as well as other cooperation partners. The Biomedical Sequencing Facility (BSF) is a technology platform specialized in next-generation sequencing in biomedicine. The Platform Austria for Chemical Biology (PLACEBO) provides researchers with access to chemical biology for studying biological processes and developing new drugs. The Proteomics and Metabolomics Facility (ProMet) has been designed to enable the determination of protein-protein interactions, drug-protein interactions, quantitative expression proteomes, post-translational modifications in cell signaling pathways and key cellular metabolites. CeMM's research facilities are also part of the newly established platform Vienna Life Science Instruments (VLSI, *www.vlsi.at*).

The Biomedical Sequencing Facility (BSF)
The BSF is Austria's leading center of expertise for next-generation sequencing in biomedicine, jointly operated by CeMM and the Medical University of Vienna. Under the scientific leadership of CeMM Principal Investigator Christoph Bock and with a dedicated team of scientists and technologists, the BSF contributes to biomedical research and whole genome medicine in Vienna and abroad. The Biomedical Sequencing Facility offers a broad range of NGS-related services, including library preparation (genome, epigenome, transcriptome, single-cell sequencing, etc.), sequencing of custom libraries (Illumina NovaSeq/HiSeq 4000/Next/MiSeq and Oxford Nanopore platforms), and bio-informatic data processing.

Platform Austria for Chemical Biology (PLACEBO)
PLACEBO was initiated as a partnership between CeMM and seven other Austrian research groups and has developed into a long-term initiative open to the wider scientific community on a collaborative basis. Under the scientific leadership of CeMM Principal Investigator Stefan Kubicek, PLACEBO provides researchers in Austria access to chemical biology resources including a 92,000-compound library as well as high-throughput and high-content screening to identify and characterize small molecules that affect new targets for studying biological processes and developing new drugs. A new acoustic transfer system facilitates highly accelerated compound transfer. The transfer of aqueous solutions in addition to DMSO is now possible, allowing application of our screening pipeline to test nucleic acids (e.g. siRNAs), peptides and proteins (e.g. therapeutic antibodies).

The Proteomics and Metabolomics Facility (ProMet)
ProMet provides state-of-the-art technologies accommodated in a custom-designed laboratory, incorporating modern industrial and academic concepts. A highly skilled and motivated team provides analysis with the goal to extend activities beyond sample measurements and take on an active role in research. The instrument park consists of triple quadrupole mass spectrometry (MS) systems as well as high-end Orbitrap-based MS instruments. The combination of mass spectrometers with ultra-high-performance liquid chromatography (UHPLC) and nanoflow liquid chromatography (nano LC) provides unsurpassed performance in terms of flexibility of application, sensitivity and speed of analysis. André Müller, biochemist and head of the Proteomics and Metabolomics Facility, is an expert for various proteomics tools, in both academic and industrial settings. Kristaps Klavins is an analytical chemist with profound expertise in different mass spectrometry and separation techniques. As deputy head of metabolomics, he and his team work on the development of workflows for the analysis of wide-range metabolites and lipids in various biological systems.

More information about the CeMM facilities, its services, conditions and contact details can be found at: *cemm.at/research/facilities*

Principal Investigators

Andreas Bergthaler

Mechanisms of Viral Diseases

Andreas Bergthaler, born in 1977, joined CeMM in 2011. He studied veterinary medicine at the University of Veterinary Medicine in Vienna and spent clinical and research stays at the Royal (Dick) School of Veterinary Studies, Edinburgh, the University of Tokyo, the University of Zurich and the Danish Veterinary Institute in Copenhagen. For his graduate studies he joined the Institute of Experimental Immunology at the ETH Zurich university (Profs. Hans Hengartner and Nobel Laureate Rolf Zinkernagel). After postdoctoral work in Zurich and in the laboratory of Prof. Daniel Pinschewer at the University of Geneva, he worked with Prof. Alan Aderem at the Institute for Systems Biology in Seattle. Andreas Bergthaler's research is focused on the molecular mechanisms of infectious diseases and the highly dynamic interactions of viruses with their host. To this end, the Bergthaler laboratory studies viral infections in mouse models through an integrative approach of virology, immunology, pathology and systems biology. A particular focus rests on the interplay of metabolic and inflammatory pathways. Animal models of patho-physiological relevance to human disease provide defined experimental systems to gain mechanistic insights into viral pathogenesis through targeted perturbations and computational analyses. This may pave the way for novel preventive and/or therapeutic avenues for virus-induced diseases such as hepatitis, immunopathology, cachexia, immunosuppression and superinfections. Andreas Bergthaler is the recipient of an ERC Starting Grant and several awards including the Löffler-Frosch-Prize of the Society of Virology. Andreas Bergthaler co-founded the clinical-stage immuno-therapy company Hookipa Pharma.

Main Research Interests

+ Chronic viral infections
+ Virus-induced immunopathologies
+ Systemic crosstalk between metabolism and inflammation
+ Molecular basis of transmissible cancers
+ Evolutionary dynamics of virus-host interactions

Relevant/Important Publications

Kosack L*, Wingelhofer B*, Popa A*, Orlova A* et al.The ERBB-STAT3 axis drives Tasmanian devil facial tumor disease. *Cancer Cell*. 2019 Jan 14;35(1):125-139.

Khamina K et al. Characterization of host proteins interacting with the lymphocytic choriomeningitis virus L protein. *PLoS Pathog*. 2017;13(12).

Bhattacharya A*, Hegazy AN*, et al. Superoxide dismutase 1 protects hepatocytes from type I interferon-driven oxidative damage. *Immunity*. 2015;43(5):974-86.

Schliehe C, et al. The methyltransferase Setdb2 mediates virus-induced susceptibility to bacterial superinfection. *Nat Immunol*. 2015;16(1):67-74.

Christoph Binder

Atherosclerosis and Immunity

Christoph Binder was born in 1973 in Vienna, Austria. Following his studies of medicine at the Medical Faculty of the University of Vienna, where he obtained his MD degree in 1997, he entered a PhD program at the University of California in San Diego, where he obtained his PhD degree in 2002. In 2005, he joined the Department of Laboratory Medicine at the Medical University of Vienna, where in 2009 he was appointed Professor of Atherosclerosis Research, in 2006 he joined CeMM as Principal Investigator. He is a specialist in laboratory medicine and leads a research group focusing on the role of immune functions in atherosclerosis and how these can be exploited for therapeutic interventions. He first described the atheroprotective effect of pneumococcal vaccination and the natural IgM T15/E06 (Binder et al., 2003). His research group discovered that certain oxidation-specific epitopes derived from lipid peroxidation are major targets of natural antibodies (Chou et al., 2009) and of complement factor H (Weismann et al., 2011). He also identified the athero-protective roles and mechanisms of the cytokines IL-5 (Binder et al., 2004) and IL-13 (Cardilo-Reis et al., 2012), as well as natural IgM antibodies (Gruber et al., 2016; Tsiantoulas et al., 2017). He has won numerous prestigious fellowships and awards and has authored >110 publications in renowned journals, including *Nature Medicine* and *Nature.*

Main Research Interests

+ Role of innate immunity in inflammation and oxidative stress
+ Elucidate the protective capacities of natural IgM antibodies in atherosclerosis and thrombosis
+ Discover ways to modulate natural immunity as therapy for cardiovascular diseases

Relevant/Important Publications

Tsiantoulas D, et al. B Cell-Activating Factor Neutralization Aggravates Atherosclerosis. *Circulation*. 2018 Nov 13; 138(20):2263-2273.

Binder CJ, et al. Innate sensing of oxidation-specific epitopes in health and disease. *Nat Rev Immunol*. 2016;16(8):485-97.

Gruber S, et al. Sialic Acid-Binding Immunoglobulin-like Lectin G Promotes Atherosclerosis and Liver Inflammation by Suppressing the Protective Functions of B-1 Cells. *Cell Rep*. 2016;14(10):2348-61.

Cardilo-Reis L, et al. Interleukin-13 protects from atherosclerosis and modulates plaque composition by skewing the macrophage phenotype. *EMBO Mol Med*. 2012;4(10):1072-86.

Weismann D, et al. Complement factor H binds malondialdehyde epitopes and protects from oxidative stress. *Nature.* 2011; 478(7367):76-81.

Christoph Bock

Medical Epigenomics and Next-Generation Sequencing

Christoph Bock, born in 1979, joined CeMM as Principal Investigator in 2012. His research group combines high-throughput experimental biology (genome sequencing, epigenetics, CRISPR screening, systems & synthetic biology) with computer science (bioinformatics, machine learning, artificial intelligence), in order to dissect immune regulation and to improve diagnosis and therapy for cancer and immune diseases. He is also a guest professor at the Medical University of Vienna, scientific coordinator of the Biomedical Sequencing Facility at CeMM, adjunct group leader for bioinformatics at the Max Planck Institute for Informatics and a key researcher at the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases. Christoph Bock is an elected member of the Young Academy of the Austrian Academy of Sciences and has received several major research awards, including the Max Planck Society's Otto Hahn Medal (2009), an ERC Starting Grant (2016–2021), and the Overton Prize of the International Society of Computational Biology (2017).

Main Research Interests

+ Epigenomics. Mapping epigenetic defects in cancer cells
+ Bioinformatics. Algorithms for inferring epigenetic cell states
+ Technology. Single-cell sequencing for genomic medicine
+ Diagnostics. Pilot projects in genome-based precision medicine

Relevant/Important Publications

Klughammer J*, Kiesel B* et al. The DNA methylation landscape of glioblastoma disease progression shows extensive heterogeneity in time and space. *Nat Med*. 2018;24:1611-1624.

Datlinger P, et al. Pooled CRISPR screening with single-cell transcriptome read out. *Nat Meth*. 2017;14:297-301.

Sheffield NC, et al. DNA methylation heterogeneity defines a disease spectrum in Ewing sarcoma. *Nat Med*. 2017;23:386-395.

Farlik M*, Halbritter F*, Müller F* et al. DNA methylation dynamics of human hematopoietic stem cell differentiation. *Cell Stem Cell*. 2017;19:808-822.

Mass E*, Ballesteros I*, Farlik M*, Halbritter F* et al. (2016) Specification of tissue-resident macrophages during organogenesis. *Science*. 2016;353(6304).

Sylvia Knapp

Innate Immunity and Bacterial Infections

Sylvia Knapp, MD, PhD, is Professor of Infection Biology at the Medical University of Vienna. Sylvia studied Medicine in Vienna and Berlin, is a board-certified internist and obtained her PhD at the University of Amsterdam. In 2006, she joined CeMM as a Principal Investigator and until recently, she continued her clinical duties while also running her own lab. Sylvia's research focuses on the innate immune response to bacterial infections in general, focusing specifically on the comprehensive repertoire of macrophage functions in health, development and disease. Her group discovered the molecular mechanisms linking hemolysis and susceptibility to infections. Her latest research is directed towards the inter-play of immune cells regulating lung tissue homeostasis in health and disease. Sylvia is highly committed to bridging academic medicine and basic science. She is a member of the Academia.Net circle of excellent female scientists and was elected corresponding member of the Austrian Academy of Sciences in 2014. In 2018, Sylvia was appointed to the University Board of the Medical University of Graz, and elected vice president of the Ludwig Boltzmann Society.

Main Research Interests

+ Molecular mechanisms of host-pathogen interactions
+ Impact of endogenous danger molecules in immunity
+ Macrophage plasticity in lung development, homeostasis and disease

Relevant/Important Publications

Cohen M, et al. Lung Single-Cell Signaling Interaction Map Reveals Basophil Role in Macrophage Imprinting. *Cell*. 2018; 175(4):1031-1044.e18

Saluzzo S, et al. First-Breath-Induced Type 2 Pathways Shape the Lung Immune Environment. *Cell Rep*. 2017;18(8):1893-1905.

Martins R, et al. Heme drives hemolysis-induced susceptibility to infection via disruption of phagocyte functions. *Nat Immunol*. 2016;17:1361-1372.

Warszawska JW, et al. Lipocalin-2 deactivates macrophages and worsens pneumococcal pneumonia outcomes. *J Clin Invest*. 2013;123(8):3363-3372.

Matt U, et al. WAVE-1 mediates suppression of phagocytosis by phospholipid-derived DAMPs. *J Clin Invest*. 2013;123(7): 3014-3024.

Robert Kralovics

Genetics of Hematological Disorders

Robert Kralovics has been Principal Investigator at CeMM since 2006 and a Group Leader at the Medical University of Vienna (MUV) since 2017. He earned his master's degree in Molecular Biology and Genetics at Comenius University and his PhD in Genomics at the Institute of Biophysics of the Academy of Sciences of the Czech Republic. His post-doctoral work was based on the genetics of myeloproliferative disorders working with Josef Prchal at the University of Alabama in Birmingham, USA. In 2000, Robert joined Prchal's group as Assistant Professor at Baylor College of Medicine in Houston. In 2001, he became project leader with Radek Skoda in Basel. Kralovics' research interests are primarily in myeloproliferative neoplasms (MPNs) and in myeloid malignancies in general. His major achievements so far have been the identification of disease causing mutations in the JAK2 kinase gene (V617F) in 2005 and in the calreticulin gene (CALR) in 2013. Using advanced genomic approaches, Robert Kralovics continues his research at CeMM and the MUV to identify new therapeutic strategies for MPN. His aim is understanding how genetic variability contributes to MPN and how it could be treated in a personalized manner.

Main Research Interests

+ How to trigger an immune response against CALR mutation-positive blood cells
+ How mutant stem cells evolve genetically, how they respond to therapy
+ What drugs can inhibit cells with specific genetic defects
+ How genetic variability contributes to disease
+ Identify the key factors that initiate thrombosis and myelofibrosis during MPN

Relevant/Important Publications

Nivarthi H, et al. Thrombopoietin receptor is required for the oncogenic function of CALR mutants. *Leukemia*. 2016; 30:1759–1763.

Milosevic Feenstra JD, et al. Whole-exome sequencing identifies novel MPL and JAK2 mutations in triple-negative myeloproliferative neoplasms. *Blood*. 2016;127(3):325-32.

Klampfl T, et al. Somatic mutations of calreticulin in myeloproliferative neoplasms. *N Engl J Med*. 2013; 369(25):2379-90.

Harutyunyan A, et al. p53 lesions in leukemic transformation. *N Engl J Med*. 2011;364(5):488-90.

Olcaydu D, et al. A common JAK2 haplotype confers susceptibility to myeloproliferative neoplasms. *Nat Genet*. 2009;41(4):450-454.

Kralovics R, et al. A gain-of-function mutation of JAK2 in myeloproliferative disorders. *N Engl J Med*. 2005;352(17):1779-90.

Stefan Kubicek

Chemical Biology and Epigenetics

Stefan Kubicek, born in 1978, is Austrian and joined CeMM in August, 2010. He obtained an MSc in synthetic organic chemistry from the Vienna University of Technology after writing a diploma thesis at ETH Zurich. For his PhD in Thomas Jenuwein's lab at the IMP in Vienna, he changed fields to molecular biology. He then performed post-doctoral research working on chemical biology with Stuart Schreiber at the Broad Institute of Harvard and MIT. Stefan Kubicek heads the chemical screening platform and PLACEBO (Platform Austria for Chemical Biology), a task he is well equipped for based on previous screening experience with Boehringer Ingelheim and at the Broad Institute. These activities have resulted in the identification of the first selective histone methyl transferase inhibitors and small molecule inducers of insulin expression. Since 2013, Stefan Kubicek has also been head of the Christian Doppler Laboratory for Chemical Epigenetics and Antiinfectives, a public-private partnership between CeMM, Boehringer Ingelheim and Haplogen. The Kubicek lab is working on the role of chromatin in the definition of cell types and cell states, particularly chromatin-modifying enzymes as synthetic lethal targets in cancer and chemical transdifferentiation to insulin-producing beta cells. In an ERC-funded project, the laboratory is testing the hypothesis that small molecule metabolites shape chromatin structure and thus control gene expression and cell identity .

Main Research Interests

+ Chemical epigenetics and metabolism of the cell nucleus
+ Small molecule probes for chromatin modifiers and host factors in infectious diseases
+ Chromatin in cancer development and progression
+ Role of chromatin in the specification of pancreatic cell types

Relevant/Important Publications

Licciardello MP, et al. A combinatorial screen of the CLOUD uncovers a synergy targeting the androgen receptor. *Nat Chem Biol*. 2017; 13(7):771-778.

Li J, et al. Artemisinins Target GABAA Receptor Signaling and Impair α Cell Identity. *Cell*. 2017;168(1-2):86-100.

Sdelci S, et al. Mapping the chemical chromatin reactivation landscape identifies BRD4-TAF1 crosstalk. *Nat Chem Biol*. 2016; 12(7):504-10.

Li J, et al. Single-cell transcriptomes reveal characteristic features of human pancreatic islet cell types. *EMBO Rep*. 2016;17(2):178-87.

Licciardello MP, et al. NOTCH1 activation in breast cancer confers sensitivity to inhibition of SUMOylation. *Oncogene*. 2015; 34(29):3780-90.

Joanna I. Loizou

DNA Repair and Genomic Stability

Joanna Loizou joined CeMM in 2011. She completed her undergraduate studies in the UK, moving there from Cyprus. Subsequently, she commenced PhD work at the University of Manchester UK, investigating mechanisms of DNA repair. Postdoctoral work followed at the International Agency for Research on Cancer (IARC), WHO, France where Joanna investigated the regulation and importance of epigenetic modifications in DNA repair. During this time, she chose to work on the immune system and demonstrated that histone acetylation is important in maintaining hematopoietic stem cells. Building on this experience she focused on the role of genomic instability in cancers of the blood and at the London Research Institute (LRI), Cancer Research UK (CR-UK), she investigated DNA repair in the development of the immune system and in suppressing lymphoma. At CeMM, Joanna's group investigates the mechanisms by which cells respond to – and repair – DNA damage to maintain genomic stability and suppress tumorigenesis and other rare hereditary diseases.

Main Research Interests

+ Consequences of DNA damage and repair on genomic mutation signatures
+ Synthetic lethal and viable interactions
+ Repair of CRISPR-Cas9 generated DNA breaks

Relevant/Important Publications

Velimezi G*, Robinson-Garcia L*, et al. Map of synthetic rescue interactions for the Fanconi anemia DNA repair pathway identifies USP48. *Nat Commun*. 2018 Jun 11;9(1):2280.

Zou X, Owusu M, et al. Validating the concept of mutational signatures with isogenic cell models. *Nat Commun*. 2018 May 1; 9(1):1744.

Mazouzi A, et al. Repair of UV-Induced DNA Damage Independent of Nucleotide Excision Repair Is Masked by MUTYH. *Mol Cell*. 2017; 68(4):797-807.e7.

Moder M*, Velimezi G*, et al. Parallel genome-wide screens identify synthetic viable interactions between the BLM helicase complex and Fanconi anemia. *Nat Comm*. 2017;8(1):1238.

Mazouzi A, et al. A Comprehensive Analysis of the Dynamic Response to Aphidicolin-Mediated Replication Stress Uncovers Targets for ATM and ATMIN. *Cell Rep*. 2016; pii:S2211-1247(16)30366-7.

Prochazkova J, et al. DNA Repair Cofactors ATMIN and NBS1 are Required to Suppress T Cell Activation. *PLoS Genetics*. 2015; 11(11):e1005645.

Jörg Menche

Network Medicine

Jörg Menche studied physics in Leipzig, Recife and Berlin. During his PhD with Reinhard Lipowsky at the Max Planck Institute of Colloids and Interfaces in Potsdam he specialized in network theory. He then moved to Boston to work as a postdoctoral fellow with Albert-László Barabási at Northeastern University and at the Center for Cancer Systems Biology at Dana Farber Cancer Institute. In close collaboration with Joseph Loscalzo from Harvard Medical School and Marc Vidal from Dana Farber Cancer Institute, he applied tools and concepts from network theory to elucidate the complex machinery of interacting molecules that constitutes the basis of (patho-)physiological states. Jörg joined CeMM as Principal Investigator in 2015. He applies diverse computational approaches to help understand and interpret the large datasets derived from the broad range of powerful post-genomic technologies that CeMM researchers employ, from next-generation sequencing of genomes, epigenomes and transcriptomes, to high-throughput proteomics and chemical screening. Two major areas of interest of his group are network-based approaches to rare diseases and understanding the basic principles of drug-drug interactions. His research group is supported by a Vienna Research Groups for Young Investigators career integration grant by the Vienna Science and Technology Fund (WWTF).

Main Research Interests

+ Network-based approaches to rare diseases
+ Basic principles of drug-drug interactions
+ Virtual reality approaches for visualizing and exploring large datasets

Relevant/Important Publications

Caldera M*, Buphamalai P*, et al. Interactome-based approaches to human disease. *Curr Opin Syst Biol*. 2017;3:88.

Menche J*, Guney E*, et al. Integrating personalized gene expression profiles into predictive disease-associated gene pools. *NPJ Syst Biol Appl*. 2017;3:10.

Guney E, et al. Network-based in silico drug efficacy screening. *Nat Comm*. 2016;7:10331.

Menche J, et al. Uncovering disease-disease relationships through the incomplete interactome. *Science*. 2015;347(6224):1257601.

Zhou XZ*, Menche J *, Barabási AL, Sharma A. Human symptoms disease network. *Nat Comm*. 2014;5:4212.

Adjunct Principal Investigators

Giulio Superti-Furga

Drug Transporters

Giulio Superti-Furga, Commander of the Order of Merit of the Italian Republic, is an Italian molecular and systems biologist, Scientific Director of CeMM, Professor for Systems Pharmacology at the Medical University of Vienna and member of the Scientific Council of the European Research Council (ERC). He completed his studies at the University of Zurich, Genentech and IMP/Vienna. He was a post-doctoral fellow and team leader at EMBL. He co-founded the biotech companies Cellzome, Haplogen and Allcyte. Since 2005, he has been Director of CeMM. His major scientific achievements to date include the elucidation of basic regulatory mechanisms of tyrosine kinases in human cancers, the discovery of fundamental organization principles of the proteome and metabolome of higher organisms and the development of integrated approaches to understand the mechanism of drug action at the molecular level. For the past five years, he has focused on unlocking the human "transportome" for medicine and drug discovery, trying to de-orphanize members of the solute carrier family (SLCs) and mapping their role in cell biology and drug transport. He is the academic coordinator of the Innovative Medicines Initiative consortium "RESOLUTE" focusing on SLCs. He is a member of EMBO, the Austrian Academy of Sciences, the German Academy of Sciences Leopoldina, the European Academy of Cancer Sciences, and Academia Europaea.

Main Research Interests

+ Systems biology of membrane transporters
+ Mechanism of action of drugs
+ Molecular networks affecting leukemia
+ Metabolism

Relevant/Important Publications

Bigenzahn JW, et al. LZTR1 is a regulator of RAS ubiquitination and signaling. *Science*. 2018 Dec 7;362(6419):1171-1177.

Vladimer GI, Snijder B, et al. Global survey of the immunomodulatory potential of common drugs. *Nat Chem Biol*. 2017;13(6):681-690.

César-Razquin A, et al. A Call for Systematic Research on Solute Carriers. *Cell*. 2015 Jul 30;162(3):478-87.

Rebsamen M, et al. SLC38A9 is a component of the lysosomal amino-acid-sensing machinery that controls mTORC1. *Nature*. 2015;519(7544):477-81.

Köberlin MS, et al. A conserved circular network of coregulated lipids modulates innate immune responses. *Cell*. 2015; 162(1):170-83.

Georg Winter

Chemical Biology of Oncogenic Gene Regulation

Georg Winter obtained his PhD from the Medical University of Vienna, working on elucidating the mechanism of action of anti-neoplastic drugs under the supervision of Prof. Giulio Superti-Furga at CeMM. He specialized in proteomics as well as chemical genetic approaches to identifying drug resistance mechanisms and on mechanistically elucidating synergistic drug combinations. He continued his training in chemical biology, working as a postdoctoral fellow with Dr. James Bradner at the Dana Farber Cancer Institute/ Harvard Medical School. There, he innovated a generalizable pharmacological solution to in vivo target protein degradation and applied this strategy to the study of leukemic gene regulation. Georg Winter was recruited as a CeMM Principal Investigator in June 2016. His lab develops and applies methods for target protein degradation with the ultimate goal of understanding and disrupting oncogenic transcriptional circuits. To that end, the Winter laboratory combines pheno-typic drug screens, chemical genetics and drug-target identification approaches with holistic measurements of global gene activity and genome structure. The ultimate goal of the research conducted in the Winter laboratory is to connect basic research in gene regulation and the ubiquitin-proteasome system with functional genomics and chemical probe development to develop novel and personalized therapeutic paradigms.

Main Research Interests

+ Chemical biology and chemical genetics
+ Targeted protein degradation
+ Oncogenic gene regulation and genome organization
+ Pharmacologic disruption of transcription

Relevant/Important Publications

Winter GE, et al. BET bromodomain proteins function as master transcription elongation factors independent of CDK9 recruitment. *Mol Cell*. 2017;67(1):5-18.e19.

Erb MA, et al. Transcriptional control by the ENL YEATS domain in acute leukemia. *Nature*. 2017;543(7644):270-274.

Winter GE, et al. Phthalimide Conjugation as a Strategy for in vivo Target Protein Degradation. *Science*. 2015;348(6241):1376-81.

Winter GE, et al. The solute carrier SLC35F2 enables YM155-mediated DNA damage toxicity. *Nat Chem Biol*. 2014; 10(9):768-73.

Winter GE, et al. Systems-pharmacology dissection of a drug synergy in imatinib-resistant CML. *Nat Chem Biol*. 2012; 8(11):905-912.

Kate Ackerman

Developmental Origins of Health and Disease in the Pulmonary System

Kate Ackerman was a recent Guest Principal Investigator at CeMM. She is currently an Associate Professor of Pediatrics (Critical Care) and Biomedical Genetics with leadership roles in research, strategy and innovation. While at CeMM, she worked with the laboratories of Christoph Bock and Sylvia Knapp on projects aimed at identifying potential epigenetic mechanisms of long-term disease resulting from critical events during the perinatal period of life. In the USA, one of Kate's leadership roles includes organization of the largest international Pediatric Research meeting (PAS, Pediatric Academic Societies). In addition to the PAS meeting, Kate holds many other advisory and leadership roles including the Board of Scientific Counselors for the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the advisory board for the Mouse Genome Database (MGD) at The Jackson Laboratories, the Strategic and Operations Officer/Sec-Treasurer for the Society for Pediatric Research (SPR) and the Board of the Federation of Pediatric Organizations (FOPO). Kate's research has previously focused on genetic and developmental mechanisms of birth defects that cause critical illness in children. She completed her undergraduate degree at Cornell University, her medical degree at the University at Buffalo, pediatrics residency in Denver, Colorado, clinical fellowship (Critical Care) at Boston Children's Hospital, and research fellowships at Brigham and Women's Hospital/ Harvard Medical School.

Main Research Interests

+ Gene identification and disease mechanisms for diseases of the lung, heart and diaphragm
+ Developmental origins of health and disease in the pulmonary system
+ Genetic and epigenetic mechanisms of co-morbidities in children and adults with isolated birth defects

Relevant/Important Publications

Kardon G, et al. Congenital diaphragmatic hernias: from genes to mechanisms to therapies. *Dis Model Mech*. 2017;10(8):955-970.

Coles GL, et al. Kif7 Maintains Respiratory Airway Architecture by Regulating Microtubule Dynamics and Cellular Proliferation. *PloS Genetics*. 2015;11(10):e1005525.

Paris ND, et al. Wt1 and B-Catenin Cooperatively Regulate Diaphragm Development in the Mouse. *Developmental Biology*. 2015;407(1):40-56.

Kaan Boztug

Genetics of Malignant and Immune System Disorders

Kaan Boztug, born in 1977, joined CeMM as Principal Investigator in 2011. He studied Medicine at the Universities of Dusseldorf, Freiburg (DE) and London (UK), followed by his graduate training with Iain L. Campbell at the Scripps Research Institute, La Jolla, USA and postgraduate research and clinical training with Christoph Klein at Hannover Medical School, DE. His laboratory combines next-generation sequencing and molecular biological techniques with system biology approaches to understand the genetics and molecular pathomechanisms of rare disorders of hematopoiesis and immunity. Kaan Boztug is director of the CeRUD Vienna Center for Rare and Undiagnosed Diseases and Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD). He holds a dual appointment as Associate Professor of Pediatrics and Adolescent Medicine at MedUni Vienna and as a consultant in Pediatric Hematology and Oncology and is Head of Immunology at St. Anna Children's Hospital. In 2012, he received a Starting Grant of the European Research Council (ERC). In 2018, Kaan Boztug received an ERC Consolidator Grant and was awarded the Clemens von Pirquet Prize of the Austrian Society of Pediatrics. In 2019, Kaan is scheduled to take on the position of Scientific Director of the Vienna Children's Cancer Research Institute.

Main Research Interests

+ Genetics and molecular pathomechanisms of rare inherited disorders of hematopoiesis and immunity
+ Systems biology and network medicine diagnostics and targeted treatment of rare and undiagnosed diseases
+ Molecular dissection of shared mechanisms underlying immune dysregulation and pediatric cancer

Relevant/Important Publications

van Rijn JM*, Ardy RC*, Kuloğlu Z*, Härter B*, van Haaften-Visser DY*, et al. Intestinal failure and aberrant lipid metabolism in patients with DGAT1 deficiency. *Gastroenterology*. 2018;155(1):130-143.e15 .

Ozen A*, Comrie WA*, Ardy RC*, et al. CD55 deficiency, early-onset protein-losing enteropathy, and thrombosis. *N Engl J Med*. 2017;377(1):52-61.

Salzer E, et al. RASGRP1 deficiency causes immunodeficiency with impaired cytoskeletal dynamics. *Nat Immunol*. 2016; 17(12):1352-1360.

Dobbs K*, Dominguez Conde C*, Zhan S-Y*, Parolini S*, et al. Inherited DOCK2 Deficiency in Patients with Early-Onset Invasive Infections. *N Engl J Med*. 2015;372(25):2409-2422.

Boztug K, et al. JAGN1 deficiency causes aberrant myeloid cell homeostasis and congenital neutropenia. *Nat Genet*. 2014; 46(9):1021-7.

Thijn Brummelkamp

Cancer Research, Infectious Diseases and Drug Action

Thijn Brummelkamp uses genetics in human cells to pinpoint genes that play a role in human disease. His interests are cancer research, infectious disease and drug action. During his PhD studies he developed a system for the expression of shRNA molecules, enabling gene inhibition through "stable RNA interference". More recently he has developed an approach for haploid genetic screens in human cells using insertional mutagenesis. He has used this approach to identify host factors used by a variety of pathogens, which led to the identification of the lysosomal cholesterol transporter NPC1 as the long-sought intracellular receptor for Ebola virus. He received his MS in biology from the Free University, Amsterdam in 1998 and did his graduate research at the Netherlands Cancer Institute in the laboratory of Prof. Rene Bernards. In 2004, he was appointed as a Whitehead Fellow to initiate his independent research program in Cambridge, USA, and in 2011, his laboratory moved to the Netherlands Cancer Institute and he became an Adjunct Principal Investigator at CeMM. For his studies, he received the Antoni van Leeuwenhoek Award (2003), the Annual NVBMB Award (2004, Dutch Association for Biochemistry and Molecular Biology), he was chosen as one of the world's top 35 Young Innovators by MIT's Technology Review magazine (2005) and received EMBO's gold medal in 2013.

Main Research Interests

+ Cancer research
+ Infectious diseases
+ Drug action

Relevant/Important Publications

Nieuwenhuis J, et al. Vasohibins encode tubulin detyrosinating activity. *Science*. 2017;pii:eaao5676.

Brockmann M, et al. Genetic wiring maps of single-cell protein states reveal an off-switch for GPCR signalling. *Nature*. 2017; 546:307-311.

Staring J, et al. PLA2G16, a Switch between Entry and Clearance of Picornaviridae. *Nature*. 2017;541:412-416.

Blomen V, et al. Gene essentiality and synthetic lethality in haploid human cells. *Science*. 2015;350(6264):1092-1096.

Carette JE, et al. Ebola virus entry requires the cholesterol transporter Niemann-Pick C1. *Nature*. 2011;477(7364):340-343.

Nuno Maulide

Precision Design Enabled by Organic Synthesis

Nuno Maulide is a trained chemist. He underwent doctoral studies in the Université catholique de Louvain and, in 2007, obtained his PhD under the supervision of Prof. Istvan Markó, working on the application of functionalized orthoesters in organic synthesis. He then moved to Stanford University for a postdoctoral stay in the group of Prof. Barry Trost. Nuno started his independent career in 2009, when he was appointed group leader at the Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr. In 2013, at age 33, he was appointed a Full Professor of Organic Synthesis at the University of Vienna, which is the position he continues to hold today. He is the holder of an ERC Consolidator Grant (2017–2021) and an ERC Proof of Concept Grant (awarded 2018), after having held an ERC Starting Grant (2011–2016). Nuno will also lead a Christian Doppler Laboratory starting in 2019 and was named "Austria's Scientist of the Year 2018". Nuno Maulide joined CeMM as Adjunct PI in November 2018.

Main research interests

+ Development of new synthetic methodology
+ Total synthesis of natural products
+ "Precision modification" of C-H bonds, with the vision of systematically exploiting such modifications in particular contexts
+ Interrogating possible benefits using in silico techniques prior to actual synthesis

Relevant/Important Publications

Kaldre D, et al. Stereodivergent synthesis of 1.4-dicarbonyls by traceless charge-accelerated sulfonium rearrangement. *Science* 2018, 361, 664–667.

Adler P, et al. α-Fluorination of carbonyls with nucleophilic fluorine. *Nature Chemistry* 2019, just accepted (DOI: 10.1038/ s41557-019-0215-z).

Li J, et al. Enantioselective Redox-Neutral Coupling of Aldehydes and Alkenes by an Iron-Catalyzed "Catch-Release" Tethering Approach. *Journal of the American Chemical Society* 2019, 141, 143–147.

Daniel H. O' Donovan, et al. C-H Activation Enables a Concise Total Synthesis of Quinine and Analogues with Enhanced Antimalarial Activity. *Angewandte Chemie International Edition* 2018, 57, 10737-10741. *Angewandte Chemie* 2018, 130, 10897-10901.

De la Torre A, et al. Flexible and Chemoselective Oxidation of Amides to α-Keto Amides and α-Hydroxy Amides. *Journal of the American Chemical Society* 2017, 139, 6578–6581.

Vanja Nagy

Development, Function and Pathology of the Nervous System

Vanja Nagy joined the LBI-RUD as Key Researcher and CeMM as Adjunct PI in 2016. She obtained her PhD at the Icahn School of Medicine at Mount Sinai, USA and received postdoctoral training in the groups of Ivan Dikic and Josef Penninger. In the USA, she studied basic molecular neuroscience and described a novel role for extracellular proteolysis supporting structural and functional synaptic remodeling underlining learning and memory. In Austria, she focused on preclinical phenotyping of mouse models of genetic disorders affecting basic functions of the nervous system. At LBI-RUD, her group concentrates on identifying and characterizing causative genes that underlie rare neurodevelopmental disorders, with a focus on intellectual disability. To gain insight into disease pathophysiology, her group applies a multidisciplinary approach: from behavioral phenotyping of genetic mouse models to detailed molecular and cellular characterization of both mouse and human neurons. Her studies will uncover common therapeutic targets, predict genes deleterious to neuronal function, and shed light on the basic biology of the neuron.

Main Research Interests

+ Preclinical phenotyping of rare neuropathologies
+ Cellular and molecular basis of rare neurodevelopmental diseases
+ Basic molecular mechanisms underlining synaptic plasticity

Relevant/Important Publications

Nagy V, et al. HACE1 deficiency leads to structural and functional neurodevelopmental defects. Accepted *Neurol Genet*.

Desiderio S*, Vermeiren S*, et al. Prdm12 directs nociceptive sensory neuron development by regulating the expression of the NGF receptor TrkA. Accepted to *Cell Reports*.

Nagy V*, et al. The evolutionarily conserved transcription factor PRDM12 controls sensory neuron development and pain perception. *Cell Cycle*. 2015;14(12):1799-1808.

Ikeda F, et al. SHARPIN forms a linear ubiquitin ligase complex regulating NF-κB activity and apoptosis. *Nature*. 2011;471(7340):637-641.

Nagy V, et al. The extracellular protease matrix metalloproteinase-9 is activated by inhibitory avoidance learning and required for long-term memory. *Learn Mem*. 2007;14(10):655-664.

Nagy V*, et al. Matrix Metalloproteinase-9 Is Required for Hippocampal Late-Phase Long-Term Potentiation and Memory. *J Neurosci*. 2006;26(7):1923-1934.

Thomas Reiberger

Rare Liver Diseases and Hepatic Microcirculation

Thomas Reiberger, born in 1982, joined the LBI-RUD and CeMM in November 2018 as an Adjunct PI. After obtaining his MD at the Medical University of Vienna, he did a first postdoc at the Department of Pathophysiology at the Medical University of Vienna focusing on ex-situ liver perfusion and liver cell biology. During his residency for Internal Medicine at the Divison of Gastroenterology and Hepatology at the Medical University of Vienna, Thomas pursued a career as a physician-scientist by performing translational clinical studies on portal hypertension and fibrosis in patients with viral hepatitis. In addition to his clinical activity, he established the Vienna Hepatic Experimental (HEPEX) Laboratory at the Medical University of Vienna. In 2011, he received his venia docendi and in 2012 he obtained his board certification for Internal Medicine. After another post-doctoral fellowship in the United States from 2012 to 2015, Thomas Reiberger was appointed Associate Professor of Gastroenterology and Hepatology at the Medical University of Vienna. Thomas conducted seminal studies for optimizing the role of non-selective betablocker therapy in patients with cirrhosis and portal hypertension. The main mission of his HEPEX research team is the exploration of novel treatment options for liver fibrosis and portal hypertension, such as anti-angiogenic drugs, FXR agonists and modulators of the soluble guanylyl cyclase. Thomas Reiberger is also the director of the Cirrhosis Outpatient Clinic and the Vienna Hepatic Hemodynamic Laboratory at the Medical University of Vienna.

Main Research Interests

+ Liver fibrogenesis and inflammation
+ Portal hypertension
+ Rare liver diseases
+ Gut-liver axis

Relevant/Important Publications

Reiberger T, et al. Beta adrenergic blockade and decompensated cirrhosis. *J Hepatol.* 2017 Apr;66(4):849-859.

Reiberger T, et al. An orthotopic mouse model of hepatocellular carcinoma with underlying liver cirrhosis. *Nature Protocols* 2015; 10(8):1264-74.

Reiberger T, et al. Carvedilol for primary prophylaxis of variceal bleeding in cirrhotic patients with haemodynamic non-response to propranolol. *Gut.* 2013 Nov;62(11):1634-41.

Reiberger T, et al. Non-selective betablocker therapy decreases intestinal permeability and serum levels of LBP and IL-6 in patients with cirrhosis. *J Hepatol.* 2013 May;58(5):911-21.

Reiberger T, et al. Sorafenib attenuates the portal hypertensive syndrome in partial portal vein-ligated rats. *J Hepatol.* 2009 Nov; 51(5):865-73.

Georg Stary

Translational Immunology of the Skin and Mucous Membranes

Georg Stary is a fully trained dermatovenereologist with direct contact to patients and ample experience in research with human tissue and mouse models. After a 4-year fellowship in the Von Andrian Laboratory at Harvard Medical School, he became a senior physician and Principal Investigator in the Department of Dermatology of the Medical University of Vienna in 2014. He was appointed Assistant Professor in 2015 and Associate Professor in 2016. Since November 2018, he has been an Adjunct Principal Investigator at LBI-RUD and CeMM. His research projects focus on different aspects of host-pathogen interactions and the contribution of tissue-resident leukocytes to physiological and pathological immune responses. His research projects are in the areas of biology, longevity, turn-over and function of tissue-resident leukocytes in peripheral tissue with the skin being an optimal and accessible organ on which to perform meaningful human experiments. He is a member of the Immuno-Board for Rare and Undiagnosed Diseases organized by LBI-RUD and CeRUD Director Kaan Boztug.

Main Research Interests

+ Host-pathogen interactions
+ Tissue-resident leukocytes in peripheral tissue

Relevant/Important Publications

Stary G, et al. A mucosal vaccine against Chlamydia trachomatis generates two waves of protective memory T cells. *Science.* 015;348(6241):aaa8205.

Brüggen MC, et al. Epidermal elafin expression is an indicator of poor prognosis in cutaneous graft-versus-host disease. *J Invest Dermatol.* 2015; 135:999-1006.

Brüggen MC, et al. Diverse T-cell responses characterize the different manifestations of cutaneous graft-versus-host disease. *Blood.* 2013;123:290-299.

Stary G, et al. Plasmacytoid dendritic cells express TRAIL and induce CD4+ T-cell apoptosis in HIV-1 viremic patients. *Blood.* 2009;114:3854-3863.

Stary G, et al. Tumoricidal activity of TLR7/8- activated inflammatory dendritic cells. *Blood.* 2009;114:3854-3863.

Miriam Unterlass

Materials Chemistry, Dyes for Life Sciences

Miriam M. Unterlass studied chemistry, materials science and chemical engineering in Würzburg, Southampton and Lyon. Between 2009 and 2011 she worked on her PhD thesis at the Max Planck Institute of Colloids and Interfaces, Potsdam-Golm, supervised by Markus Antonietti. Miriam then worked as a postdoc with Ludwik Leibler at the ESPCI in Paris. In December 2012, she established her research group "Advanced Organic Materials" at the Institute of Materials Chemistry of the Vienna University of Technology (TU Wien). In September 2018, Miriam obtained her habilitation (venia docendi) in "materials chemistry". She joined CeMM as an Adjunct Principal Investigator in 2018. The research interests of Miriam Unterlass are centered on compounds that are rich in aromatic and heterocyclic moieties. The materials the Unterlass Lab investigates are low-molecular weight dyes, high-performance polymers, covalent organic frameworks (COFs), and inorganic-organic hybrids. A major focus lies on the development of novel, environmentally-friendly, non-toxic and highly efficient synthetic techniques especially via hydrothermal synthesis and solid-state reactions. Miriam is committed to seeing her research implemented: in 2017, she co-founded her first company, UGP materials, where she holds the position of CSO.

Main Research Interests

+ Non-classical synthesis of advanced organic compounds
+ Heterocycles, dyes and pigments, fluorescent compounds
+ Crystalline organic materials, crystal engineering, crystal morphology

Relevant/Important Publications

Taublaender MJ, et al. Green and Rapid Hydrothermal Crystallization and Synthesis of Fully Conjugated Aromatic Compounds, *Angew. Chem. Int. Ed.* 2018, doi:10.1002/anie.201801277

Unterlass MM. Hot water generates crystalline organic materials, *Angewandte Chemie International Edition*, 2018, 57(9), 2292–2294

Baumgartner B, et al. Geomimetics for Green Polymer Synthesis: Highly Ordered Polyimides via Hydrothermal Techniques, *Polymer Chemistry* 2014, 5, 3771–3776

Baumgartner B, et al. Green and highly efficient synthesis of perylene and naphthalene bisimides is nothing but water, *Chemical Communications* 2017, 53, 1229–1232

Leimhofer L, et al. Green one-pot synthesis and processing of polyimidesilica hybrid materials, *Journal of Materials Chemistry* A 2017, 5, 16326-16335

Andreas Villunger

Cell Death Signaling in Health and Disease

Andreas Villunger, born in 1967, is a full professor at the Medical University in Innsbruck, Austria, where he heads the Division of Developmental Immunology at the MUI Biocenter. He joined CeMM in November 2018 as an Adjunct PI. He studied biology at the Universities of Salzburg and Innsbruck, completed his PhD and early post-doctoral studies in Innsbruck, before moving to the Walter and Eliza Hall Institute in Melbourne, Australia. There, he investigated the role of BCL2 family proteins in immune cell development and immune tolerance together with his mentor Prof. Andreas Strasser. Back in Innsbruck, he established his own research group supported by the FWF START Prize in 2003. In the more recent past, his team has begun to explore the crosstalk between the cell cycle and cell death machineries, focusing on mitotic cell death and post-mitotic cell fate.

Main Research Interests

+ BCL2 family proteins in tissue homeostasis
+ DNA damage & checkpoint signaling
+ Cell cycle – cell death crosstalk
+ Polyploidization in health and disease

Relevant/Important Publications

Haschka M, et al. Perturbing mitosis for anti-cancer therapy: is cell death the only answer? EMBO Rep. 2018 Mar;19(3). pii: e45440.

Schuler F, et al. Checkpoint kinase 1 is essential for normal B cell development and lymphomagenesis. *Nat Commun.* 2017 Nov 22;8(1):1697.

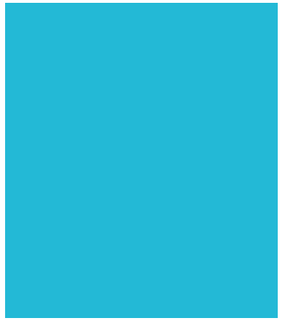
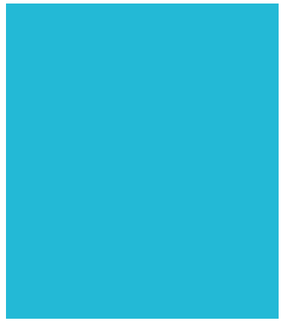
Sladky V, et al. The resurrection of the PIDDosome - emerging roles in the DNA damage response and centrosome surveillance. *J Cell Sci.* 2017 Nov 15;130(22):3779-3787.

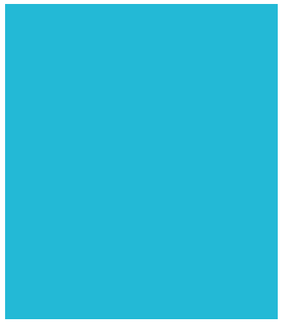
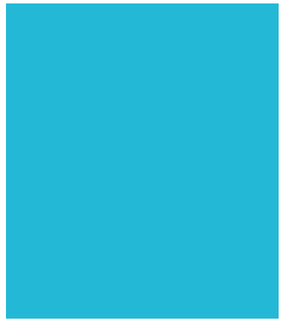
Fava LL, et al.The PIDDosome activates p53 in response to supernumerary centrosomes. *Genes Dev.* 2017 Jan 1;31(1):34-45.

Haschka MD, et al. The NOXA-MCL1-BIM axis defines lifespan on extended mitotic arrest. *Nat Commun.* 2015 Apr 29;6:6891.

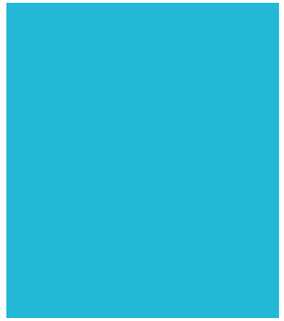
Labi V, et al. Deregulated cell death and lymphocyte homeostasis cause premature lethality in mice lacking the BH3-only proteins Bim and Bmf. *Blood.* 2014 Apr 24;123(17):2652-62.










from top left to bottom right
Andreas Bergthaler,
Miriam Unterlass, Georg Winter,
Giulio Superti-Furga, Sylvia Knapp,
Christoph Binder, Kate Ackerman,
Thijn Brummelkamp,
Christoph Bock, Stefan Kubicek,
Georg Stary, Robert Kralovics,
Jörg Menche, Thomas Reiberger,
Kaan Boztug, Nuno Maulide,
Andreas Villunger, Joanna Loizou,
Vanja Nagy

Life at CeMM

"The CeMM Scientific Director and I were PhD students together at the IMP in the late eighties. Science was a blast in those days and we created a culture of serious work and fun that has continued at the IMP over the decades and permeated the new institutions that grew around it. Among these 'IMP buds', CeMM is special. CeMM is the center of translational medicine in Vienna. 'Bench to bedside' is realized there every day, impacting diagnosis and treatment. Keep up the good work and stay special!"

Prof. Dr. Angelika Amon
Kathleen and Curtis Marble Professor of Cancer Research,
Howard Hughes Medical Institute, Massachusetts, United States
2019 Breakthrough Prize in Life Sciences Awardee

"Never before in history has the importance of research for humanity been more evident. I am personally and particularly passionate for research in the medical and life-science field, a key for a better future and a longer, healthier life for as many people as possible. Since I have been chairing the University Council of the Medical University of Vienna, I have been a great fan and supporter of CeMM as one of the key MedUni partners in research and innovation. I wish all researchers at CeMM a steady stream of victories against our ignorance about disease mechanisms."

Dr. Eva Dichand
Chair of the University Council of MedUni Vienna
Publisher of the daily newspaper "Heute"
CEO of the healthcare portal netdoktor.at.

"Science is not just for the sake of science. Science has to have an impact and should be for the benefit of society. It must lead to the gaining of knowledge in order to address societal questions and needs. It must give rise to innovations that are taken up by society and the economy. Science shall provide an inspiring environment that supports the education and training of young and talented people and prepares them for their future career path. I highly recognize that CeMM is holding up exactly such a spirit. I welcome the vision of CeMM to bridge the gap between healthcare and the research lab, from bench to bedside and vice versa. Under its renowned and inspiring leadership and with its talented and open-minded staff, CeMM resembles a vibrant incubator of translation and innovation on the forefront of molecular medicine. In particular, passing on such a holistic research approach to CeMM's PhDs and postdocs, who will belong to tomorrow's generation of medical scientists, is a value not to underestimate."

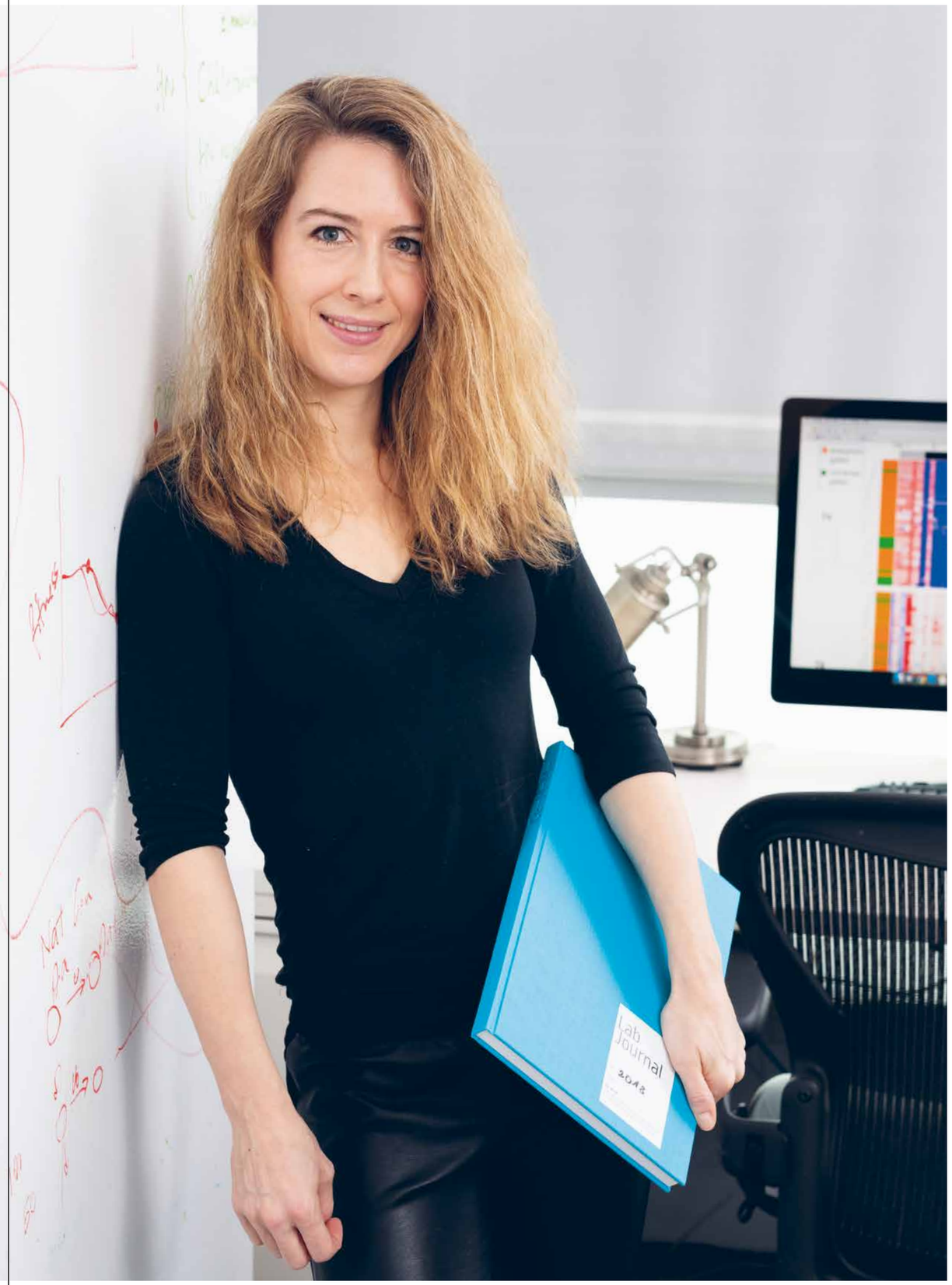
Prof. Dr. Heinz Faßmann
Federal Minister of Education, Science and Research

"Both EMBO and CeMM attach great importance to excellence and international interactions. EMBO provides support for great science, but the researchers at institutions such as CeMM are the ones who actually do the great science. CeMM provides a cheerful hub in the middle of Vienna and the middle of Europe for a community of impressively dedicated and creative scientists. So much life, energy and ideas: all the ingredients coming together for cutting-edge research to contribute to the advancement of knowledge and innovation at the interface between molecular sciences and medicine."

Professor Maria Leptin, PhD
EMBO Director, Heidelberg, Germany

"I have been a regular visitor and collaborator of CeMM throughout its existence, from discussions on cancer evolution with its new faculty when CeMM was just setting up space in Mariannengasse, through a legendary systems medicine workshop in Portofino in 2007 that CeMM coorganized, to today. Each year, I have productive scientific exchanges during seminars at CeMM. From my East Coast perspective, it is wonderful to be able to use such a modern place as CeMM as my Austrian academic HQ. In my heart, I am a CeMMie!"

Professor Franziska Michor, PhD
Dana-Farber Cancer Institute and Harvard University,
Boston and Cambridge, United States



Lectures, Symposia and Workshops

To network with scientists of different disciplines and to communicate with the public, CeMM has established several lecture series. In 2018, 38 lectures, symposia, seminars and scientific meetings took place at CeMM.

8th S.M.A.R.T Lecture – Livable Cities for the 21st Century

The 8th CeMM S.M.A.R.T. Lecture, held by Jan Gehl, architect and world-renowned expert in all things related to urban design and public spaces, took place on March 19, 2018. In his talk, Jan Gehl illustrated how city planning in the 20th century focused on objects and thoroughfares rather than on the well-being of people: Because of the emphasis on "mobility", meaning the use of automobiles, a lack of physical exercise, the so-called "sitting syndrome", has become a major health threat. To counteract those developments, Jan Gehl pioneered observation-based city planning by systematically documenting urban spaces, making gradual incremental improvements, then documenting them again. Measures like banning cars from city centers, creating extensive and coherent biking lanes and designing nice and "sticky" places, turned Copenhagen from a car-dominated city into one of the most "livable" places in the world. Some 150 people with all kinds of backgrounds attended this S.M.A.R.T. Lecture eagerly and engaged in lively discussions. His take-home message will remain firmly etched into their memories: The world is not about getting from A to B, the world is about having nice places to be!

9th S.M.A.R.T Lecture – Population Trends and the Global Sustainable Development Goals

On December 10, 2018, Wolfgang Lutz, Founding Director of the Wittgenstein Centre for Demography and Global Human Capital (IIASA, VID/ÖAW, WU) delivered the 9th CeMM S.M.A.R.T. Lecture: a plea for education. He proclaimed that essentially people are not very different all over the world. However, we face a universal development of "demographic modernization", with countries currently at different stages of the same process: In the first stage, falling death rates due to better sanitation and medical advance, together with a culturally determined high birth rate, result in high population growth. In a later stage, birth rates fall as well, leading to low or even negative population growth. Studies show that the most transformative social changes are associated with female literacy. The future of world population growth and adaptive capacity to environmental change will depend on female education. The "homo sapiens literata" (MPI-EVA, McElreath) – a subspecies of homo sapiens characterized by high abstraction, literacy, and modern science – will make the change. Education matters!

8th S.M.A.R.T Lecture
Urban design expert Jan Gehl explained how measures like banning cars from city centers, creating biking lanes and designing enjoyable places contribute to livable cities and the well-being of people.

9th S.M.A.R.T Lecture
Wolfgang Lutz talk was a plea for (female) education: empirical studies show that the most transformative social changes are associated with female literacy.

12th CeMM Landsteiner Lecture – Can Bacteria Defend our Body? Role of Microbiota in the Control of Immunity

At the 12th CeMM Landsteiner Lecture, on May 14, 2018, Yasmine Belkaid, Director of the NIH Center for Human Immunology and Director of the NIAID Microbiome Program, explained how microorganisms living in and on our bodies influence every aspect of our immune system, and why research in this field will change the medicine of the future.

The communities of bacteria, protists, fungi and viruses that reside throughout the human body affect many aspects of its physiology. However, the immune system is by far the most tightly interwoven part. Refuting the old paradigm of an immunity whose sole purpose is to defend the body against invading pathogens, Yasmine Belkaid showed how it constantly interacts with the commensal microbes and how those single-celled organisms control immune cells with mind-blowing precision. In the conclusion to her talk, Yasmine Belkaid stated that understanding the profound alliance between the microbiota and the immune system in detail will be a major step forward in combating a wide range of medical conditions, from infection to inflammation to cancer.

370 scientists from different fields and interested lay people attended the talk at the Baroque Ceremonial Hall of the Austrian Academy of Sciences and via video stream in an adjacent room. Music by Bela Koreny and Ethel Merhaut, who delightfully performed two Viennese songs, a cocktail reception and lively discussions rounded off the evening.

6th NGS Symposium and Workshop

On November 15, 2018, the 6th "Next Generation Sequencing Vienna Symposium & Workshop" brought together researchers from Vienna and beyond, to discuss the latest questions of next-generation sequencing technology. A symposium in the morning was dedicated to sequencing in biology and medicine and addressed both medical issues and evolutionary anthropology. In his keynote lecture, Robert P. Zinzen from the Max Delbrück Center Berlin highlighted the topic "Single-cell sequencing of whole organisms". In the afternoon, four parallel workshops provided an opportunity for further information and a hands-on discussion of NGS-related topics. The program ranged from a seminar for newcomers, "Getting started with next generation sequencing", to in-depth introductions to technology and application, "Single-cell sequencing technologies" and "Medical applications of NGS technology", to special workshop contributed by the Vienna Life Science Instruments consortium (www.vlsi.at), "Beyond NGS: flow and mass cytometry". The NGS Symposium and Workshop series was jointly organized by Christoph Bock, Coordinator of the Biomedical Sequencing Facility (BSF) of CeMM and the Medical University of Vienna, and Andreas Sommer, Coordinator of the NGS unit at the Vienna Biocenter Core Facilities (VBCF), the NGS Symposium and Workshop.

Landsteiner Lecture
Named in honor of Karl Landsteiner, the Viennese discoverer of blood groups, the CeMM Landsteiner Lecture has taken place annually since 2007. The speakers, carefully selected by the faculty at CeMM, are prominent scientists whose molecular research has had a significant impact on medicine. The lecture given at the festive hall of the Austrian Academy of Sciences aims to reach the wider scientific community as well as the public.

Scientific Meetings
A fine blend of top-class speakers holds numerous seminars, workshops, symposia and scientific meetings throughout the year, providing a broad range of opportunities for scientists to keep up to date on the latest developments in their fields of interest, expand their networks and strengthen collaboration.

Overview Seminars and Scientific Meetings in 2018

10 Jan 2018
Impromptu
Ivan Yudushkin
Group Leader, Department of Structural and Computational Biology, Max F Perutz Laboratories (MFPL), Vienna, Austria
"Biochemistry illustrated: Observing enzymes in their natural habitat"
Host: Kaan Boztug

15 Jan 2018
Impromptu
Tugce Aktas Ilik
Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany
"Taming the repetitive transcriptome with RNA binding proteins"
Host: Kaan Boztug

22 Jan 2018
Impromptu
Lisenka E L M Vissers
Principal Investigator Translational Genomics, Department of Human Genetics, Radboud UMC, Nijmegen, The Netherlands
"NGS in clinic: From research to diagnosis and back"
Host: Vanja Nagy

25 Jan 2018
Impromptu
Marco Prunotto
Senior Clinical Scientist, Roche/Genentech, Basel, Switzerland
"Drug discovery strategies to prevent renal function loss in Alport Syndrome"
Host: Kaan Boztug

26 Jan 2018
Impromptu
Andreas Mayer
Group Leader, Max Planck Institute for Molecular Genetics, Berlin, Germany
"Genome transcription at nucleotide resolution"
Host: Georg Winter

22 Feb 2018
Special Seminar
Christoph Huber
Professor Emeritus Department of Hematology-Oncology, University Medical Center of the Johannes Gutenberg University Mainz, Germany
"Exploiting the mutanome for tumor vaccination"
Host: Robert Kralovics

19 Mar 2018
Smart Lecture
Jan Gehl
Architect MAA, Professor (ret.), Royal Danish Academy of Fine Arts. Founder, Senior Advisor: Gehl Architects – Urban Quality Consultants
"Livable cities for the 21st century"
Host: Giulio Superti-Furga

4 Apr 2018
Impromptu
Marco Vignuzzi
Institut Pasteur, Paris, France
"Monitoring and altering RNA virus evolution"
Host: Andreas Bergthaler

9 Apr 2018
CeMMinar
Dan Kastner
Scientific Director of the Division of Intramural Research of the National Human Genome Research Institute Maryland, United States
"Horror autoinflammaticus: the expanding universe of systemic autoinflammatory diseases"
Host: Kaan Boztug

16 Apr 2018
CeMMinar
Patrick Stover
Professor and Director of the Division of Nutritional Sciences at Cornell University, United States
"Systems understanding of the one-carbon metabolism network in health and disease"
Host: Stefan Kubicek

14 May 2018
Landsteiner Lecture
Yasmine Belkaid
Director of the NIH Center for Human Immunology, Director NIAID Microbiome Program
"Can Bacteria Defend our Body? Role of Microbiota in the Control of Immunity."
Host: Giulio Superti-Furga

16 May 2018
EU-Life Special Seminar
Anna Sablina
Group Leader at VIB-KU Leuven Center for Cancer Biology, Campus Gasthuisberg of the University of Leuven, Belgium
"The ubiquitin system in RAS driven disease"
Host: Giulio Superti-Furga

15 Jun 2018
Impromptu
Marlies Meisel
University of Chicago
"Gut commensal microbiota shapes local and systemic immunity"
Reinhard Hinterleitner
University of Chicago
"Aftertaste of protective immunity to enteric microbes"
Host: Andreas Bergthaler

18 Jun 2018
Impromptu
Raz Somech
Director of the Department of Pediatrics, the Edmond and Lily Safra Children's Hospital Director of the Pediatric Immunology Unit, Jeffrey Modell Foundation Center
"Diagnosing, understanding and treating primary immunodeficiencies – from bed to bench and back"
Host: Kaan Boztug

20 Jun 2018
Impromptu
Raz Somech
Director of the Department of Pediatrics, the Edmond and Lily Safra Children's Hospital Director of the Pediatric Immunology Unit, Jeffrey Modell Foundation Center
"Diagnosing, understanding and treating primary immunodeficiencies – from bed to bench and back"
Host: Kaan Boztug

25-26 Jun 2018
Translational Proteomics Minisymposium & Workshops
Organizers:
André Müller (CeMM)
Viktoria Dorfer (FHOÖ)
Klaus Kratochwill (MUV)

28 Jun 2018
Impromptu
Katharina Jungnickel
University of Hamburg and Centre for Ultrafast Imaging in the group of Henning Tidow
"Structural and mechanistic surprises of proton-coupled amino acid transport in the SLC7/CAT family"
Host: Giulio Superti-Furga

4 Jul 2018
Impromptu
Sai Reddy
ETH Zurich, Department of Biosystems Science and Engineering, Basel, Switzerland
"Molecular decryption of antibody responses"
Host: Christoph Bock

10 Jul 2018
Impromptu
Mathias Woidy
Medical Doctor, Group of Søren W. Gerting, University Medical Center Hamburg-Eppendorf
"A BRET-based platform for protein interaction analysis in living cells and multi-layer networks"
Host: Jörg Menche

13 Aug 2018
Impromptu
Lauren Peters
Head of Disease Discovery, Sema4, Mount Sinai Health System Venture, Icahn School of Medicine at Mount Sinai, Department of Genetics and Genomic Sciences, United States
"Defining the missing link between rare early onset and common adult IBD genetic networks"
Host: Kaan Boztug

29-31 Aug 2018
Austrian Proteomics and Metabolomics Research Symposium 2018: Building Blocks of Life – from Metabolomics and Proteomics to Systems Biology
Organizers:
André Müller (CeMM)
Wolfram Weckwerth (University of Vienna)
Klaus Kratochwill (MUV)

10 Sep 2018
CeMMinar
Alexander Meissner
Director, Max Planck Institute for Molecular Genetics, Berlin, Germany "DNA Methylation in Development and Disease"
Host: Christoph Bock

10–11 Sep 2018
LBI-RUD Workshop on Human Phenotype Ontology for Immune-Mediated Disorders
Organizer: Kaan Boztug (CeMM, LBI-RUD)

17 Sep 2018
Impromptu
Martin Prlic
Fred Hutchinson Cancer Research Center, United States
"A single-cell analysis pipeline to define immune responses in human mucosal tissues"
Host: Andreas Bergthaler

1 Oct 2018
Special Seminar
Yigong Shi
Tsinghua University, The Shi Laboratory, Beijing, China
"Mechanism of pre-RNA splicing by the spliceosome"
Host: Giulio Superti-Furga

17 Oct 2018
Special Lecture
Karl Sigmund
University of Vienna, Austria
"Einstein's Vienna – The history of the Vienna Circle"
Hosts: Andreas Bergthaler and Jörg Menche

18 Oct 2018
Special Lecture
Jürgen Meier and Leopold Zapp
"Patenting for CeMM – Do's and Don'ts" (Legal View)
Host: Anita Ender

18 Oct 2018
Impromptu
Franz Herzog
LMU, Gene Center Munich, Herzog Lab, Biological Mass Spectrometry, Germany
"Kinetochore Assembly and Function: Chemical Crosslinking and Mass Spectrometry Insights"
Host: Stefan Kubicek

6 Nov 2018
FH Symposium: Familiäre Hypercholesterinämie und andere angeborene Fettstoffwechselstörungen Effektives Management mit bewährten und neuen Therapien
Organizers:
Christoph Binder (CeMM, MUV)
Gabriele Hanauer-Mader (FHchol Austria)

12 Nov 2018
Impromptu
Benjamin Schuster-Böckler
Ludwig Institute for Cancer Research, University of Oxford, United Kingdom
"The influence of cell-intrinsic processes on mutation rate"
Host: Joanna Loizou

15 Nov 2018
6th Next Generation Sequencing Vienna Symposium & Workshop
Organizers:
Christoph Bock (CeMM, MUV)
Andreas Sommer (VBCF)

23 Nov 2018
Impromptu
Bruno Amati
European Institute of Oncology, Director of Oncogenes, Chromatin and Cell Cycle Control Unit, Milan, Italy
"Transcriptional programs and therapeutic targets in MYC-driven tumors"
Host: Giulio Superti-Furga

26 Nov 2018
Impromptu
Andreas Pichlmair
Immunopathology of Virus Infections, Institute of Virology, Technical University of Munich, Germany
"Mass spectrometry-based survey of infected cells and antiviral responses – Inhibitom vs Defendome"
Host: Giulio Superti-Furga

7 Dec 2018
Impromptu
Jacques Colinge
Montpellier Cancer Research Institute (IRCM), France
"In vivo large scale mapping of protein power"
Host: Jörg Menche

10 Dec 2018
Smart Lecture
Wolfgang Lutz
Wittgenstein Centre for Demography and Global Human Capital (IISA, VID/ÖAW, WU)
"Population Trends and the Global Sustainable Development Goals"
Host: Giulio Superti-Furga

11 Dec 2018
Impromptu
Noelia Urban
Institute of Molecular Biotechnology, Vienna, Austria
"Intrinsic and systemic regulation of adult neural stem cells"
Host: Vanja Nagy

17 Dec 2018
CeMMinar
Matthew Vander Heiden
Associate Director, Koch Institute for Integrative Cancer Research at MIT, Cambridge MA, United States
"Metabolic limitations of tumor growth"
Host: Giulio Superti-Furga

19 Dec 2018
Impromptu
Franziska Michor
Dana-Farber Cancer Institute, Department of Biostatistics and Computational Biology, Boston, United States
"DNA methylation profiling for non-invasive early cancer diagnosis"
Host: Giulio Superti-Furga

Awards

We would like to highlight the following prizes and recognitions garnered by CeMM members in 2018. CeMM is particularly proud of its successful team members. Congratulations on the prestigious honors and awards!

Sylvia Knapp elected vice president of the board of LBG
In November 2018, Sylvia Knapp, Professor of Infection Biology at the Medical University of Vienna and Principal Investigator at CeMM was elected vice president of the board of the Ludwig Boltzmann Gesellschaft (LBG). We congratulate Sylvia Knapp on her new responsibilities in one of the most innovative organizations in Austria's research landscape. Together with academic and implementing partners, the LBG currently operates 19 research institutes – among them the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD) which is located at CeMM.

Elisabeth Lutz Prize awarded to Georg Winter
On December 10, 2018, CeMM Principal Investigator Georg Winter received the Elisabeth Lutz Award for outstanding research achievements in chemical biology in the ceremonial hall of the Austrian Academy of Sciences, in the presence of the sponsor. Following an international peer review process, the Academy awards the prize to young researchers in the field of life sciences, who received their doctorate no longer than eight years ago, especially for new findings or innovative research approaches that could help develop new therapeutic methods. The award comes with a purse of €15,000.

Three prestigious awards to Kaan Boztug
For his outstanding research into rare diseases, Kaan Boztug received not only the Pirquet Prize as well as the Austrian Science Prize for Pediatric and Adolescent Medicine, both awarded annually by the Austrian Society for Pediatric and Adolescent Medicine (ÖGKJ), but he was also awarded a Consolidator Grant by the European Research Council (ERC) for a five-year project researching the causes of human immune system regulation disorders. Well-deserved honors for a dedicated pediatrician and brilliant scientist. Kaan Boztug joined CeMM as a Principal Investigator in 2011, where he is still a faculty member. He works both at MedUni Vienna/Vienna General Hospital and at St. Anna Children's Hospital as a doctor of pediatric and adolescent medicine. He has been head of the Vienna Center for Rare and Undiagnosed Diseases (CeRUD) since 2014 and Director of the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD) since 2016. In 2019 Kaan Boztug will become the Scientific Director of the Vienna Children's Cancer Research Institute.

Georg Winter and Elisabeth Lutz

Outreach Activities

CeMM is always eager to explain the benefits of its research to the public. The participation in events, like the Long Night of Research or art exhibitions is a good opportunity to share knowledge and to engage with people. No need to say, that all activities are two-way communication, and CeMM benefits highly from the input of several dialogue partners.

Long Night of Research
During the Long Night of Research, on April 13, 2018, a vast number of knowledge-hungry people called at the two CeMM booths. While typically students and adults discussed genomic research with CeMM's Genom Austria team at the MedUni of Vienna's research mile, mostly families enjoyed the interactive program at Heldenplatz from which myriads of children came away with a newly instilled enthusiasm for science.

Virtual Reality at the art exhibit "Bodyscan"
On November 20, three CeMM scientists traveled to Munich on a very special mission: Sebastian Pirch, Felix Müller and Jörg Menche were guests at the opening of "Bodyscan – Anatomy in Art and Science". Following an invitation by the artist Peter Kogler and Sabine Adler from the Eres Foundation, the CeMM team contributed a virtual reality installation to the exhibition, which covered a wide spectrum of art, from Baroque anatomical sculptures to contemporary works by John Baldessari, Gerhard Richter, Meret Oppenheim and many others.

Stiegenhaus, 11 Square Albin Cachot, 75013 Paris-13E / RC01-BDJ 2018
On October 4, 2018, CeMM inaugurated the multi-part wall sculpture "Stiegenhaus, 11 Square Albin Cachot, 75013 Paris-13E / RC01-BDJ 2018". The artwork, made of lacquered balsa wood, is a generous gift from friend and artist Klaus Pamminger for CeMM's lecture hall. About 270 × 520 × 32 cm in size, it refers to the staircase that Séverine Sérizy (Catherine Deneuve) climbs in Luis Buñuel's movie "Belle de Jour" (1967), in order to leave her old bourgeois life behind.

BEOPEN
The Austrian Science Fund FWF's 50th anniversary served as an opportunity to launch the "BE OPEN – Science & Society Festival" together with partners from science, research, business and society. CeMM participated with a "Medicine of the Future Quiz", presented by actors of the Business Theater. The characters Virus, Miss DNA, and Monsieur Macrophage engaged visitors and families in lively discussions and distributed a card game with questions about biomedical and basic research.

Social Events

Social events play an important role when it comes to maintaining the CeMM spirit. From a yearly outing, an illustrious Halloween party, to a Christmas Party with all the CeMMies and their families, from regular happy hours, to sports activities – there are several opportunities for communication and networking.

Social activities specifically support CeMM's strong intellectual environment that stems from the international nature of its employees (currently 46 nationalities represented). Diversity and different cultural backgrounds and the formal and informal exchange are clearly conducive to successful research, collaborations, and day-to-day business.

Vienna Science Ball
For the fourth time, CeMMies had a great evening at the Vienna Ball of Sciences, a wonderful event at which the scientific community celebrates its profession, diversity and internationality. Together with their guests of honor, Jo Bury and Els Coopman, some 100 CeMMies enjoyed Austrian ball culture in the beautiful and historical setting of the Vienna City Hall.

Vienna City Marathon and Cancer Research Run
On Sunday, April 22, 15 CeMM relay teams and colleagues from LBI-RUD and Allcyte participated in the 35th Vienna City Marathon. On October 6, 2018, a large group of CeMMies took part in the 12th Cancer Research Run ta the Old General Hospital University Campus. For every lap completed on the circular course (1 mile), a donation was made to an innovative cancer research project at the Medical University of Vienna.

Outing and Photo Challenge
To start the academic year with a community experience, CeMM had its Annual Outing on October 5, 2018. The thematic focus was on traffic and public transport, taking inspiration from Jan Gehl's talk "Livable cities for the 21st century". We had the opportunity to visit the light rail manufacturing plant of Siemens Mobility GmbH in Vienna, which is usually not open to visitors. The afternoon was dedicated to a photo and group challenge on mobility, related to the topics, "Public Transportation", "Vehicles", "Street Life", "History Meets Future", "Movement" and "Signs and Signals".

Welcome New Adjunct PIs
On November 6, 2018, CeMMies and our colleagues from LBI-RUD met to welcome five new faculty members: Miriam Unterlass, Technical University of Vienna, Nuno Maulide, University of Vienna, Andreas Villunger, Medical University of Innsbruck, Georg Stary and Thomas Reiberger, Medical University of Vienna.

Halloween
Every year, the first-year students organize a Halloween Party, just one month after beginning their studies at CeMM. They always surprise with even more creativity and inventiveness, despite having big shoes to fill! The big question at the event, on October 25, 2018: "What is your superpower, to defend CeMM against the hordes of evil?"

Charity: Movember and Pink Ribbon
At the initiative of CeMM PhD student Benedikt Agerer, CeMM raised donations for cancer awareness during November 2018: more than €2.000 were donated to Movember, an awareness initiative for men's health issues (men all over the world grow moustaches in support of the campaign), and to Pink Ribbon, a symbol for breast cancer awareness. The initiative's highlight at CeMM was the charity closing event, where several CeMMie beards were auctioned off for a good cause.

VBCeMM Kick-Off Event
On November 27, 2018, PhD students from five life science institutes met to kick off a new event series. "VBCeMM" aims to strengthen the connection between life science campuses in Vienna by creating a platform for scientific exchange in an informal setting. In a scientific speed dating format, the participants from IMBA, IMP, GMI, MFPL, and CeMM exchanged bright ideas, shared expertise and enjoyed a good laugh.

Christmas Party
On December 14, 2018, CeMM celebrated its traditional Christmas party at Casino Baumgarten, a spectacular ballroom established in 1890. On a lovely winter's night, some 200 adults and 56 children enjoyed roasted chestnuts and punch on the terrace, followed by a delicious dinner in the spectacular festive hall. The children received gift books from a jolly Santa Claus and games and an entertainment program were provided by the Kinder Events team. The second-year students prepared a wonderful quiz show with faculty. A dance party with the band "Hot Five" completed the marvelous evening.

Community Service

CeMM is very proud of its role as a flagship institute in molecular medicine. The mandate to shape the medicine of the future through a new understanding of molecular physiology and pathology of humans and to invent new therapies and diagnostics comes with great social responsibility. CeMM's management, faculty and all its co-workers are well aware of their accountability towards society. An open dialogue with politics and the public aims to improve the understanding of science, and vice versa, to better understand public interest in priorities for science and the public's concerns.

Science meets Politics, November 9, 2018
Thanks to the initiative of Anton Zeilinger, President of the Austrian Academy of Sciences, and Wolfgang Sobotka, President of the National Council, there was a kick-off meeting for a new dialogue format on November 9, 2018, bringing together "Science and Politics". CeMM Director Giulio Superti-Furga was one of eight top scientists who met representatives of the Austrian National Council at Palais Epstein for a knowledge-based discussion and exchange on topics around Quantum Physics, Life Sciences, Space Research and Demography.

Visit from Singapore's Minister for Foreign Affairs
On October 17, 2018, CeMM had the pleasure to welcome Dr. Vivian Balakrishnan, Singapore's Minister for Foreign Affairs, and his delegation for a visit to our research institute. CeMM's Administrative Director Anita Ender and Principal Investigator Christoph Bock introduced CeMM to the guests, detailing its research focus, cooperation culture and mission to achieve maximum scientific innovation in molecular medicine. In accordance with their special interest in translational initiatives, Nikolaus Krall (CEO and founding member of Allcyte) and CeMM PI Robert Kralovics (founding member of MyeloPro) gave examples for spin-offs based on CeMM basic research findings and inventions that promise to have an impact on medicine and healthcare. After a tour through CeMM's technical facilities, the Minister engaged in a conversation with his compatriot Marini Ng, PhD student at LBI-RUD and CeMM.

Giulio Superti-Furga at European Forum Alpbach 2018
On August 23, 2018, a panel discussion on "Precision medicine – medicine's solution to diversity?" took place at the European Forum Alpbach. Michaela Fritz (VR MedUni Vienna), Patrice Milos (Medley Genomics), Christian Herold (MedUni Vienna), Peter Nilsson (SciLifeLab Stockholm), and Giulio Superti-Furga (CeMM) debated the paradigm shift in the field of medicine: in a revolutionary development, precision medicine based on diversity is significantly changing medicine towards personalized methods of treatment. A lively discussion focused on promising advantages for individual patients and the possible impact on the technologies of tomorrow. Are we facing a revolution?

FACE IT – Jörg Menche at TEDxDornbirn
CeMM PI Jörg Menche systematically investigates the molecular basis of human diseases. The way he does that and how it works was at the core of what he shared with the TEDx audience on July 21, 2018 in Spielboden Dornbirn. With this year's theme 'Face It' the organizers tried to find speakers able to deliver insights into technology, science, personal stories, challenges and to face topics we usually don't come in touch with. What should we share in public? What should we keep to ourselves? Determining where this border is, was the challenge for this year's event.

Flashmob – Dance for Science
On April 13, 2018 many CeMMies took part in the "Dance for Science", at the Campus of the University of Vienna. Following up the 2017 "March of Science", the event was organized by the University and the team for Science March Vienna to connect science and society, to promote the important value of robust science, and to conclude the Long Night of Science joyfully.

Sience meets Politics
On November 9, 2018, Giulio Superti-Furga was one of eight scientists who met representatives of the Austrian National Council in a kick-off meeting for a new dialogue format bringing together scientists and policymakers.

Visit from Singapore's Minister for Foreign Affairs
As one of Austria's leading centers for research and training, CeMM is attractive to delegations from all over the world. During his visit, Singapore's Minister for Foreign Affairs was especially interested in CeMM's successful translational initiatives.

Giulio Superti-Furga at European Forum Alpbach 2018
In 2018, the Forum Alpbach focused on "Diversity and Resilience". Together with Michaela Fritz, Patrice Milos, Christian Herold and Peter Nilsson, Giulio Superti-Furga debated on precision medicine, a paradigm shift in the field of medicine.

FACE IT – Jörg Menche at TEDxDornbirn
On July 11, 2018, CeMM Principal Investigator Jörg Menche delivered a TEDx talk about the links between humans, genes and machines and the potential of network science to revolutionize the way medicine and science are generally done.

CeMM Facts

Facts

Co-Workers

46 Nationalities
Armenia, Australia, Austria, Belgium, Bosnia and Herzegovina, Brazil, Bulgaria, Canada, China, Croatia, Cyprus, Czech Republic, Finland, France, Germany, Great Britain, Greece, Hungary, India, Indonesia, Iran, Ireland, Israel, Italy, Japan, Jordania, Latvia, Lebanon, Macedonia, Mexico, Netherlands, Poland, Portugal, Romania, Russia, Saudi Arabia, Serbia, Slovakia, Spain, Switzerland, Taiwan, Thailand, Tunesia, Turkey, Ukraine, USA

Directory

Management

Giulio Superti-Furga
Scientific Director, CEO

Anita Ender
Administrative Director, CEO

Principal Investigators

Andreas Bergthaler

Christoph Binder

Christoph Bock

Sylvia Knapp

Robert Kralovics

Stefan Kubicek

Joanna Loizou

Jörg Menche

Giulio Superti-Furga

Georg Winter

Adjunct Principal Investigators

Kate Ackerman
University of Rochester Medical Center

Kaan Boztug
LBI-RUD, CeRUD, CCRI

Thijn Brummelkamp
Netherlands Cancer Institute

Nuno Maulide
University of Vienna

Vanja Nagy
LBI-RUD

Thomas Reiberger
Medical University of Vienna

Georg Stary
Medical University of Vienna

Miriam Unterlass
Technical University of Vienna

Andreas Villunger
Medical University of Innsbruck

Administrative Team Leaders

Binia Maria Meixner
Head of Human Resources

Gabriel O'Riordain
Head of Scientific Support

Michael Pilz
Head of IT Services

Eva Schweng
Head of Public Relations

Sigrid Strodl
Head of Finance, Division Grants & Controlling

Kathrin Wiesendorfer
Head of Finance, Division Grants & Controlling

Facility Heads

Christoph Bock
Head of Biomedical Sequencing Facility (BSF)

Stefan Kubicek
Head of Platform Austria for Chemical Biology (PLACEBO)

André Müller
Head of the Proteomics and Metabolomics Facility

Kristaps Klavins
Deputy Head for Metabolomics

Postdoctoral Fellows

Taras Afonyushkin
Medical University of Vienna

Ariel Bensimon
ERC GAMEOFGATES

Johannes Wolfgang Bigenzahn
FWF F4711

Larissa Cardilo dos Reis Weismann
Medical University of Vienna

Ruth Eichner°
EMBO Long-Term Fellowship ALTF 245-2017

Matthias Farlik-Födinger
ÖAW Innovationsfonds, FWF F6102, FWF I2798

Lukas Folkman
FWF F6102

Nikolaus Fortelny
EMBO Long-Term Fellowship ALTF 241-2017

Riem Gawish
Medical University of Vienna

Enrico Girardi
FWF P29250

Michaela Gruber
ÖAW New Frontier 2014

Florian Halbritter
DFG Fellowship, FWF I1575, FWF I2798

Mari Hashimoto*
ERC GAMEOFGATES

Leonhard Heinz
BI SLC

Birgit Höger
LBI-RUD

Hana Imrichova
FWF P30271, FWF I2798

Alvaro Ingles-Prieto
ERC GAMEOFGATES, IMI RESOLUTE

Vasyl Ivashov

Roland Jäger
FWF P29018

Artem Kalinichenko
LBI-RUD

Anton Kamnev
LBI-RUD

Nikolaus Krall*
MSCA SLIM

Thomas Krausgruber
ÖAW New Frontier 2014, FWF M2403

David Lara-Astiaso*
ÖAW New Frontier 2014

Kai-Chun Li
ERC GAMEOFGATES

Jung-Ming George Lin
ERC CHROMABOLISM

Andrea Majoros
FWF P30041

Cristina Mayor-Ruiz
EMBO Long-Term Fellowship ALTF 676-2017

David Medgyesi*
LBI-RUD

Amandine Moretton
FWF P29555

Harini Nivarthi°
FWF P30041

Yael Nossent
Medical University of Vienna

Nikolina Papac-Milicevic
Medical University of Vienna

Konstantinos Papakostas
BI SLC

Tea Pemovska
EMBO Long-Term Fellowship ALTF 733-2016

Manuele Rebsamen
ERC GAMEOFGATES

Elisabeth Salzer
LBI-RUD

Sandra Schick
CDG Laboratory

Michael Schuster

Sara Sdelci*
JDRF 2-SRA-2017-416-S-B

Vitaly Sedlyarov
IMI RESOLUTE

Celine Sin
WWTF LS16-060

Philipp Starkl
FWF P31113

Georgia Velimezi*
FWF P29555

Bojan Vilagos*
FWF P30047

Stefanie Widder
Medical University of Vienna

Tabea Wiedmer
IMI RESOLUTE

PhD Students

Naga Sarada Achyutuni
FWF F4702

Benedikt Agerer
FWF W1212

Rico Ardy
ÖAW DOC Fellowship 24486

Hatoon Baazim
ERC CMIL

Jana Block
LBI-RUD

Bernhard Karl Boidol#*
CDG Laboratory

Matthias Brand
FWF P30271

Pisanu Buphamalai
WWTF VRG15-005

Michael Caldera

Tamara Casteels
JDRF 3-SRA-2015-20-Q-R, JDRF 2-SRA-2017-416-S-B

Adrián Cesar Razquin*

Paul Datlinger
ÖAW New Frontier 2014, FWF I1575

Justine Deroissart
Medical University of Vienna

Cecilia Dominguez Conde#*
ERC IMMUNOCORE

Vojtech Dvorak
WWTF LS17-059

Lennart Enders
JDRF 2-SRA-2017-416-S-B

Patrick Essletzbichler
ERC GAMEOFGATES

Asma Farhat

Christopher Fell
LBI-RUD

Joana Ferreira Da Silva
FWF P29763, ÖAW DOC Fellowship 25035

Jakob-Wendelin Genger
ERC CMIL

Anna-Dorothea Gorki
Medical University of Vienna

Anna Hakobyan
WWTF VRG15-005

Ben Haladik
LBI-RUD

Joel Hancock

Alexander Hanzl
FWF P30271

Jakob Huemer
LBI-RUD

Martin Jäger
BIF PhD Fellowship

Ruochen Jia
FWF F4702

Felix Kartnig
FWF F4711

Kseniya Khamina#
FWF P30047

Mate Kiss
Medical University of Vienna

Johanna Klughammer#*
FWF I1575

Tomislav Kokotovic
LBI-RUD

Alexander Lercher
ERC CMIL, ÖAW DOC Fellowship 24955

Brenda Marquina Sanchez
CDG Laboratory, JDRF 3-SRA-2015-20-Q-R, BIF PhD Fellowship

Mathilde Meyenberg
FWF P29555

Anna Moskovskich*
ERC GAMEOFGATES

Marini Ng
LBI-RUD

Georg Obermayer
Medical University of Vienna

Michel Owusu#
FWF P29763

Robert Pazdzior
ÖAW DOC Fellowship 24721

Julia Pazmandi
LBI-RUD

Florentina Porsch
Medical University of Vienna

Florian Puhm
Medical University of Vienna

Federica Quattrone
Medical University of Vienna

Mariem Radhouani
FWF P31113

Bernhard Ransmayr
LBI-RUD

Andreas Reicher
WWTF LS17-059

André Rendeiro
ÖAW New Frontier 2014

Lydia Robinson-Garcia
BIF PhD Fellowship

Daria Romanovskaia
FWF I2798

Sejla Salic*

Fiorella Schischlik*

Anna Schrempf
FWF P29763

Christina Schüller
FWF P30041

Tala Shahin
LBI-RUD

Anna Skucha#*
ERC GAMEOFGATES, IMI RESOLUTE

Mark Smyth
ÖAW DOC Fellowship 24813

Peter Traxler
ERC Epigenome Programming

Loan Vulliard
WWTF VRG15-005

Martin Watzenböck
Medical University of Vienna

Juliane Weißer#*

Sophie Zahalka
Medical University of Vienna

Fangwen Zhao
LBI-RUD

Diploma Students

Mirlinda Ademi*
Medical University of Vienna

Tyler Artner*
Medical University of Vienna

Stefanie Haslinger-Hutter*
Medical University of Vienna

Regina Jin
Medical University of Vienna

Isabel Kaltenbrunner*
FFG FEMtech 864423, WWTF VRG15-005

Rebecca Kresnik*
Medical University of Vienna

Leon Kutzner*
FWF F4702

Nevena Milosavljevic*
FWF P30041

Michael Moschinger*

Theresa Pinter*
FWF P30047

Daniel Roden
Medical University of Vienna

Shirin Shargh*
Medical University of Vienna

Thomas Jan Streef*
Medical University of Vienna

Nadine Tüchler

Markus Youssef*

Guest Scientists

Ayse Bal
ERC IMMUNOCORE, JMF Translational Research Program, LBI-RUD

Loïc Dupré
LBI-RUD

Aysu Eshref
Medical University of Vienna

Yolla German
LBI-RUD

Dorothea Holter*

Evgeniia Pankevich
ERC Epigenome Programming

Lauréne Pfajfer
LBI-RUD

Mattia Pizzagalli

Lisa Poeltl*

Moritz Schlapansky*
ERC CMIL

Dörte Symmank
Medical University of Vienna

Samaneh Zoghi
ERC IMMUNOCORE, JMF Translational Research Program

Technical Assistants and Computer Scientists

Donat Alpar
BSF Technologist

Daniele Barreca
Bioinformatician

Sophie Bauer
FWF P30271

Thorina Boenke
NGS Technologist

Edith Bogner°

Manuela Bruckner
ERC GAMEOFGATES

Luna D'Angelo
ERC CHROMABOLISM

Jasmin Dmytrus
ERC IMMUNOCORE, LBI-RUD

Bekir Ergüner
Bioinformatician

Noel Fitzgerald

Giuseppe Fiume
FWF P29250

Frederic Fontaine

Elisabeth Fuchs
FWF P29018

Wojciech Garncarz
ERC IMMUNOCORE, LBI-RUD

Victoria Gernedl
ÖAW New Frontier 2014, ÖAW Innovationsfonds

Laura Göderle
Medical University of Vienna

Ulrich Goldmann
Data Scientist
ERC GAMEOFGATES, IMI RESOLUTE

Bettina Gürtl

Matthias Haimel
Bioinformatician
LBI-RUD

Anastasiya Hladik
Medical University of Vienna

Gerald Hofstätter*~
CDG Laboratory

Raimund Holly*
FWF P30041

Raúl Jimenez Heredia
Medical University of Vienna

Christoph Klimek
IMI RESOLUTE

Lindsay James Kosack

Vitalii Kovtunyk
ÖAW New Frontier 2014

Vesna Krajina
Medical University of Vienna

Ana Krolo°
Medical University of Vienna

Karin Lakovits
Medical University of Vienna

Ewelina Lenartowicz
LBI-RUD

Sabrina Lindinger
WWTF LS16-034

Eva Lineiro-Retes
IMI RESOLUTE

Peter Májek
Bioinformatician

Noémi Meszaros*
WWTF LS16-034

Felix Müller
Scientific Programmer
WWTF VRG15-005

Heiko Müller*
Data Analyst

Amelie Nemc
FWF I1575, FWF I2798

Matthew Oldach*
JDRF 2-SRA-2017-416-S-B

Svenja Onstein
IMI RESOLUTE

Maria Ozsvar-Kozma
Medical University of Vienna

Katja Parapatics~

Thomas Penz
BSF Technologist

Melanie Pieraks*
WWTF LS16-034

Iro Pierides*
LBI-RUD

Sebastian Pirch
Graphic Designer
WWTF VRG15-005

Alexandra-Mariela Popa
Data Analyst
ERC CMIL

Christina Rashkova
LBI-RUD

Roxanna Rehak
Medical University of Vienna

Daniela Reil

Anna Ringler

Kathrin Runggatscher

Linda Schuster*
ERC Epigenome Programming

Stefania Scorzoni
ERC GAMEOFGATES

Martin Senekowitsch
NGS Technologist

Marton Siklos
ERC CHROMABOLISM

Ismet Srndic

Adrijana Stefanovic
BI SLC

Jakob Weinzierl

Marc Wiedner

Gernot Wolf
Senior Scientist
IMI RESOLUTE

Wanhui You
CDG Laboratory

Özlem Yüce Petronczki
ERC IMMUNOCORE, LBI-RUD

Scientific Support

Susanne Barcanec*
Cleaning Staff

Sylvia Bolz*
Wash and Media Kitchen

Jana Brandlova*
Cleaning Staff

Amisi Fundi Nyembo
Wash and Media Kitchen

Paul Kletzl~
Internal Logistics

Alisa Kokorovic
Cleaning Staff

Faith Lang
Cleaning Staff

Daliborka Nedeljkovic
Cleaning Staff

Sarah Niggemeyer
Animal Care

Peter Pelz
House Logistics

Anton Johann Peisser
Facility Manager

Sona Rettenbacherova
Cleaning Staff

Jenny Riede
Animal Care

Mate Sebök
Wash and Media Kitchen

Patrick Stangl~
Purchaser, Deputy Head of Scientific Support

Zeljka Stanusic*
Cleaning Staff

Administration and Scientific Project Management

Mitra Eva Baghai
Personal Assistant to Robert Kralovics

Sonja Baier°
Assistant

Thomas Brandl
Funding Manager

Patricia Ann Carey
Senior IT Systems Engineer

Wolfgang Georg Däuble*
Media Relations Manager

Sabine Forster
Assistant

Alexandra Gavalaki
HR Project Assistant

Isabel Grießhammer°
Personal & Scientific Assistant to Kaan Boztug
LBI-RUD

Oliwia Hadjiaghai
Assistant

Patrick Haiger
Senior Accountant

Daniel Lackner
Scientific Project Manager
IMI RESOLUTE

Lasse Matias Kalevi
Senior IT Systems Administrator

Peter Kotzan
Purchaser

Karin Kukla°
Senior Accountant

Victoria Kulcsar-Mecsery
Accountant

Catherine May Lloyd°
HR Project Manager
EU LIBRA

Johannes Pfeifenschneider
Business Development Officer
LBI-RUD

Veronika Poschenreithner
Junior Controller

Maximilian Rau
Executive Assistant to Kaan Boztug
LBI-RUD

Nina Rezac
Personal Assistant to Sylvia Knapp
Medical University of Vienna

Elisabeth Simböck*
Project Assistant Genom Austria

Vera-Desiree Sodl
Executive Assistant to Giulio Superti-Furga

Matthew Spencer
PhD and Postdoc Program Manager

Alexandra Stadler*
Executive Assistant

Michaela Corinna Steiner*
PhD and Postdoc Program Manager
EU LIBRA

Te Fung Fiona Tseng
Human Resources Administrator

Cafeteria

Erdzhan Alekov*

Borbala Terez Ando*

Marika Cappella*

Tuende Fuchs

Magdalena Legierska

Janek Leszczynski

Walter Steinbrecher

graduated in 2018
° on parental leave
~ on education leave
* left CeMM in 2018

Legend of Grants

BIF PhD Fellowship
Lydia Robinson-Garcia
Boehringer Ingelheim Fonds PhD Fellowship

BIF PhD Fellowship
Martin Jäger
Boehringer Ingelheim Fonds PhD Fellowship

BIF PhD Fellowship
Brenda Marquina Sanchez
Boehringer Ingelheim Fonds PhD Fellowship

Boehringer Ingelheim Collaborative Research Agreement Boehringer Ingelheim International GmbH

CDG Laboratory, Christian Doppler Laboratory for Chemical Epigenetics and Antiinfectives

CeRUD Vienna Center for Rare and Undiagnosed Diseases

DFG Fellowship
Florian Halbritter
Deutsche Forschungs-gemeinschaft Fellowship

EMBO Long-Term Fellowship
ALTF 733-2016
European Molecular Biology Organization Fellowship

EMBO Long-Term Fellowship
ALTF 245-2017
European Molecular Biology Organization Fellowship

EMBO Long-Term Fellowship
ALTF 241-2017
European Molecular Biology Organization Fellowship

EMBO Long-Term Fellowship
ALTF 676-2017
European Molecular Biology Organization Fellowship

ERC CMIL
Starting Grant "Crosstalk between Metabolism and Inflammation"

ERC CHROMABOLISM
Consolidator Grant
"Chromatin-localized central metabolism regulating gene expression and cell identity"

ERC EPIGENOMEPROGRAMMING
Starting Grant
"An experimental and bioinformatics toolbox for functional epigenomics and its application to epigenetically making and breaking a cancer cell – EpigenomeProgramming"

ERC GAMEOFGATES
Advanced Grant
"Solute carrier proteins as the gates managing chemical access to cells – GameofGates"

ERC IMMUNOCORE
Starting Grant "Inborn errors of innate immunity"

EU IMI RESOLUTE
Innovative Medicines Initiative, "Research Empowerment on Solute Carriers (RESOLUTE)"

EU LIBRA
Coordination and Support Action "Leading Innovative Measures to Reach Gender Balance in Research Activities"

EU MSCA SLIM
PostDoc Fellowship, "Crosstalk between Metabolism and Inflammation"

FFG FEMtech 864423
FEMtech Praktika Studentinnen 2017

FFG Bridge 851289
"Mimicking isoform-specific inhibitors – Genetic engineering of histone deacetylases"

FWF F4702
Special Research Program "Myeloproliferative Neoplasms"

FWF F4711
Special Research Program "Myeloproliferative Neoplasms"

FWF F6102
Special Research Program "Dissecting cell type-specific chromatin dynamics driven by oncogenic JAK-STAT signaling"

FWF I1575
ERA-NET "Epigenetic risk assessment and biomarker development for breast cancer (EpiMark)"

FWF I2192,
ERA-NET "Evaluating viral RNA/DNA-bound proteins Across SpeciEs (ERASE)"

FWF I2798,
International Project, "Cancer evolution and identification of relapse-initiating cells (CEVIR)"

FWF M2403
Lise Meitner Fellowship, "Systems-level analysis of the T-bet Interaction network"

FWF P29018
Stand-Alone Project, "Inherited susceptibility for thrombosis in MPN"

FWF P29250
Stand-Alone Project, "The viral transportome (VITra)"

FWF P29555
Stand Alone Project, "Correcting Nucleotide Excision Repair-Associated Diseases"

FWF P29763
Stand-Alone Project, "Kinases and DNA Damage"

FWF P30041
Stand-Alone Project, "Mechanism of CALR Mutants in Myeloproliferative Neoplasms"

FWF P30047
Stand-Alone Project, "Role of Chromatin-Associated Proteins in Inflammation"

FWF P30271
Stand-Alone Project, "Charting and Disrupting the Gene-Regulatory Function of CDK6"

FWF P31113
Stand-Alone Project, "Bacteria-Induced Type 2 Immunity in Host Defense and Disease"

FWF W1212 DK
Doctoral Program, "IAI: Inflammation and Immunity"

JDRF 3-SRA-2015-Q-R
Strategic Research Agreement, "Generation of functional beta cells from alternative pancreatic cell subtypes"

JDRF 2-SRA-2017-416-S-B
Strategic Research Agreement, "Novel therapeutic targets from artemisinin-mediated alpha to beta cell transdifferentiation"

JMF
Jeffrey Modell Foundation, "New insights into DNA repair disorders: integrating genomics and functional studies for developing diagnostic and therapeutic approaches"

LBI-RUD
Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases

Medical University of Innsbruck

Medical University of Vienna

Netherlands Cancer Institute

ÖAW DOC Fellowship 24486
Doctoral Fellowship Program of the Austrian Academy of Sciences

ÖAW DOC Fellowship 24721
Doctoral Fellowship Program of the Austrian Academy of Sciences

ÖAW DOC Fellowship 24813
Doctoral Fellowship Program of the Austrian Academy of Sciences

ÖAW DOC Fellowship 25035
Doctoral Fellowship Program of the Austrian Academy of Sciences

ÖAW DOC Fellowship 24955
Doctoral Fellowship Program of the Austrian Academy of Sciences

ÖAW New Frontier 2014
"High-throughput dissection and reprogramming of epigenetic drug resistance in leukemia"

ÖAW New Frontier 2015
"High-Throughput Metabolomics in Homeostasis and Disease"

ÖAW Innovationsfonds
"Small Cell Colider: dissecting the regulatory impact of physical interactions between single immune cells"

Technical University of Vienna

University of Rochester Medical Center

University of Vienna

WWTF VRG15-005
Vienna Research Group Leader, "Network Medicine – an interactome-based approach to rare diseases"

WWTF LS16-034
"PHARMACOSCOPY: Breaking resistance of refractory blood cancers through ex vivo automated image-based analysis of drug action"

WWTF LS16-060
"Systems precision medicine of inborn errors of the immune system (PrecisePID)"

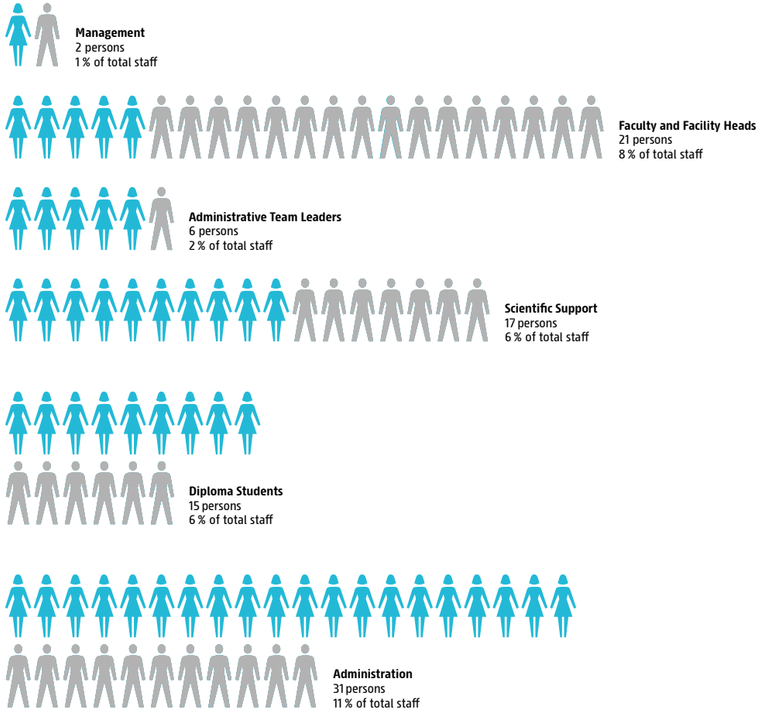
WWTF LS17-059
"3C Cellular Color Chart"

Facts & Figures

Staff

Listed by number of persons per field of work. In the observation period, an average of 153 people not comprising Adjunct Principal Investigators, the colleagues from the Medical University of Vienna, and the LBI-RUD are equal to 138.63 full-time equivalents.

CeMM has a good gender balance, and the average age of its staff is 33.



Management
2 persons
1 % of total staff

Faculty and Facility Heads
21 persons
8 % of total staff

Administrative Team Leaders
6 persons
2 % of total staff

Scientific Support
17 persons
6 % of total staff

Diploma Students
15 persons
6 % of total staff

Administration
31 persons
11 % of total staff

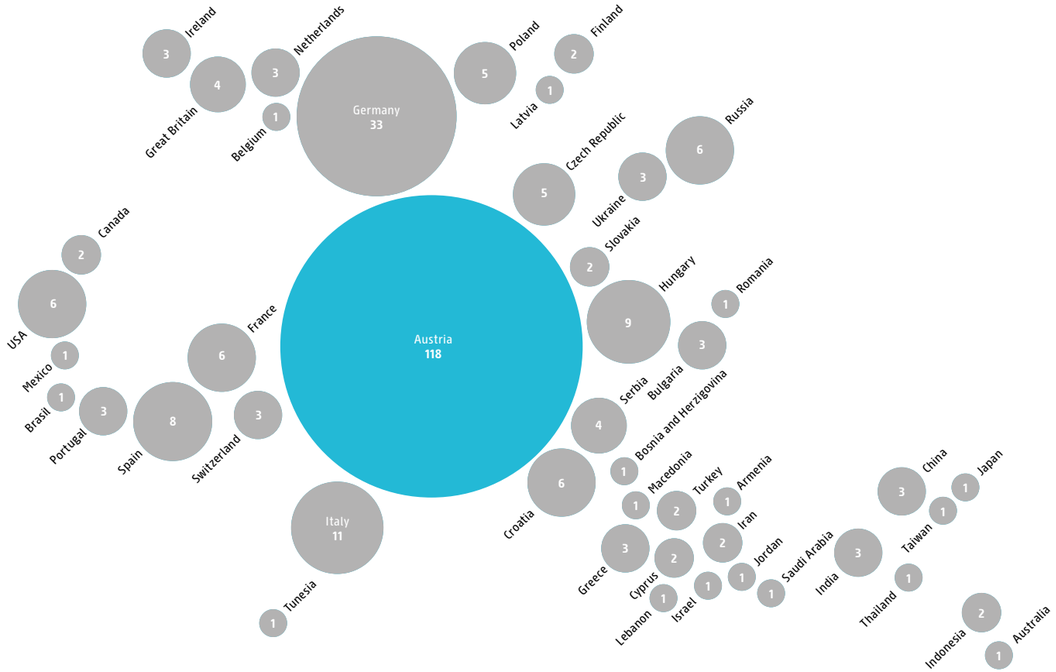
Postdoctoral Fellows
47 persons
17 % of total staff

PhD Students
66 persons
25 % of total staff

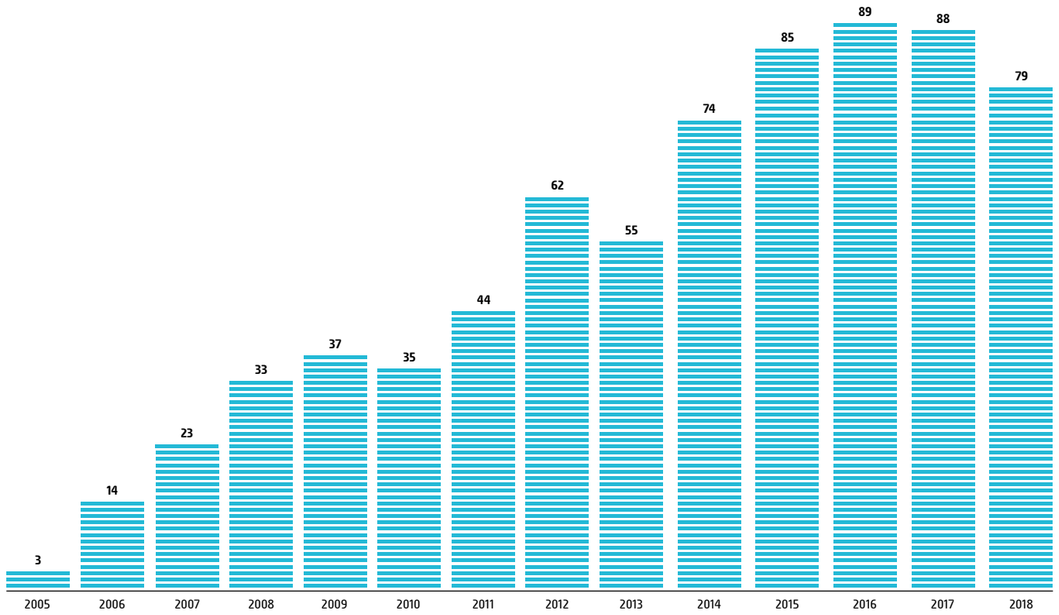
Technical Assistants, Technologists, Computer Scientists
64 persons
24 % of total staff

Nationalities at CeMM

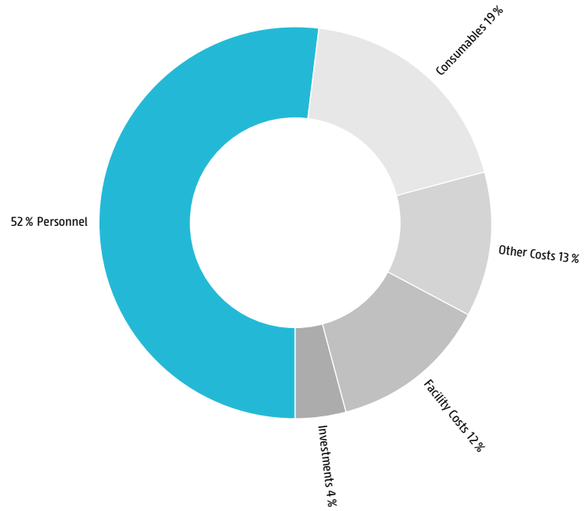
46 different nationalities
are represented at CeMM.



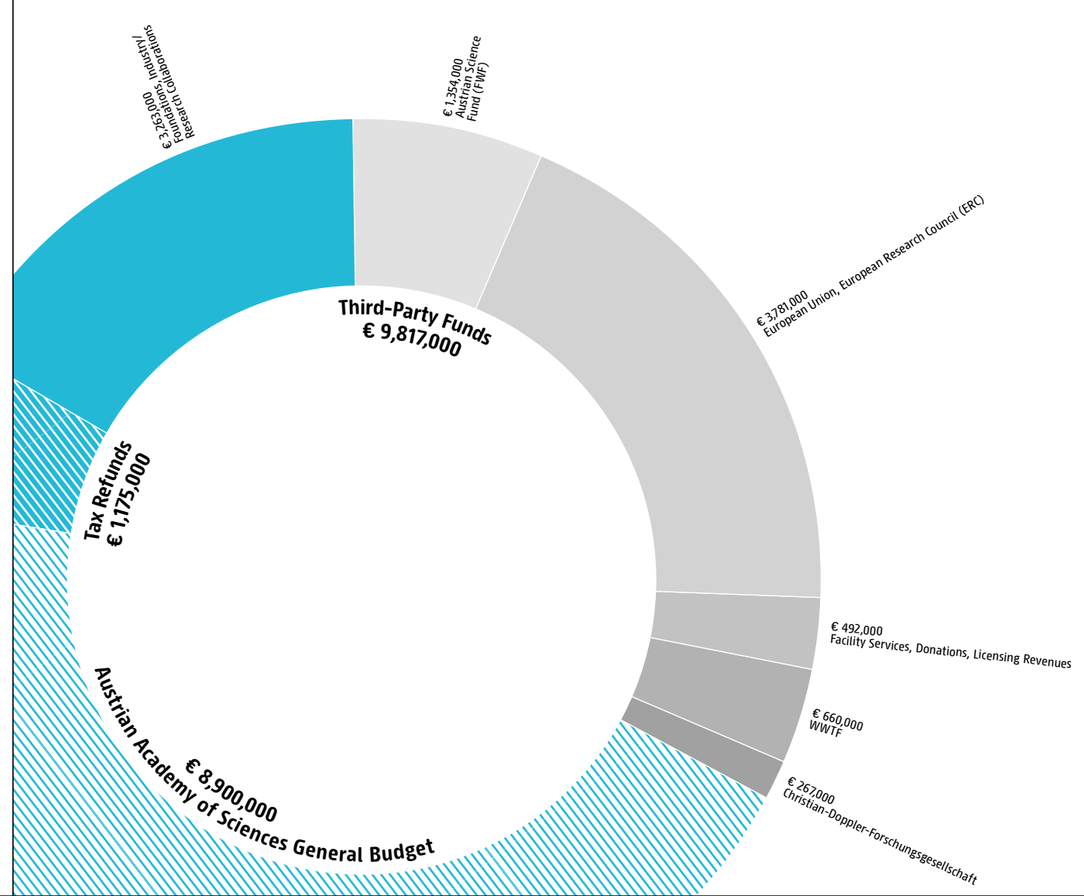
Publications



Expenses in 2018



Money Sources in 2018



Publications 2018

1. Afonyushkin T, Binder CJ. **Extracellular Vesicles Act as Messengers of Macrophages Sensing Atherogenic Stimuli.** *Arterioscler Thromb Vasc Biol.* 2018 Jan;38(1):2-3. doi: 10.1161/ATVBAHA.117.310257.

2. Afonyushkin T, Oskolkova OV, Bochkov VN. **Oxidized phospholipids stimulate production of stem cell factor via NRF2-dependent mechanisms.** *Angiogenesis.* 2018 May; 21(2):229-236. doi: 10.1007/s10456-017-9590-5. Epub 2018 Jan 12.

3. Aguirre-Plans J, Piñero J, Menche J, Sanz F, Furlong LI, Schmidt HHHW, Oliva B, Guney E. **Proximal Pathway Enrichment Analysis for Targeting Comorbid Diseases via Network Endopharmacology.** *Pharmaceuticals (Basel).* 2018 Jun 22;11(3). pii: E61. doi: 10.3390/ph11030061.

4. Aldape K, Amin SB, Ashley DM, Barnholtz-Sloan JS, Bates AJ, Beroukhim R, Bock C, et al. **Glioma through the looking GLASS: molecular evolution of diffuse gliomas and the Glioma Longitudinal Analysis Consortium.** *Neuro Oncol.* 2018 Jun 18;20(7):873-884. doi: 10.1093/neuonc/noy020.

5. Allison TF, Andrews PW, Avior Y, Barbaric I, Benvenisty N, Bock C, et al. **Assessment of established techniques to determine developmental and malignant potential of human pluripotent stem cells.** *Nat Commun.* 2018 May 15;9(1):1925. doi: 10.1038/s41467-018-04011-3.

6. Asp J, Skov V, Bellosillo B, Kristensen T, Lippert E, Dicker F, Schwarz J, Wojtaszewska M, Palmqvist L, Akiki S, Aggerholm A, Tolstrup Andersen M, Girodon F, Kjær L, Oppliger Leibundgut E, Pancrazzi A, Vorland M, Andrikovics H, Kralovics R, et al. **International external quality assurance of JAK2 V617F quantification.** *Ann Hematol.* 2018 Dec 8. doi: 10.1007/s00277-018-3570-8.

7. Avery DT, Kane A, Nguyen T, Lau A, Nguyen A, Lenthall H, Payne K, Shi W, Brigden H, French E, Bier J, Hermes JR, Zahra D, Sewell WA, Butt D, Elliott M, Boztug K, et al. **Germline-activating mutations in PIK3CD compromise B cell development and function.** *J Exp Med.* 2018 Aug 6;215(8):2073-2095. doi: 10.1084/jem.20180010. Epub 2018 Jul 17.

8. Balbino B, Conde E, Marichal T, Starkl P, Reber LL. **Approaches to target IgE antibodies in allergic diseases.** *Pharmacol Ther.* 2018 Nov;191:50-64. doi: 10.1016/j.pharmthera.2018.05.015. Epub 2018 Jun 27. Review.

9. Barakat TS, Halbritter F, Zhang M, Rendeiro AF, Perenthaler E, Bock C, Chambers I. **Functional Dissection of the Enhancer Repertoire in Human Embryonic Stem Cells.** *Cell Stem Cell.* 2018 Aug 2; 23(2):276-288.e8. doi: 10.1016/j.stem.2018.06.014. Epub 2018 Jul 19.

10. Baumgartner C, Toifl S, Farlik M, Halbritter F, Scheicher R, Fischer I, Sexl V, Bock C, Baccarini M. **An ERK-Dependent Feedback Mechanism Prevents Hematopoietic Stem Cell Exhaustion.** *Cell Stem Cell.* 2018 Jun 1;22(6):879-892.e6. doi: 10.1016/j.stem.2018.05.003. Epub 2018 May 24.

11. Bellutti F, Tigan AS, Nebenfuehr S, Dolezal M, Zojer M, Grausenburger R, Hartenberger S, Kollmann S, Doma E, Prchal-Murphy M, Uras IZ, Höllein A, Neuberg DS, Ebert BL, Ringler A, Mueller AC, Loizou JI, et al. **CDK6 Antagonizes p53-Induced Responses during Tumorigenesis.** *Cancer Discov.* 2018 Jul; 8(7):884-897. doi: 10.1158/2159-8290.CD-17-0912. Epub 2018 Jun 13.

12. Benke S, Agerer B, Haas L, Stöger M, Lercher A, Gabler L, Kiss I, Scinicariello S, Berger W, Bergthaler A, Obenauf AC, Versteeg GA. **Human tripartite motif protein 52 is required for cell context-dependent proliferation.** *Oncotarget.* 2018 Feb 5;9(17):13565-13581. doi: 10.18632/oncotarget.24422. eCollection 2018 Mar 2.

13. Bigenzahn JW, Collu GM, Kartnig F, Pieraks M, Vladimer GI, Heinz LX, Sedlyarov V, Schischlik F, Fauster A, Rebsamen M, Parapatics K, Blomen VA, Müller AC, Winter GE, Kralovics R, Brummelkamp TR, Mlodzik M, Superti-Furga G. **LZTR1 is a regulator of RAS ubiquitination and signaling.** *Science.* 2018 Nov 15. pii: eaap8210. doi: 10.1126/science.aap8210. [Epub ahead of print]

14. Bomken S, van der Werff Ten Bosch J, Attarbaschi A, Bacon CM, Borkhardt A, Boztug K, et al. **Current Understanding and Future Research Priorities in Malignancy Associated With Inborn Errors of Immunity and DNA Repair Disorders: The Perspective of an Interdisciplinary Working Group.** *Front Immunol.* 2018 Dec 12;9:2912. doi: 10.3389/fimmu.2018.02912.

15. Brand M, Jiang B, Bauer S, Donovan KA, Liang Y, Wang ES, Nowak RP, Yuan JC, Zhang T, Kwiatkowski N, Müller AC, Fischer ES, Gray NS, Winter GE. **Homolog-Selective Degradation as a Strategy to Probe the Function of CDK6 in AML.** *Cell Chem Biol.* 2018 Nov 22. pii: S2451-9456(18)30413-6. doi: 10.1016/j.chembiol.2018.11.006.

16. Brigida I, Zoccolillo M, Cicalese MP, Pfajfer L, et al. **T-cell defects in patients with ARPC1B germline mutations account for combined immunodeficiency.** *Blood.* 2018 Nov 29; 132(22):2362-2374. doi: 10.1182/blood-2018-07-863431.

17. Brown M, Johnson LA, Leone DA, Majek P, Vaahtomeri K, Senfter D, Bukosza N, Schachner H, Asfour G, Langer B, Hauschild R, Parapatics K, Hong YK, Bennett KL, Kain R, Detmar M, Sixt M, Jackson DG, Kerjaschki D. **Lymphatic exosomes promote dendritic cell migration along guidance cues.** *J Cell Biol.* 2018 Jun 4; 217(6):2205-2221. doi: 10.1083/jcb.201612051. Epub 2018 Apr 12.

18. Cagdas D, Gur Cetinkaya P, Karaatmaca B, Esenboga S, Tan C, Yılmaz T, Gümüş E, Barış S, Kuşkonmaz B, Ozgur TT, Bali P, Santisteban I, Orhan D, Yüce A, Cetinkaya D, Boztug K, Hershfield M, Sanal O, Tezcan İ. **ADA Deficiency: Evaluation of the Clinical and Laboratory Features and the Outcome.** *J Clin Immunol.* 2018 May 9. doi: 10.1007/s10875-018-0496-9. [Epub ahead of print]

19. Centa M, Prokopec KE, Garimella MG, Habir K, Hofste L, Stark JM, Dahdah A, Tibbitt CA, Polyzos KA, Gisterå A, Johansson DK, Maeda NN, Hansson GK, Ketelhuth DFJ, Coquet JM, Binder CJ, Karlsson MCI, Malin S. **Acute Loss of Apolipoprotein E Triggers an Autoimmune Response That Accelerates Atherosclerosis.** *Arterioscler Thromb Vasc Biol.* 2018 Aug;38(8):e145-e158. doi: 10.1161/ATVBAHA.118.310802.

20. César-Razquin A, Girardi E, Yang M, Brehme M, Saez-Rodriguez J, Superti-Furga G. **In Silico Prioritization of Transporter-Drug Relationships From Drug Sensitivity Screens.** *Front Pharmacol.* 2018 Sep 7; 9:1011. doi: 10.3389/fphar.2018.01011. eCollection 2018.

21. Cipe FE, Aydogmus C, Serwas NK, Keskindemirci G, Boztuğ K. **Novel Mutation in CECR1 Leads to Deficiency of ADA2 with Associated Neutropenia.** *J Clin Immunol.* 2018 Apr; 38(3):273-277. doi: 10.1007/s10875-018-0487-x. Epub 2018 Mar 21.

22. Clément M, Haddad Y, Raffort J, Lareyre F, Newland SA, Master L, Harrison J, Ozsvar-Kozma M, Bruneval P, Binder CJ, Taleb S, Mallat Z. **Deletion of IRF8 (Interferon Regulatory Factor 8)-Dependent Dendritic Cells Abrogates Proatherogenic Adaptive Immunity.** *Circ Res.*2018 Mar 16;122(6):813-820. doi: 10.1161/CIRCRESAHA.118.312713. Epub 2018 Feb 7.

23. Cohen M, Giladi A, Gorki AD, Solodkin DG, Zada M, Hladik A, Miklosi A, Salame TM, Halpern KB, David E, Itzkovitz S, Harkany T, Knapp S, Amit I. **Lung Single-Cell Signaling Interaction Map Reveals Basophil Role in Macrophage Imprinting.** *Cell.* 2018 Nov 1; 175(4):1031-1044.e18. doi: 10.1016/j.cell.2018.09.009. Epub 2018 Oct 11.

24. Edwards ESJ, Bier J, Cole TS, Wong M, Hsu P, Berglund LJ, Boztug K, et al. **Activating PIK3CD mutations impair human cytotoxic lymphocyte differentiation and function and EBV immunity.** *J Allergy Clin Immunol.* 2018 May 22. pii: S0091-6749(18)30702-4. doi: 10.1016/j.jaci.2018.04.030. [Epub ahead of print]

25. Faust K, Bauchinger F, Laroche B, de Buyl S, Lahti L, Washburne AD, Gonze D, Widder S. **Signatures of ecological processes in microbial community time series.** *Microbiome.* 2018 Jun 28;6(1):120. doi: 10.1186/s40168-018-0496-2.

26. Fauster A, Rebsamen M, Willmann KL, César-Razquin A, Girardi E, Bigenzahn JW, Schischlik F, Scorzoni S, Bruckner M, Konecka J, Hörmann K, Heinz LX, Boztug K, Superti-Furga G. **Systematic genetic mapping of necroptosis identifies SLC39A7 as modulator of death receptor trafficking.** *Cell Death Differ.* 2018 Sep 20. doi: 10.1038/s41418-018-0192-6. [Epub ahead of print]

27. Fontana MC, Marconi G, Feenstra JDM, et al. **Chromothripsis in acute myeloid leukemia: biological features and impact on survival.** *Leukemia.* 2018 Jul; 32(7):1609-1620. doi: 10.1038/s41375-018-0035-y. Epub 2018 Feb 23.

28. Hashimoto M, Girardi E, Eichner R, Superti-Furga G. **Detection of Chemical Engagement of Solute Carrier Proteins by a Cellular Thermal Shift Assay.** *ACS Chem Biol.* 2018 Jun 15; 13(6):1480-1486. doi: 10.1021/acschembio.8b00270. Epub 2018 Jun 6.

29. Higareda-Almaraz JC, Karbiener M, Giroud M, Pauler FM, Gerhalter T, Herzig S, Scheideler M. **Norepinephrine triggers an immediate-early regulatory network response in primary human white adipocytes.** *BMC Genomics.* 2018 Nov 3;19(1):794. doi: 10.1186/s12864-018-5173-0.

30. Ishoey M, Chorn S, Singh N, Jaeger MG, Brand M, Paulk J, Bauer S, Erb MA, Parapatics K, Müller AC, Bennett KL, Ecker GF, Bradner JE, Winter GE. **Translation Termination Factor GSPT1 Is a Phenotypically Relevant Off-Target of Heterobifunctional Phthalimide Degraders.** *ACS Chem Biol.* 2018 Mar 16; 13(3):553-560. doi: 10.1021/acschembio.7b00969. Epub 2018 Jan 29.

31. Jangra RK, Herbert AS, Li R, Jae LT, Kleinfelter LM, et al. **Protocadherin-1 is essential for cell entry by New World hantaviruses.** *Nature.* 2018 Nov; 563(7732):559-563. doi: 10.1038/s41586-018-0702-1.

32. Kager L, Jimenez Heredia R, Hirschmugl T, Dmytrus J, Krolo A, Müller H, Bock C, Zeitlhofer P, Dworzak M, Mann G, Holter W, Haas O, Boztug K. **Targeted mutation screening of 292 candidate genes in 38 children with inborn haematological cytopenias efficiently identifies novel disease-causing mutations.** *Br J Haematol.* 2018 Jul;182(2):251-258. doi: 10.1111/bjh.15389.

33. Kanduri C, Bock C, Gundersen S, Hovig E, Sandve GK. **Colocalization analyses of genomic elements: approaches, recommendations and challenges.** *Bioinformatics.* 2018 Oct 11. doi: 10.1093/bioinformatics/bty835. [Epub ahead of print]

34. Karonitsch T, Kandasamy RK, Kartnig F, Herdy B, Dalwigk K, Niederreiter B, Holinka J, Sevelda F, Windhager R, Bilban M, Weichhart T, Säemann M, Pap T, Steiner G, Smolen JS, Kiener HP, Superti-Furga G. **mTOR Senses Environmental Cues to Shape the Fibroblast-like Synoviocyte Response to Inflammation.** *Cell Rep.* 2018 May 15; 23(7):2157-2167. doi: 10.1016/j.celrep.2018.04.044.

35. Klughammer J, Kiesel B, Roetzer T, Fortelny N, Nemc A, Nenning KH, Furtner J, Sheffield NC, Datlinger P, et al. **The DNA methylation landscape of glioblastoma disease progression shows extensive heterogeneity in time and space.** *Nat Med.* 2018 Oct;24(10):1611-1624. doi: 10.1038/s41591-018-0156-x. Epub 2018 Aug 27.

36. Lawson JT, Tomazou EM, Bock C, Sheffield NC. **MIRA: an R package for DNA methylation-based inference of regulatory activity.** *Bioinformatics.* 2018 Aug 1;34(15):2649-2650. doi: 10.1093/bioinformatics/bty083.

37. Lee SE, Song J, Bösl K, Müller AC, Vitko D, Bennett KL, Superti-Furga G, Pandey A, Kandasamy RK, Kim MS. **Proteogenomic Analysis to Identify Missing Proteins from Haploid Cell Lines.** *Proteomics.* 2018 Apr;18(8):e1700386. doi: 10.1002/pmic.201700386.

38. Lowe R, Barton C, Jenkins CA, Ernst C, Forman O, Fernandez-Twinn DS, Bock C, Rossiter SJ, Faulkes CG, Ozanne SE, Walter L, Odom DT, Mellersh C, Rakyan VK. **Ageing-associated DNA methylation dynamics are a molecular readout of lifespan variation among mammalian species.** *Genome Biol.* 2018 Feb 16; 19(1):22. doi: 10.1186/s13059-018-1397-1.

39. Maas C, Lüftinger R, Krois W, Matthes-Martin S, Bayer G, Boztug K, Metzelder M. **EBV-positive B-cell lymphoma manifestation of the liver in an infant with RAG1 severe combined immunodeficiency disease.** *Pediatr Blood Cancer.* 2018 Sep; 65(9):e27258. doi: 10.1002/pbc.27258. Epub 2018 Jun 1.

40. Mughal TI, Lion T, Abdel-Wahab O, Mesa R, Scherber RM, Perrotti D, Mauro M, Verstovsek S, Saglio G, Van Etten RA, Kralovics R. **Precision immunotherapy, mutational landscape, and emerging tools to optimize clinical outcomes in patients with classical myeloproliferative neoplasms.** *Hematol Oncol.* 2018 Dec;36(5):740-748. doi: 10.1002/hon.2537.

41. Mullapudi ST, Helker CS, Boezio GL, Maischein HM, Sokol AM, Guenther S, Matsuda H, Kubicek S, Graumann J, Yang YHC, Stainier DY. **Screening for insulin-independent pathways that modulate glucose homeostasis identifies androgen receptor antagonists.** *Elife.* 2018 Dec 6;7. pii: e42209. doi: 10.7554/eLife.42209.

42. Nabet B, Roberts JM, Buckley DL, Paulk J, Dastjerdi S, Yang A, Leggett AL, Erb MA, Lawlor MA, Souza A, Scott TG, Vittori S, Perry JA, Qi J, Winter GE, Wong KK, Gray NS, Bradner JE. **The dTAG system for immediate and target-specific protein degradation.** *Nat Chem Biol.* 2018 May;14(5):431-441. doi: 10.1038/s41589-018-0021-8. Epub 2018 Mar 26.

43. Nieuwenhuis J, Brummelkamp TR. **The Tubulin Detyrosination Cycle: Function and Enzymes.** *Trends Cell Biol.* 2018 Sep 10. pii: S0962-8924(18)30141-7. doi: 10.1016/j.tcb.2018.08.003. [Epub ahead of print] Review.

44. Obermayer G, Afonyushkin T, Binder CJ. **Oxidized low-density lipoprotein in inflammation-driven thrombosis.** *J Thromb Haemost.* 2018 Mar;16(3):418-428. doi: 10.1111/jth.13925.

45. Pattaroni C, Watzenboeck ML, Schneidegger S, Kieser S, Wong NC, Bernasconi E, Pernot J, Mercier L, Knapp S, Nicod LP, Marsland CP, Roth-Kleiner M, Marsland BJ. **Early-Life Formation of the Microbial and Immunological Environment of the Human Airways.** *Cell Host Microbe.* 2018 Dec 12; 24(6):857-865.e4. doi: 10.1016/j.chom.2018.10.019.

46. Pemovska T, Bigenzahn JW, Superti-Furga G. **Recent advances in combinatorial drug screening and synergy scoring.** *Curr Opin Pharmacol.* 2018 Oct; 42:102-110. doi: 10.1016/j.coph.2018.07.008. Epub 2018 Sep 5. Review.

47. Perugorria MJ, Esparza-Baquer A, Oakley F, Labiano I, Korosec A, Jais A, Mann J, Tiniakos D, Santos-Laso A, Arbelaiz A, Gawish R, Sampedro A, Fontanellas A, Hijona E, Jimenez-Agüero R, Esterbauer H, Stoiber D, Bujanda L, Banales JM, Knapp S, Sharif O, Mann DA. **Non-parenchymal TREM-2 protects the liver from immune-mediated hepatocellular damage.** *Gut.* 2018 Jan 27. pii: gutjnl-2017-314107. doi: 10.1136/gutjnl-2017-314107. [Epub ahead of print]

48. Pfajfer L, Mair NK, Jiménez-Heredia R, Genel F, Gulez N, Ardeniz Ö, Hoeger B, Bal SK, Madritsch C, Kalinichenko A, ChandraArdy R, Gerçeker B, Rey-Barroso J, Ijspeert H, Tangye SG, Simonitsch-Klupp I, Huppa JB, van der Burg M, Dupré L, Boztug K. **Mutations affecting the actin regulator WD repeat-containing protein 1 lead to aberrant lymphoid immunity.** *J Allergy Clin Immunol.* 2018 Nov; 142(5):1589-1604.e11. doi: 10.1016/j.jaci.2018. 04.023. Epub 2018 May 8.

49. Porpaczy E, Tripolt S, Hoelbl-Kovacic A, Gisslinger B, Bago-Horvath Z, Casanova-Hevia E, Clappier E, Decker T, Fajmann S, Fux DA, Greiner G, Gueltekin S, Heller G, Herkner H, Hoermann G, Kiladjian JJ, Kolbe T, Kornauth C, Krauth MT, Kralovics R, et al. **Aggressive B-cell lymphomas in patients with myelofibrosis receiving JAK1/2 inhibitor therapy.** *Blood.* 2018 Aug 16; 132(7):694-706. doi: 10.1182/blood-2017-10-810739. Epub 2018 Jun 14.

50. Prusty BK, Gulve N, Chowdhury SR, Schuster M, Strempel S, Descamps V, Rudel T. **HHV-6 encoded small non-coding RNAs define an intermediate and early stage in viral reactivation.** *NPJ Genom Med.* 2018 Sep 5;3:25. doi: 10.1038/s41525-018-0064-5.

51. Puchner A, Saferding V, Bonelli M, Mikami Y, Hofmann M, Brunner JS, Caldera M, Goncalves-Alves E, Binder NB, Fischer A, Simader E, Steiner CW, Leiss H, Hayer S, Niederreiter B, Karonitsch T, Koenders MI, Podesser BK, O'Shea JJ, Menche J, Smolen JS, Redlich K, Blüml S. **Non-classical monocytes as mediators of tissue destruction in arthritis.** *Ann Rheum Dis.* 2018 Oct;77(10):1490-1497. doi: 10.1136/annrheumdis-2018-213250. Epub 2018 Jun 29.

52. Que X, Hung MY, Yeang C, Gonen A, Prohaska TA, Sun X, Diehl C, Määttä A, Gaddis DE, Bowden K, Pattison J, MacDonald JG, Ylä-Herttuala S, Mellon PL, Hedrick CC, Ley K, Miller YI, Glass CK, Peterson KL, Binder CJ, Tsimikas S, Witztum JL. **Oxidized phospholipids are proinflammatory and proatherogenic in hypercholesterolaemic mice.** *Nature.* 2018 Jun; 558(7709):301-306. doi: 10.1038/s41586-018-0198-8. Epub 2018 Jun 6.

53. Ronceray L, Friesenbichler W, Hutter C, Lakatos K, Krizmanich W, Amann G, Boztug K, Kager L, Mann G, Attarbaschi A. **Thoracic Actinomycosis With Infiltration of the Spine: An Oncological Pitfall.** *J Pediatr Hematol Oncol.* 2018 Aug; 40(6):468-471. doi: 10.1097/MPH. 0000000000001035.

54. Rudnick RB, Chen Q, Stea ED, Hartmann A, Papac-Milicevic N, Person F, Wiesener M, Binder CJ, Wiech T, Skerka C, Zipfel PF. **FHR5 Binds to Laminins, Uses Separate C3b and Surface-Binding Sites, and Activates Complement on Malondialdehyde-Acetaldehyde Surfaces.** *J Immunol.* 2018 Apr 1; 200(7):2280-2290. doi: 10.4049/jimmunol.1701641.

55. Sage AP, Tsiantoulas D, Binder CJ, Mallat Z. **The role of B cells in atherosclerosis.** *Nat Rev Cardiol.* 2018 Nov 8. doi: 10.1038/s41569-018-0106-9. [Epub ahead of print] Review.

Saulnier-Blache JS, Wilson R, Klavins K, Graham D, et al. **Ldlr$^{-/-}$ and ApoE$^{-/-}$ mice better mimic the human metabolite signature of increased carotid intima media thickness compared to other animal models of cardiovascular disease.** *Atherosclerosis.* 2018 Sep; 276:140-147. doi: 10.1016/j.atherosclerosis.2018.07.024. Epub 2018 Jul 21.

56. Schwinger W, Urban C, Ulreich R, Sperl D, Karastaneva A, Strenger V, Lackner H, Boztug K, Albert MH, Benesch M, Seidel MG. **The Phenotype and Treatment of WIP Deficiency: Literature Synopsis and Review of a Patient With Pre-transplant Serial Donor Lymphocyte Infusions to Eliminate CMV.** *Front Immunol.* 2018 Nov 2; 9:2554. doi: 10.3389/fimmu.2018.02554. eCollection 2018. Review.

57. Sedlyarov V, Eichner R, Girardi E, Essletzbichler P, Goldmann U, Nunes-Hasler P, Srndic I, Moskovskich A, Heinz LX, Kartnig F, Bigenzahn JW, Rebsamen M, Kovarik P, Demaurex N, Superti-Furga G. **The Bicarbonate Transporter SLC4A7 Plays a Key Role in Macrophage Phagosome Acidification.** *Cell Host Microbe.* 2018 Jun 13; 23(6):766-774.e5. doi: 10.1016/j.chom.2018.04.013. Epub 2018 May 17.

58. Serwas NK, Huemer J, Dieckmann R, Mejstrikova E, Garncarz W, Litzman J, Hoeger B, Zapletal O, Janda A, Bennett KL, Kain R, Kerjaschky D, Boztug K. **CEBPE-Mutant Specific Granule Deficiency Correlates With Aberrant Granule Organization and Substantial Proteome Alterations in Neutrophils.** *Front Immunol.* 2018 Mar 29; 9:588. doi: 10.3389/fimmu.2018.00588. eCollection 2018.

59. Sharma A, Halu A, Decano JL, Padi M, Liu YY, Prasad RB, Fadista J, Santolini M, Menche J, et al. **Controllability in an islet specific regulatory network identifies the transcriptional factor NFATC4, which regulates Type 2 Diabetes associated genes.** *NPJ Syst Biol Appl.* 2018 Jul 3; 4:25. doi: 10.1038/s41540-018-0057-0. eCollection 2018.

60. Sharma A, Kitsak M, Cho MH, Ameli A, Zhou X, Jiang Z, Crapo JD, Beaty TH, Menche J, Bakke PS, Santolini M, Silverman EK. **Integration of Molecular Interactome and Targeted Interaction Analysis to Identify a COPD Disease Network Module.** *Sci Rep.* 2018 Sep 27;8(1):14439. doi: 10.1038/s41598-018-32173-z.

61. Simovski B, Kanduri C, Gundersen S, Titov D, Domanska D, Bock C, Bossini-Castillo L, Chikina M, Favorov A, Layer RM, Mironov AA, Quinlan AR, Sheffield NC, Trynka G, Sandve GK. **Coloc-stats: a unified web interface to perform colocalization analysis of genomic features.** *Nucleic Acids Res.* 2018 Jul 2;46(W1):W186-W193. doi: 10.1093/nar/gky474.

62. Skjærven KH, Jakt LM, Fernandes JMO, Dahl JA, Adam AC, Klughammer J, Bock C, Espe M. **Parental micronutrient deficiency distorts liver DNA methylation and expression of lipid genes associated with a fatty-liver-like phenotype in offspring.** *Sci Rep.* 2018 Feb 14; 8(1):3055. doi: 10.1038/s41598-018-21211-5.

63. Skucha A, Ebner J, Schmöllerl J, Roth M, Eder T, César-Razquin A, Stukalov A, Vittori S, Muhar M, Lu B, Aichinger M, Jude J, Müller AC, Győrffy B, Vakoc CR, Valent P, Bennett KL, Zuber J, Superti-Furga G, Grebien F. **MLL-fusion-driven leukemia requires SETD2 to safeguard genomic integrity.** *Nat Commun.* 2018 May 18; 9(1):1983. doi: 10.1038/s41467-018-04329-y.

64. Skucha A, Ebner J, Grebien F. **SETD2 in MLL-rearranged leukemia - a complex case.** *Mol Cell Oncol.* 2018 Aug 13; 5(4):e1503492. doi: 10.1080/23723556.2018.1503492. eCollection 2018.

65. Spel L, Nieuwenhuis J, Haarsma R, Stickel E, Bleijerveld OB, Altelaar M, Boelens JJ, Brummelkamp TR, Nierkens S, Boes M. **Nedd4-Binding Protein 1 and TNFAIP3-Interacting Protein 1 Control MHC-1 Display in Neuroblastoma.** *Cancer Res.* 2018 Dec 1; 78(23):6621-6631. doi: 10.1158/0008-5472.CAN-18-0545.

66. Staring J, van den Hengel LG, Raaben M, Blomen VA, Carette JE, Brummelkamp TR. **KREMEN1 Is a Host Entry Receptor for a Major Group of Enteroviruses.** *Cell Host Microbe.* 2018 May 9;23(5):636-643.e5. doi: 10.1016/j.chom.2018.03.019. Epub 2018 Apr 19.

67. Staring J, Raaben M, Brummelkamp TR. **Viral escape from endosomes and host detection at a glance.** *J Cell Sci.* 2018 Aug 3; 131(15). pii: jcs216259. doi: 10.1242/jcs.216259. Review.

68. Szappanos D, Tschismarov R, Perlot T, Westermayer S, Fischer K, Platanitis E, Kallinger F, Novatchkova M, Lassnig C, Müller M, Sexl V, Bennett KL, Foong-Sobis M, Penninger JM, Decker T. **The RNA helicase DDX3X is an essential mediator of innate antimicrobial immunity.** *PLoS Pathog.* 2018 Nov 26;14(11):e1007397. doi: 10.1371/journal.ppat.1007397.

69. Tsafou K, Katschnig AM, Radic-Sarikas B, Mutz CN, Iljin K, Schwentner R, Kauer MO, Mühlbacher K, Aryee DNT, Westergaard D, Haapa-Paananen S, Fey V, Superti-Furga G, Toretsky J, Brunak S, Kovar H. **Identifying the druggable interactome of EWS-FLI1 reveals MCL-1 dependent differential sensitivities of Ewing sarcoma cells to apoptosis inducers.** *Oncotarget.* 2018 Jul 24; 9(57):31018-31031. doi: 10.18632/oncotarget.25760. eCollection 2018 Jul 24.

70. Tsiantoulas D, Sage AP, Göderle L, Ozsvar-Kozma M, Murphy D, Porsch F, Pasterkamp G, Menche J, Schneider P, Mallat Z, Binder CJ. **B Cell-Activating Factor Neutralization Aggravates Atherosclerosis.** *Circulation.* 2018 Jun 1. pii CIRCULATIONAHA.117.032790. doi: 10.1161/CIRCULATIONAHA.117.032790. [Epub ahead of print]

71. van Mierlo G, Dirks RAM, De Clerck L, Brinkman AB, Huth M, Kloet SL, Saksouk N, Kroeze LI, Willems S, Farlik M, Bock C, Jansen JH, Deforce D, Vermeulen M, Déjardin J, Dhaenens M, Marks H. **Integrative Proteomic Profiling Reveals PRC2-Dependent Epigenetic Crosstalk Maintains Ground-State Pluripotency.** *Cell Stem Cell.* 2018 Nov 14. pii: S1934-5909(18)30498-3. doi: 10.1016/j.stem.2018.10.017.

72. van Rijn JM, Ardy RC, Kuloğlu Z, Härter B, van Haaften-Visser DY, van der Doef HPJ, van Hoesel M, Kansu A, van Vugt AHM, Thian M, Kokke FTM, Krolo A, et al. **Intestinal Failure and Aberrant Lipid Metabolism in Patients With DGAT1 Deficiency.** *Gastroenterology.* 2018 Jul; 155(1):130-143.e15. doi: 10.1053/j.gastro.2018.03.040. Epub 2018 Mar 29.

73. Velimezi G, Robinson-Garcia L, Muñoz-Martínez F, Wiegant WW, Ferreira da Silva J, Owusu M, Moder M, Wiedner M, Rosenthal SB, Fisch KM, Moffat J, Menche J, van Attikum H, Jackson SP, Loizou JI. **Map of synthetic rescue interactions for the Fanconi anemia DNA repair pathway identifies USP48.** *Nat Commun.* 2018 Jun 11;9(1):2280. doi: 10.1038/s41467-018-04649-z.

74. Verger E, Soret-Dulphy J, Maslah N, Roy L, Rey J, Ghrieb Z, Kralovics R, Gisslinger H, Grohmann-Izay B, Klade C, Chomienne C, Giraudier S, Cassinat B, Kiladjian JJ. **Ropeginterferon alpha-2b targets JAK2V617F-positive polycythemia vera cells in vitro and in vivo.** *Blood Cancer J.* 2018 Oct 4;8(10):94. doi: 10.1038/s41408-018-0133-0.

75. Wingelhofer B, Maurer B, Heyes EC, Cumaraswamy AA, Berger-Becvar A, de Araujo ED, Orlova A, Freund P, Ruge F, Park J, Tin G, Ahmar S, Lardeau CH, Sadovnik I, Bajusz D, Keser GM, Grebien F, Kubicek S, Valent P, Gunning PT, Moriggl R. **Pharmacologic inhibition of STAT5 in acute myeloid leukemia.** *Leukemia.* 2018 May;32(5):1135-1146. doi: 10.1038/s41375-017-0005-9.

76. Wuerth JD, Habjan M, Wulle J, Superti-Furga G, Pichlmair A, Weber F. **NSs Protein of Sandfly Fever Sicilian Phlebovirus Counteracts Interferon (IFN) Induction by Masking the DNA-Binding Domain of IFN Regulatory Factor 3.** *J Virol.* 2018 Nov 12; 92(23). pii: e01202-18. doi: 10.1128/JVI.01202-18. Print 2018 Dec 1.

77. Zoghi S, Ziaee V, Hirschmugl T, Jimenez-Heredia R, Krolo A, Boztug K, Rezaei N. **Exome sequencing revealed C1Q homozygous mutation in Pediatric Systemic Lupus Erythematosus.** *Allergol Immunopathol (Madr).* 2018 Nov - Dec;46(6):594-598. doi: 10.1016/j.aller.2018.02.004. Epub 2018 May 5.

78. Zou X, Owusu M, Harris R, Jackson SP, Loizou JI, Nik-Zainal S. **Validating the concept of mutational signatures with isogenic cell models.** *Nat Commun.* 2018 May 1; 9(1):1744. doi: 10.1038/s41467-018-04052-8.

CeMM International PhD Program in Molecular Technologies and Systems Medicine

In 2018, eight PhD students successfully graduated from the CeMM PhD program:

Kseniya Khamina (Bergthaler group),
Cecilia Domínguez Conde (Boztug group),
Bernd Boidol (Kubicek group),
Martin Moder (Loizou group),
Simona Saluzzo (Knapp group),
Anna Skucha (Superti-Furga group),
Juliane Weißer (Binder group),
Michel Owusu (Loizou group).

Kseniya Khamina's graduation marked a milestone with 50 PhD students graduating from CeMM since the program started in 2006.

In the 12 years since the founding of the CeMM PhD program in 2006, we have welcomed over 100 international and enthusiastic students through our doors and 57 students have already successfully completed their PhD studies. We are proud of each individual student who has added his or her scientific and personal contributions to the growing legacy of the program.

Each year over 700 candidates from around the world apply to CeMM's international PhD program. We seek students whose keen interest in interdisciplinary teamwork and science will allow them to nurture the precise, personalized, predictive and preventive medicine of the future. To identify the best candidates, CeMM has established a multistep selection process, building up to a final three-day selection in Vienna. The successful candidates are offered a four-year scholarship, which covers university fees, work-related travel, salary and health insurance. The Medical University of Vienna awards the PhD degree.

Giulio Superti-Furga, Scientific Director and CEO of the Research Center of Molecular Medicine of the Austrian Academy of Sciences and Professor of Medical Systems Biology at the Medical University of Vienna, has been the Dean of the PhD program and responsible for all student affairs.

The goal of the PhD program is to enable and empower students with the ability to successfully design, execute, manage and explain a research project in modern molecular medicine. This is achieved through a strongly participatory and interactive program conceptualized in five 'modes': onboarding, collecting, connecting, contributing, offboarding. These guide the students through scientific excellence in data generation and validation to responsible and professional scientific citizenship.

In 2018, 13 new PhD students, from 8 different countries, joined our ranks. They commenced our PhD program with an introductory lecture series, covering a wide variety of topics, ranging from safety, sex and gender issues in research to ethical issues, patenting and soft skills. Additionally, all CeMM Principal Investigators introduced themselves and their research topics in detail. An additional faculty of experts from the Medical University of Vienna and beyond complemented our faculty on many subjects, anchoring the program in a wider context and providing practical examples. The introductory program capitalizes on the small-group dynamic and actively encourages a highly interactive discussion-based environment that strengthens the group dynamic and encourages participation and critical thinking.

The second phase of the introductory program is a one-month lab rotation. By dint of small projects carried out by the PhD students, they benefit from exposure to new labs, people and techniques. This has proven to be an excellent introduction to the collaborative nature and strong sense of community that characterize CeMM.

The introductory phase concludes with a 2-week-long in-house bioinformatics course. This is organized and led by Jörg Menche, Principal Investigator and Head of Bioinformatics at CeMM, and provides the students with the necessary knowledge on statistics and basic programming to process and analyze their data adequately.

After the introductory three months, students embark on their own PhD research while simultaneously completing all necessary university courses and checkpoints over the next 3-4 years. As part of this, they regularly attend the in-house Hot Topics Journal Club, where they present a critical review of recently published scientific papers, and take the opportunity to present their own work at our CeMM institute-wide seminars, held every Friday.

A PhD program is only as good as the students in it and this is why we invest so much time and effort in ensuring that, having selected the best, we nurture and allow them to grow and flourish. They are also the best placed to explain the CeMM difference and why it is such a special place to carry out a PhD:

Jakob-Wendelin Genger
1st-year PhD student, Bergthaler group
"Out of all the places I have seen so far, CeMM offers the best individual support for PhD students – ranging from the chance to present your work to the whole institute at the CeMM Recess to social activities like the CeMM Outings and the Social Hours to the fact that everyone in the building is open to give you input and support for your project. This makes CeMM a unique place that allows you to explore your full academic potential."

Christina Schüller,
1st-year PhD student, Kralovics group
"You might come to CeMM or even to Austria alone but as soon as you enter, you are part of a community. Starting here makes the whole expertise gathered at CeMM available to you, which ranges from sequencing to compound screening to medical knowledge."

Loan Vulliard,
2nd-year PhD student, Menche group
"CeMM's international PhD program is an amazing opportunity to learn and grow in a supportive environment, in which we can reach our full scientific potential. Thanks to an open-minded and collaborative mindset, CeMM is everything needed to transform the curiosity of its researchers into rigorous and innovative scientific papers, and to share them not only within our fields but with the general audience at large. Regular social events and the general kindness of everyone here turns this process into an enjoyable and empowering experience."

Peter Traxler,
3rd-year PhD student, Bock group
"Starting a PhD at CeMM meant joining not just a lab but a whole institute. The strong collaborative mind-set is reflected in the everyday life of PhD students beginning with a placement in another laboratory within CeMM to scientific retreats fostering shared projects as well as getting valuable input during Friday seminar presentations in front of the entire scientific community. This open and informed culture enabled many a perspective-changing elevator ride and provides a strong network for future endeavors."

Federica Quattrone,
4th-year PhD student, Knapp group
"The core strength of CeMM is the bright and cheerful community that builds it. The variety of educational and cultural backgrounds is what makes the local community extraordinary. Here you can build meaningful lifetime connections with your peers, who will be there to cheer you up and help whenever needed. Whenever you need to discuss your research project, or a friend to celebrate with, or someone to help assemble your furniture, you can be sure: you'll find a CeMMie by your side."

Michael Caldera,
4th-year PhD student, Menche group
"One of the great things for me is that you become a part of a scientific community, where you can benefit from a stimulating and collaborative studying and working environment, collaborating with people from different areas of work and departments on exciting and groundbreaking projects. As a computational biologist especially, there have been many great opportunities for me to work on various interesting projects from different fields over the last few years."

EU Libra Project Activities

LIBRA is an EC H2020-funded project with the stated aim of unifying innovative efforts of European research centers to achieve gender equality in academia. It involves ten life sciences research institutes from ten European countries, all members of the EU-Life group, promoting excellence in life sciences. CeMM, in collaboration with the Max Delbrück Center for Molecular Medicine, Berlin, coordinates LIBRA's centralized activities to recruit without gender bias. Further topics covered by the LIBRA project will be career development and training, work-life balance, and sex and gender dimensions of research.

Unconscious Bias Workshops
On Tuesday, June 19, we invited Femi Otitoju from Challenge Consultancy Limited, UK, back to CeMM to hold additional workshops on unconscious bias. This time she gave sessions for technicians, PhD students and postdocs. With examples from mass media, various case studies and evidence-based reports from academia, the workshop helped our colleagues examine their unconscious bias and develop tools to recognize and combat it.

Sex and Gender in Research Workshop
In September 2018, CeMM was represented at a workshop on Sex and Gender in Research and Experimental Design at the Babraham Institute in Cambridge by Gabriel Ó Ríordáin, Head of Scientific Support at CeMM. After introductions, there were lectures by Sabine Oertelt-Prigione, Natasha Karp, Peter Brown, Irene Miguel-Aliga, Stephane Berghmans, Pavel Ovseiko and Wilbert Zwart. There was also a panel discussion on the topic. The audience was varied with representatives from funding organizations, publishers, EU-Life partners, scientists, administrators, pharma and outreach.

Annual LIBRA Meeting
Also in September, the annual LIBRA meeting was held at the Babraham Institute in Cambridge, attended By Binia Meixner, Head of HR at CeMM.

LIBRA Poster Campaign
In November, a poster campaign on promoting the benefits of work-life balance (WLB) was started at CeMM using posters developed and kindly shared as part of the H2020 LIBRA consortium. Posted throughout the building and on our information screens, the posters challenged family roles and stimulated awareness and discussion about issues such as career aspirations, the gender pay gap and sharing care work.

For more information about LIBRA and CeMM's activities in this project please visit:
www.eu-libra.eu and *cemm.at/career/libra*

Technology Transfer

An integral component of CeMM's strategy is to identify and support translational initiatives that promise to have an impact on medicine. CeMM therefore considers that safeguarding and valorizing its research output is an integral part of its societal responsibility.

CeMM offers regular trainings to its scientific staff on the practical and conceptual issues of patenting. Patent experts from Vossius & Partner Munich assist the researchers and the CeMM Directors in the generation, management and commercialization of CeMM's Intellectual Property Portfolio. Business opportunities arising from its research projects and the innovative ideas of CeMM's employees can result in the founding of new start-up companies, the enrichment of the portfolio of existing companies, and in the out-licensing of patents or in partnerships involving consultancy, know-how and technology transfer. Boehringer Ingelheim, Qiagen and Diagenode, to name a few, have been valuable industry and pharma partners in this respect.

Research and Technology Transfer Highlights of the Past Years:

+ Pharmacoscopy is a method developed at CeMM that combines high-content imaging of individual cell behavior, computational analysis, as well as hematological and immunological competence in a translational/medical setting – all with a focus on determining the therapeutic value of hundreds to thousands of (single or synergistic) chemotherapy options for an individual patient at a given time in their treatment.
+ In collaboration with the Medical University of Vienna, CeMM has been able to decode a genetic mutation (CALR) responsible for about 15% of myeloproliferative neoplasia cases. This newly identified mutation filled the gap in the molecular pathogenesis of MPN and brought a new diagnostic kit to many MPN patients.

CeMM currently holds about 10 patent families, has several licensing agreements and is a founding partner of the following spin-off companies to further develop and apply its research results:

Haplogen is a biopharmaceutical company with the mission to improve human health by combating infectious disease. Employing a proprietary genetics technology to identify host factors, Haplogen is building a pipeline of therapeutic programs in the area of virus-caused diseases. *www.haplogen.com*

MyeloPro is a research stage biopharmaceutical company, aiming to develop innovative therapeutics for the treatment of blood diseases/myeloproliferative neoplasms (MPNs). MyeloPro's research focuses on the development of antibodies that target the mutated form of the protein called calreticulin (CALR). *www.myelopro.com*

Allcyte is a biotech start-up company focused on functional drug testing in primary human material. With the so-called "Pharmacoscopy" high-content imaging platform, Allcyte supports pre-clinical drug development and clinical decision-making services by helping physicians find the right drug for the right patients, and pharmaceutical companies identify the most promising indications for their drugs and drug candidates. *www.allcyte.com*

Aelian Biotechnology combines CRISPR screening with single-cell sequencing, leveraging two transformative technologies to enable genetic screening for complex phenotypes. The approach has broad applications in identifying novel drug targets or elucidating unknown mechanisms of action of drugs. *www.aelianbio.com*

CeMM is in contact with several companies to build even more strategic and sustainable partnerships for commercialization and translational activities. For more information, please contact Anita Ender, Administrative Director of CeMM: *ip@cemm.oeaw.ac.at*

CeMM's Mother Organization, Strategic Partnerships and Collaborations

Austrian Academy of Sciences
CeMM, the Research Center for Molecular Medicine is a constituent institute falling under the auspices of the Austrian Academy of Sciences. Founded in 1847 as a learned society, the Austrian Academy of Sciences has since developed to become the pre-eminent, "non-university" academic research organization in Austria. Cognizant of its social, cultural and economic responsibilities, the Academy conducts basic research, much of which is developed into practical application, and its members support this function by making their broad range of expertise available in both a practical sense and in an advisory capacity to the public and to decision-makers across the business and political spectrum. The Academy has its headquarters in the historic and impressive old university building in the very heart of Vienna. The Academy has constituted 28 research institutions employing 1,700 scientists and support staff located all over Austria. CeMM was founded in 2005 as an interdisciplinary research institute committed to advancing the understanding of human diseases through basic and biomedical research. Its research profile is based upon the quality of its science, its potential for innovation, and the sustainability of its output, which together, in the few years since its inception, have already made CeMM a flagship institute of the Academy and a key player for biomedical research and precision medicine in the heart of Europe. *www.oeaw.ac.at*

The Medical University of Vienna
The Medical University of Vienna (MUV) is one of CeMM's most important research partners and plays a key role in the career development of CeMM students and faculty. The MUV is a highly dynamic research organization, competent in the treatment of a very wide range of human ailments with a tradition of innovation that goes back centuries. Situated in its purpose-built building on the campus of the MUV and the General Hospital (AKH), CeMM is in a prime location within Austria's largest medical research complex to fulfill its mission which, by its very nature, implies and requires close collaboration between basic researchers and clinicians and an indispensable interactive mindset. *www.meduniwien.ac.at*

EU-LIFE
EU-LIFE, established in 2012, is a life sciences research partnership set up to support and strengthen European excellence in research. It is an alliance of 13 renowned research centers (~540 research groups, 7,400 scientists). Partners operate with similar principles of excellence, external reviews, independence, competitiveness and with the same international perspective. During difficult economic times and within a highly competitive international research landscape, the alliance partners decided to join forces to address complex questions, share knowledge and influence research policy in life sciences, with a view to pushing European science forward. To reach EU-LIFE goals, the partners established dedicated working groups to reflect on specific topics of common interest, such as technology transfer, translational research, training, science communication and others. *www.eu-life.eu*

LBI-RUD
The Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD) was founded by the Ludwig Boltzmann Gesellschaft in 2016 in conjunction with its partner institutions CeMM, the Medical University of Vienna, and the Children's Cancer Research Institute (CCRI) of the St. Anna Children's Hospital. The research focus of the LBI-RUD under the leadership of Kaan Boztug is on rare diseases of the immune system, hematopoiesis and the nervous system, which all together account for more than 50% of all rare diseases. The goal of LBI-RUD is to perform top-level science that seminally contributes to diagnostics and therapeutics, but also to address societal, ethical and economical aspects of rare diseases. *www.rud.lbg.ac.at*

National and International Collaborations
CeMM operates in a unique mode of super-cooperation, connecting biology with medicine, experiments with computation, discovery with translation, and science with society and the arts. In addition to many international connections, CeMM has excellent collaborative partnerships with the Austrian research community. In 2018, we were particularly grateful to the University of Vienna, the Vienna University of Technology (TU Wien) and the Medical University of Innsbruck for generously supporting our call for Adjunct Principal Investigators to broaden CeMM's scientific competence but also to further strengthen institutional ties and collaborations.

Supporters

It has been a long and so-far successful tradition to invite notable people to give us their take on CeMM's philosophies and performance, which we include in our annual research reports. These people are both advisors and supporters of CeMM and have included holders of prominent positions in government, industry and academia, accomplished artists, comedians and a sporting World Champion.

The photographs of those who have imparted their testimonials in the past are presented in the following pages. We believe that we can learn from their opinions and benefit from their approval and encouragement.

The statements of the supporters can be found on the CeMM website: *cemm.at/artssociety/supporters*

Prof. Dr. Josef Penninger Scientific Director, Life Sciences Institute Vancouver, UBC

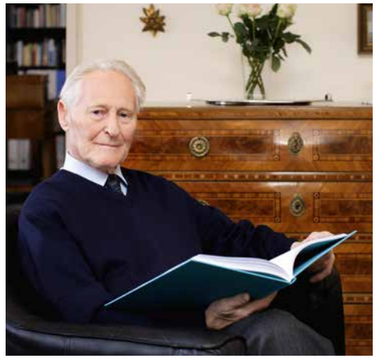
Mag. Georg Kapsch
President of the Federation of Austrian Industries

Dr. Henrietta Egerth Managing Director of the Austrian Research Promotion Agency (FFG)

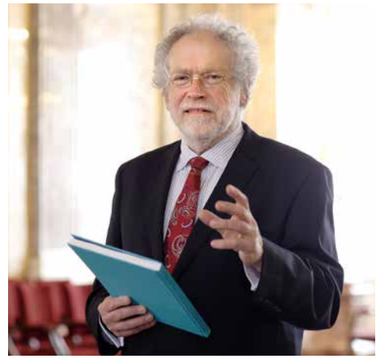
Margit Fischer
Chairwoman of the Science Center Network Foundation

Prof. Dr. Gaia Novarino Institute of Science and Technology Austria, Klosterneuburg

Dr. Hannes Androsch Chair, Austrian Council for Research and Technology Development



Prof. Dr. Hans Tuppy Former Federal Minister, Former President of FWF and ÖAW



Prof. Dr. Anton Zeilinger
President of the Austrian Academy of Sciences

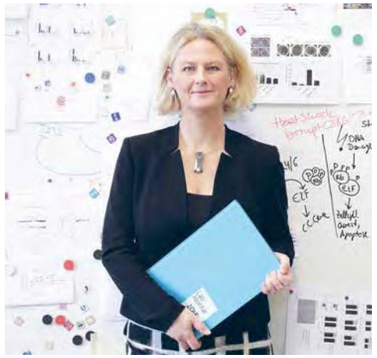
Prof. Dr. Gabriela-Verena Kornek
Medical Director of the Vienna General Hospital

Prof. Dr. Alexander Van der Bellen
President of the Austrian Republic

Professor Jean-Pierre Bourguignon
President of the European Research Council

Prof. Dr. Carl-Henrik Heldin Director, LICR, Uppsala Univ., SE, Chairman Board of the Nobel Foundation

Dr. Sigrid Pilz
Patient Advocate of the City of Vienna

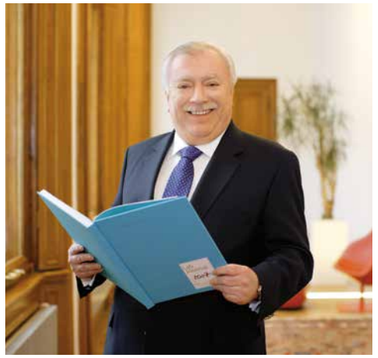


Professor Dr. Veronika Sexl Institute of Pharmacology and Toxicology, University of Veterinary Medicine, Vienna

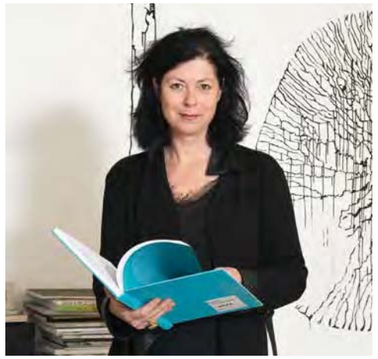
Prof. Dr. Ewald Nowotny
Governor Oesterreichische Nationalbank

Walking Chair
Artists

Dr. Johanna Rachinger Director General of the Austrian National Library, Member of the Senate of the ÖAW



Dr. Michael Häupl
Mayor of the City of Vienna



Eva Schlegel
Artist

Prof. Dr. Richard Flavell Sterling Professor of Immunobiology, Yale School of Medicine, USA

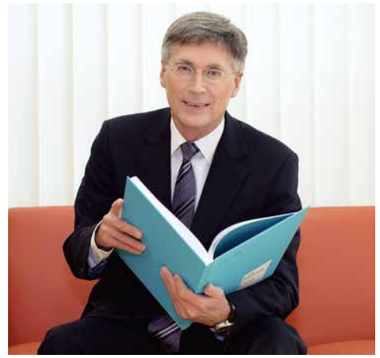
Prof. Dr. Markus Aspelmeyer
Faculty of Physics, University of Vienna and VCQ

Dr. Werner Lanthaler, MBA, MPA
Chief Executive Officer of Evotec AG

Dipl. Ing. Dr. Sabine Herlitschka, MBA Chief Executive Officer and Chief Technology Officer, Infineon Technologies Austria AG

Prof. Dr. Peter Schuster
Former President of the Austrian Academy of Sciences

Mag.ª Brigitte Ederer
Former Member of the Executive Board of Siemens AG



Prof. Dr. Reinhard Krepler
Former Director of the Vienna General Hospital

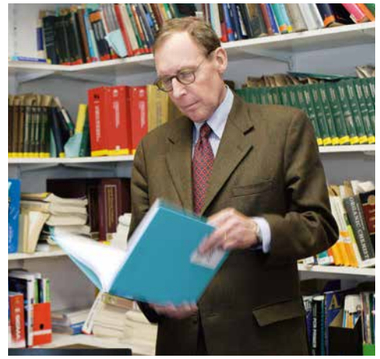
Dr. Andreas Mailath-Pokorny
former City Councilor for Culture and Science, Vienna

Prof. Dr. Fabiola Gianotti
Director-General of CERN, Geneva

Prof. Dr. David Livingston Deputy Director, Dana-Farber/Harvard Cancer Center, Boston

Dr. Sonja Hammerschmid
Former Federal Minister for Education

Prof. Dr. Georg Stingl Former President of the Section for Natural Sciences of the ÖAW

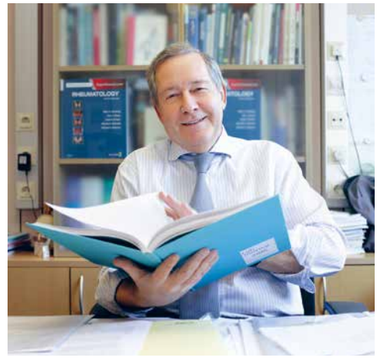


Prof. Dr. Bernd Binder † Department of Vascular Biology and Thrombosis Research, MUV

Prof. Dr. Gustav Ammerer Group Leader, Max F. Perutz Laboratories, Business Angel, Vienna

Peter Kogler
Artist

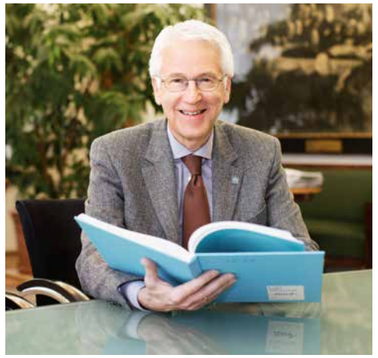
Brigitte Kowanz
Artist



Prof. Dr. Josef Smolen Head of Division of Rheumatology, Medical University of Vienna

Mag.ª Monika Kircher-Kohl Former Chief Executive Officer, Infineon Technologies Austria AG

Stermann & Grissemann
Comedians, TV Stars, Compères "Willkommen Österreich"



Prof. Dr. Wolfgang Schütz
Former Rector, Medical University of Vienna

Dorothee Golz
Artist

Dr. Johannes Hahn
Commissioner of the European Union

Dr. Beatrix Karl
Former Austrian Federal Minister of Science and Research

Mag.ª Barbara Prammer † President of the Austrian National Council, Member of the Senate of the ÖAW

Cardinal Christoph Schönborn
Archbishop of Vienna

Professor DI Dr. Edeltraud Hanappi-Egger
Rector, Vienna University of Economics and Business

Dr. Michaela Fritz
Vice Rector of the Medical University of Vienna

Prof. Dr. Markus Müller
Rector, Medical University of Vienna

Prof. Dr. Bernhard Felderer
Former Director, Institute for Advanced Studies, Vienna

Niki Lauda
F1 World Champion and Airline Founder

Dr. Heinz Fischer
Former President of the Austrian Republic

Dr. Agnes Husslein-Arco Former Director of the Belvedere Palace Museum and 21er Haus

Prof. Dr. Helmut Denk
Former President of the Austrian Academy of Sciences

Thomas Feuerstein
Artist

Prof. Dr. Christoph Zielinski former Director of the CCC Vienna and Scientific Director of the Vienna Cancer Center

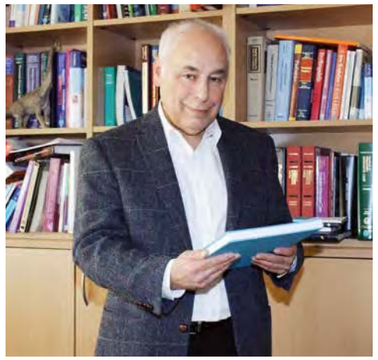
Ulrike Lunacek
Former Vice President of the European Parliament

Robert Palfrader Austrian comedian in his most famous social satire role as the (fictitious) Austrian Emperor

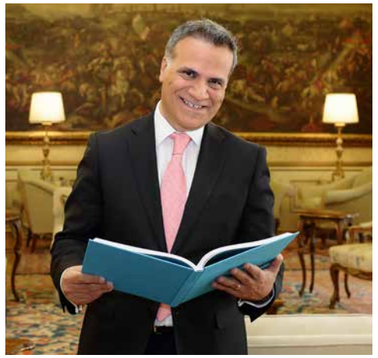
Jo Bury Managing Director, VIB Belgium
Board of Directors, eu-life

Prof. Dr. Harald zur Hausen
Winner of the Nobel Prize for Medicine 2008

Prof. Dr. Nadia Rosenthal Director, The Jackson Laboratory for Mammalian Genetics, USA

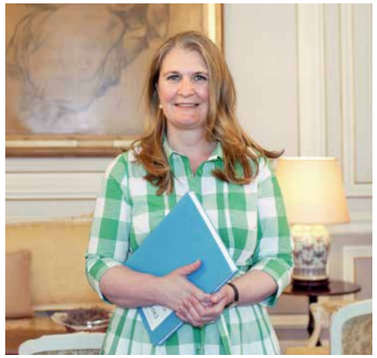


Prof. Dr. Arnold Pollak Former Head of the Department of Pediatrics and Adolescent Medicine, MUV



Giorgio Marrapodi
Former Ambassador of Italy to the Republic of Austria

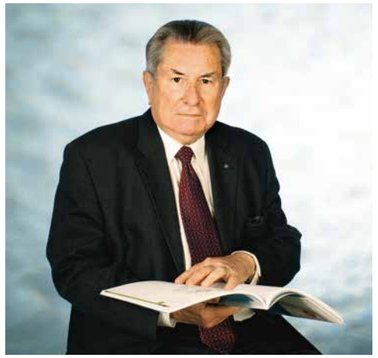
Prof. Dr. Ursula Schmidt-Erfurt Head of the Department of Ophthalmology and Optometrics at the MUV/AKH



Susan le Jeune d'Allegeershecque
Former Ambassador of the United Kingdom to Austria

Martin Walde
Artist

Dr. Benedikt and Beatrice Spiegelfeld
Sponsors



Prof. Dr. Max L. Birnstiel † Founding Director of the Research Institute of Molecular Pathology (IMP)

Prof. Dr. Isabelle Vernos member of the ERC Scientific Council, LIBRA Project Coordinator

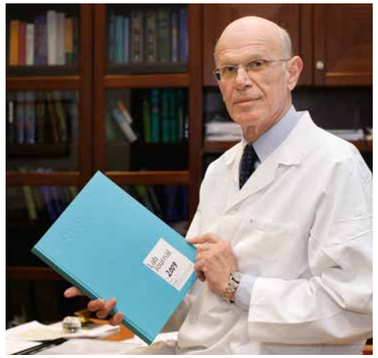
Philipp von Lattorff Country Managing Director Boehringer Ingelheim RCV Vienna

Prof. Dr. Christine Mannhalter Former Vice-President and interim President of the Austrian Science Fund

Prof. Dr. Helga Nowotny Founding Member and Former President, European Research Council

Prof. Martin A. Nowak, PhD Professor of Biology and Mathematics at Harvard University

Dr. Reinhold Mitterlehner Former Vice-Chancellor and Federal Minister of Science, Research and Economy



Prof. Dr. Helmut Gadner Former Director, St. Anna Children's Cancer Research Institute

Esther Stocker
Artist

Prof. Dr. Karlheinz Töchterle
Former Austrian Federal Minister of Science and Research

ÖAW Austrian Academy of Sciences
MUV Medical University of Vienna
AKH Vienna General Hospital

How to Reach CeMM

CeMM
Research Center for Molecular Medicine
of the Austrian Academy of Sciences
Lazarettgasse 14, AKH BT 25.3
Main Entrance, 1st Floor
1090 Vienna, Austria
Tel +43-1/40160-70 011
office@cemm.oeaw.ac.at
cemm.at

Acknowledgements

Marta Agostinho
Adriano Aguzzi
Michael Alram
Bruno Amati
Gustav Ammerer
Angelika Amon
Stylianos Antonarakis
Cheryl Arrowsmith
Anna Artaker
Markus Aspelmeyer
Patrick Auer
Gertraud Auer Borea d'Olmo
Vivian Balakrishnan
Christine Bandtlow
Sergio Barbanti
Ralf Bartenschläger
Hemma Bauer
Anette und Georg Baumann
Stephan Beck
Andreas Becker
Yasmine Belkaid
Monica Bettencourt-Dias
Andreas Bichl
Christa Binder
Ewan Birney
Margret and Kristy Birnstiel
Bruno Biton
Guido Boehmelt
Martin and Lucrezia Böhm
Stefan Böhm
Jean-Pierre Bourguignon
James Bradner
Georg Brasseur
Tilmann Bürckstümmer
Jörg Bürger
Jo Bury
Jürgen Busch
Erhard Busek
Meinrad and Irene Busslinger
Jakob Calice
Georg Casari
Claudia Caserini
Emmanuelle Charpentier
Aaron Ciechanover
Matthew Crawford
Philippe Cronet
George Daley
Thomas Decker
Nicolas Demaurex
Eva Dichand
Daniela Digles
Christiane Druml
Darren Dumlao
Katharina L. Dürr
Stefan Echinger
Gerhard Ecker
Aled Edwards
Henrietta Egerth
Alexander Ehrmann
Titanilla Eisenhart
Wilfried Ellmeier
Traudl Engelhorn
Heinz Engl
Harald Esterbauer
Heinz Faßmann
Jonas Feferle
Bernhard Felderer
Ulrike Felt
Thomas Feuerstein
Heinz und Margit Fischer
Richard Flavell
Michael Freissmuth
Michaela Fritz
Julia Fröhlich
Johannes Fröhlich
William Gahl
Jan Gehl
Fabiola Gianotti
Heinz Gisslinger
Wolfgang Gleissner
Laurie Glimcher
Dorthee Golz
Susanne Greber-Platzer
James D. Griffin
Bernhard Groehs
Barbara Hamilton
Brendon Hammer
Sonja Hammerschmid
Markus Hanakam
Edeltraud Hanappi-Egger
Michael Häupl
Hermann Hauser
Karl-Heinz Heider
Claudia Heilmann
Laura Heitman
Benjamin Hemmens
Carl-Henrik Heldin
Thomas Helleday
Markus Hengstschläger
Thomas Henzinger
David Hepworth
Sabine Herlitschka
Reinhard Hinterleitner
Helen Hobbs
Denis Hochstrasser
Wolfgang Holter
Andrew Hopkins
Barbara Horejs
Lukas Huber
Christoph Huber
Ad P. IJzerman
Harald Isemann
Ulrich Jäger
Ursula Jakubek
Kai Johnsson
Ulrich Jordis
Katharina Jungnickel
Wolfgang Kainz
Olli Kallioniemi
Georg Kapsch
Dan Kastner
Veronica Kaup-Hasler
Annie Kay
Douglas B. Kell
Janet Kelso
Bernhard Keppler
Markus Kiess
Christoph Klein
Stefan Knapp
Uta Knittel
Christian Köberl
Reinhart Kögerler
Peter Kogler
Ernst Kopper
Gabriele Kornek
Salome Koussoroplis
Nikolaus Krall
Klaus Kratochwill
Norbert Kraut
Michael Krebs
Reinhard Krepler
Hans Kupelwieser
Werner Lanthaler
Hans Lassmann
Klaus Lechner
Kriso Leinfellner
Maria Leptin
Stefanie Lichtwitz
Claudia Lingner
David Livingston
Dieter Lutz
Elisabeth Lutz
Christine Mannhalter
Vania Manolova
Iain Mattaj
Marjori Matzke
Andreas Mayer
Karl Mechtler
Jürgen Meier
Marlies Meisel
Alexander Meissner
Franziska Michor
Martin Moder
Thomas Moser
Maria Mota
Markus Müller
Michael Nentwich
Waltraud and Laurenz Niel
Magnus Nordborg
Gaia Novarino
Martin Nowak
Helga Nowotny
Primus Österreicher
Klaus Pamminger
Josef Penninger
Jan-Michael Peters
Lauren Peters
Fidel Peugeot
Klaus Pichler
Sigrid Pilz
Karl Emilio Pircher
Hidde Ploegh
Maria Polsterer-Kattus
Barbara Prainsack
Martin Prlic
Meinrad Rauchensteiner
Loredana Redaelli
Sai Reddy
Sonja Reiland
Jürgen Reinhardt
Achim Ribbe
Nadia Rosenthal
Paul Rübig
Günther Rupprechter
David Sabatini
Anna Sablina
Lia Scarabottolo
Gerhard Schadler
Ursula Schmidt-Erfurth
Georg Schneider
Renée Schröder
Dieter Schweizer
Luis Serrano
Klaus Seuwen
Veronika Sexl
Yigong Shi
Maria Sibilia
Karl Sigmund
Sabine Simmross
Jörg Simonitsch
Michael Sixt
Uwe Sleytr
Josef Smolen
Raz Somech
Andreas Sommer
Michael Speicher
Beatrix and Benedikt Spiegelfeld
Almuth Spiegler
Philipp Staber
Michael Stampfer
Claire Steppan
Georg Stingl
Esther Stocker
Patrick Stover
Alfred Strauch
Michela Stucchi
Stefanie Superti-Furga
Peter Swetly
Volkan Talazoglu
Elly Tanaka
Klement Tockner
Thomas Töller
Michael Trauner
Hans Tuppy
Jean-Robert Tyran
Alfonso Valencia
Peter Valent
Alexander van der Bellen
Matthew Vander Heiden
Isabelle Vernos
Gregory Vladimer
Philipp von Lattorff
Oswald Wagner
Martin Walde
Manfred Walkobinger
Barbara Weitgruber
Wolfgang Weninger
Georg Wick
Maria Wilhelm
Joseph Witztum
Mathias Woidy
Hans Wojta
Oleh Zagrijtschuk
Rudolf Zechner
Anton Zeilinger
Markus Zeitlinger
Christoph Zielinski
Harald zur Hausen

Copyrights
© CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences
Lazarettgasse 14, AKH BT 25.3
1090 Vienna, Austria
cemm.at

Overall Responsibility for Content
Giulio Superti-Furga, PhD
Scientific Director CeMM
Anita Ender
Administrative Director CeMM

Project Management
Eva Schweng, MAS
PR Manager CeMM

Editor Discussion Rounds
Giulio Superti-Furga

Art Direction and Design
Lichtwitz Leinfellner visuelle Kultur KG
Kriso Leinfellner
Stefanie Lichtwitz
Christina Güttl
Maximilian Strische

Photography
Lukas Beck (pp. 5, 14–15, 17, 32–33, 35, 38, 41, 42–43, 45, 48)
Roland Ferrigato (p. 104)
Thomas Fröhle (p. 139)
Niko Havranek (pp. 66, 106)
Sharona Jacobs (p. 141)
Justin A. Knight (pp. 84–85, 92–93)
Franzi Kreis (cover, pp. 9, 20–21, 23, 29, 50–51, 53, 57)
Hans Leitner (pp. 3, 139, 140, 143)
Claudia Marcelloni (p. 141)
Klaus Pichler (pp. 80–81, 95, 97, 103, 107)
Iris Ranzinger (pp. 139–145)
Michael Sazel (pp. 86–87, 88–89, 139–145)
Marietta Schupp (pp. 90–91)
Nicola Weiß (p. 109)
Laurent Ziegler (p. 109)
Johannes Zinner/Parlamentsdirektion (p. 109)

All other photos by CeMM

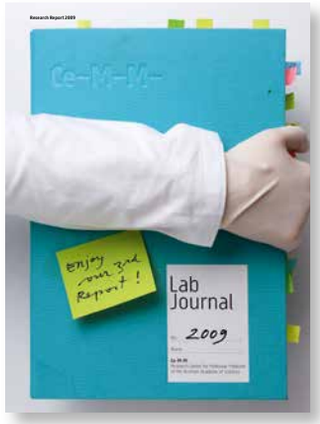
Print
Druckerei Gugler
Paper
MultiOffset, 120g

Fonts
Sys (by Fabrizio Schiavi)
DTL Documenta (by Frank E. Blokland)

Please order our previous 2007–2017 Research Reports with Eva Schweng or download at:
cemm.at/media/downloads/
CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences
eschweng@cemm.at
Lazarettgasse 14, AKH BT 25.3
1090 Vienna, Austria
Tel +43-1/40160-70 051
Fax +43-1/40160-970 000

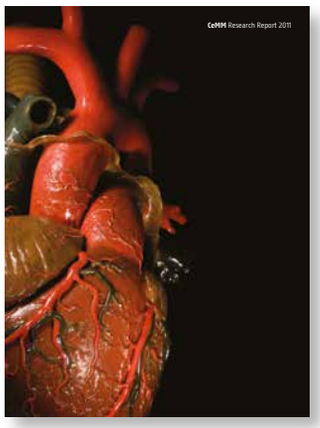
2007

2008



2009

2010

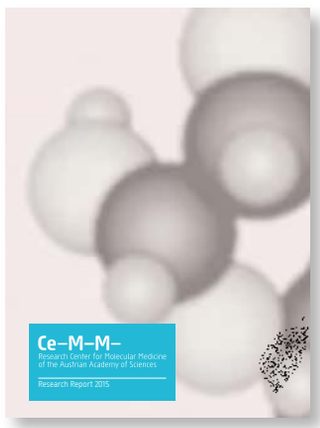


2011

2012

2013

2014



2015

2016

2017