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CeMM Research Report 2019

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Research Center for Molecular Medicine
of the Austrian Academy of Sciences

Research Report 2019

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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 2019

CeMM Directors
Anita Ender and
Giulio Superti-Furga

As we write the introduction to the 2019 CeMM Research Report, feeling privileged and proud, it is clear that it has been another extremely successful year. This is the 13th Research Report and nobody, even the most ardent enthusiasts among us, would have fully trusted that CeMM would be able to establish itself in just a decade as one of the most interesting and dynamic research powerhouses of Europe within the area of medical frontier research. Many things conspired to this outcome, numerous of which are linked to the support of the Austrian Academy of Sciences and the advantaged location and relationship with the Medical University of Vienna. We were ahead of the curve in using molecular data to understand and stratify therapy. We entertained strong, institutional and personal ties with the faculty of the Medical University, including Principal Investigators with dual affiliations. We established human genome/epigenome characterization and also proteomics, as one of the first institutions in Europe. We invested in medical bioinformatics, systems and network biology before it became fashionable. Ours was the first academic drug discovery laboratory (and possibly still is the only one in this country) to operate within a medical campus. We started collaborating with industry early on, valuing the respective areas of competence and keeping an eye-to-eye relationship, strictly avoiding contract research, but enabling basic research to go a step further towards application and medical impact. We have secured 12 ERC grants so far, in all categories. We focused on a highly attractive and competitive international PhD program early on. Importantly, we spun off laboratories for the Christian Doppler Society and Ludwig Boltzmann Society and five biotech start-ups, plus two in the making, employing an estimated number of one hundred individuals. It is this engaging and nurturing of the community that has propelled us into the fortunate state we are describing. In 2019, we obtained ample evidence of our privileged condition.

The winning of an ERC Starting Grant by Georg Winter for what are called "molecular glues", one of the areas in which CeMM is both investing and already securing a place among the prime movers, has been of major relevance. "Molecular glues" are bound to seriously upset and ultimately revolutionize traditional pharmacology in that they allosterically lead to a change in the "social" parameters of a target protein. They do not simply inhibit or activate, but can create new functions, short-circuiting regulatory interaction and, in a common desired outcome, lead to the degradation (i.e. destruction) of the target protein by arbitrating an encounter with the cell's "garbage disposal" machinery. Georg also won the 2019 Eppendorf Award for Young European Investigators. The impressive list of past winners reads as a "who's who" of Europe's leaders in molecular biology. Expect many new developments in the molecular glue field at CeMM in the years to come. The awarding of a rare and well-endowed ERC Synergy Grant to Joanna Loizou, alongside two eminent colleagues from the University of Cambridge and the ETH in Zurich, has been of exceptional importance. Joanna was the first female scientist in Austria to win such coveted support and one of the first to do so in the life sciences. This grant will propel the study of DNA repair forward, the process by which the integrity of the human genome is safeguarded against potentially disease-causing mutations caused by environmental exposure and simple genome duplication when cells divide. Because of Joanna and her collaboration network, Vienna is poised to establish itself on the research map of this highly important area of research for the years to come. We congratulate Joanna, Georg and their teams.

We are also proud that two CeMM Principal Investigators, who were recruited to Vienna by CeMM and have pioneered medical genetics on campus, have accepted positions that consolidate their involvement in medical research for the community and will secure their contributions to Austria for decades to come. Robert Kralovics, who discovered calreticulin, the "missing gene" responsible for myeloproliferative neoplasm, has moved to join the Department of Laboratory Medicine (KILM) of the Medical University of Vienna. Kaan Boztug, CeMM Principal Investigator and Director of the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases and a renowned expert in the genetics of pediatric tumors and innate immune disorders, has become Scientific Director of the St. Anna Children's Cancer Research Institute (CCRI). The laboratories of Robert and Kaan, who are now CeMM Adjunct Principal Investigators, will be close to CeMM, either in the adjacent Anna Spiegel building or in the St. Anna Research building a few hundred meters away. We wish them and their teams every success. CeMM is a place of training in all aspects and one of the measures to confirm its success and societal impact is to follow the career of its former employees. Not only group leaders, but also recent graduates and postdocs have secured excellent positions in leading laboratories worldwide or have taken the initiative to develop innovative technologies in commercial settings. In 2019, we started a CeMM Alumni Club – an initiative that will further strengthen our network and collaboration activities – for which we had an enjoyable and constructive kick-off meeting at the beginning of May.

In terms of achievements, it is impossible to summarize all the great work that was published in 2019 by "CeMMies", which is what we call ourselves. However, our colleagues will forgive that we chose to highlight papers that show the relationship of metabolism and key biological and pathophysiological processes. Two beautiful papers by Andreas Bergthaler's laboratory have shown that the metabolic "revolution" underlying wasting (or more properly cachexia) during viral infection is dependent on T-cell function, linking immunity to metabolism in a manner that we did not expect. In the second independent study, virus-induced interferon-dependent inactivation of T-cell function involves a previously unknown alteration of metabolism in the liver, again providing for an unexpected link between metabolism and immunity. In Stefan Kubicek's laboratory, metabolism was found to play a surprisingly important role even in the nucleus, where the laboratory was able to discover enzymes producing metabolites associated with chromatin, the "gene packaging machinery", and directly regulating nearby genes. Thus, 2019 was the year in which metabolism assumed center stage at CeMM. Please read the report to discover many of the other interesting findings of the year in the various laboratories. Needless to say, all these works are the result of intensive collaborations with many other laboratories on campus and all over the world.

The lion's share of research at CeMM is done by PhD students and by people generally referred to as postdocs. While every year, PhD students are chosen from almost a thousand applicants from all over the world and then enter a well-structured and intensively "nursed" training process, postdocs are less privileged. Recruited at different time points throughout the year, they are considered "adults" who should learn to take care of themselves as a way to prepare for the hardships of independence. Often, they end up on the job market for first independent positions when they are already in their late thirties, after exhausting years of non-stop, breathless research, where the only way to excel was to publish more and better than their peers. At CeMM, we decided that postdocs needed an "upgrade". To begin with, their status and responsibility should be recognized and visible, not just an afterthought to their PhDs. They should obtain specific training – including exposure to the clinical reality in hospitals and industrial research – that prepares them for independence or for any other professional development they may desire. Importantly, there should be better time-management to ensure nobody misses out on future opportunities. In 2019, CeMM started the "Pre-ERC Postdoc Program", so named specifically to address eligibility to the ERC Starting Grant scheme as a defined goal. The word "pre" – as opposed to "post" in postdoc – is to emphasize the brightness of the future to come rather than the past. In 2020, the first group of Pre-ERC postdocs will launch. We hope that this experiment will succeed and elevate the postdoc status at CeMM to a new value, hence helping us attract the most talented researchers.

Two brief comments on political issues that affect us as an international research community, one regarding Brexit: Like most researchers in Europe, we have been horrified by Brexit as it threatens to erect barriers where none previously existed, for example in the free movement of researchers across Europe and in the sharing of EU funds for common projects. Absolutely none of the great challenges that humanity faces – from life-threatening diseases and infections to climate change, from energy to food production – are local. As responsible members of the scientific community, we will do everything we can to ensure that we will be able to continue our collaboration with colleagues in the UK as well as possible. Once more, as it has in the past, research can show that shared knowledge generation and dissemination is, in itself, key to human prosperity and peace. Politics will not change the spirit in which scientists collaborate. Full stop. As we write, Europe's leaders are debating the budget of the European Union for the next seven years in light of Brexit. In the ensuing negotiations, the research budget needs to be ring-fenced and declared sacred. What more evidence of the need of more and better funded research does humanity need? From CeMM's perspective, understanding biology to comprehend, prevent and reduce disease is an absolute priority that should not be negotiable. Almost all else follows from this.

Like in science, where people from different countries, with different cultural backgrounds and resources share a common goal and motivation to advance knowledge and the search for truth, music brings together individuals, irrespective of their origin or location, and is a universal language that speaks to our emotions, in other words to our heart, brain, skin and other organs. It is therefore a perfect theme for the 2019 CeMM Research Report and we have chosen pop songs which include words and topics representing the overall research areas at CeMM. Nuno Maulide, Adjunct PI at CeMM and Professor at the University of Vienna, was our perfect ambassador of both worlds, being an excellent chemist and "Researcher of the Year", as well as a talented musician. He toured through the different CeMM and Adjunct Principal Investigator laboratories, playing the CeMM-blue piano, and giving credit to the individual groups and their research topics.

We hope you like the result and thank Eva Schweng, Stefanie Lichtwitz, Kriso Leinfellner, Christoph Burgstaller, Thomas Hötzeneder, Alexandra Tirendi, Juliett Zuza, Klaus Pichler and the entire creative team for bringing an abstract idea to life, as well as for providing us with an exceptional document and marvelous visuals and memories of a great team-building event. The result fits perfectly into the series of previous CeMM reports that have always aimed to be documents of historical significance for the institute while being a work of art in and of themselves. It summarizes CeMM's achievements, but also offers a glimpse into the unique environment, collaborative spirit, dedicated teams and corporate identity at CeMM, all of which are key components of the excellent research being performed at our institute. At the end of this report, we will give special credit to our wonderful long-term collaboration with *Lichtwitz Leinfellner visuelle Kultur KG,* who has accompanied CeMM since the beginning in terms of corporate design and has been showcasing some of our ideas. It is our common passion for music that compelled us to conceive this 13th record as our "Abbey Road" ambition, in reference to the Beatles' final masterpiece.

We thank all CeMM researchers, adjunct groups and admin staff for their participation in this collaborative Research Report "experiment" and for another year of hard and dedicated work to advance research.

The photos for the report and the video have been recorded in January and at beginning of February before the COVID-19 health crisis reached Europe. As a leading biomedical research institute, CeMM is committed to advancing the molecular understanding of the COVID-19 pandemic and the causative pathogen, SARS-CoV-2. We are willing to take up the challenge of assisting the medical world to fight the disease. Biomedical research on the virus and the disease will contribute substantially to informed policy decisions and, ultimately, the development of new treatments. Seldom has the importance of quality research for humanity been more evident.

Giulio Superti-Furga, Scientific Director
Anita Ender, Administrative Director

Science at CeMM

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Soundtrack of Research

As scientists, music accompanies us all the time. It comforts us when we work long hours. It often helps us focus. Some songs determine the rhythm of our pipetting. Good music, pop, rock, classical, jazz, hip-hop and more, makes up the soundtrack of our research lives.

When we celebrated CeMM's tenth anniversary in 2017, selected pop music gems accompanied the entrance of each actor embodying a biological entity, such as Monsieur Macrophage and the like. A highlight of 2019 was certainly the transformation of extraordinary CeMM Karl Landsteiner Lecturer Luke O'Neill into a guitar hero and bandleader who made us dance to an amazing set list of tunes for three hours. Some of you may remember the medley of songs by the Beatles, Daft Punk and other bands to which we danced (and won) the first ever "Dance your PhD" contest by *Science* magazine.

It is therefore not surprising that songs specifically referring to science, research and medicine play a special role in the collective culture defining our community. Lines at the top of the list are Sam Cooke's *"don't know much biology"* in "What a Wonderful World" or *"and all this science I don't understand"* in Elton John's "Rocket Man". The heart-wrenching ballad "The Scientist" by Coldplay takes a special place:

I was just guessing at numbers and figures
Pulling your puzzles apart
Questions of science, science and progress
Do not speak as loud as my heart

So, for this 2019 Research Report, we felt inspired to organize thematic chapters around pop songs featuring our key topics. Originally, we just wanted to refer to lyrics and artist quotes. But then, with typical CeMMish creativity and overconfidence, we decided to enact them by dancing. As we panicked about the daunting logistics thereof, we ultimately realized that the most effective musical communicator of science in the history of Austria was, in fact, a CeMMie who was willing to embrace the project. This is how fantastic chemist and pianist Nuno Maulide gained center stage. We identified six suitable songs, which inspired Nuno to a charming medley. Wonderful choreographer and dancer Alessandra Tirendi, assisted by her colleague Juliett Zuza, met with the teams of the different laboratories and created a concept.

The six songs and themes we quote are:

1. "I've got you Under my Skin" by Cole Porter and made world famous by Frank Sinatra. Clearly a dermatology/exposure/infection song. Ideal for the laboratory of Georg Stary, Joanna Loizou and Andreas Bergthaler.
2. "Light my Fire" by The Doors (mostly Robbie Krieger's song). Fire, inflammation, immunity, stress. Even personalized medicine. A good match for the research of Kaan Boztug, Thomas Reiberger and Andreas Villunger.
3. "Unchain my Heart", written by Bobby Sharp, made famous by Ray Charles first and later by Joe Cocker. Heart, pumping blood. Cardiovascular disease, blood disorders, hematopoiesis, clogged veins. Perfectly suitable for the discoveries of Christoph Binder and Robert Kralovics and their teams.
4. "Just like a Pill", by Pink, written by the singer together with Dallas Austin, a song about medication, expectation of effects, drug action, dosage. So, therapeutic innovation, chemical biology, new compounds. This is a song that represents the work of several laboratories run by CeMM Principal Investigators and Adjunct Principal Investigators, including Nuno Maulide, Miriam Unterlass, Georg Winter, Stefan Kubicek and Giulio Superti-Furga.
5. "Every Breath you Take" by Sting and performed by The Police is a song about breathing, the lungs and their complex neuronal control. Preserving the lung function. Protecting the lungs as interface to the environment. The complexity of physiological interactions. The many rare disorders affecting the body's complex homeostasis. A great fit for the research areas of Sylvia Knapp and Vanja Nagy.
6. "The Scientist", written and performed by the band Coldplay. This is a song about love but also about the fact that when you are in love, not even science matters. But it is cryptic – not clear who the scientist is. It is a deeply beautiful song. The song fits in with the activities of three groups whose work spans across everyone else at CeMM, like a network: Christoph Bock, Jörg Menche and Anita Ender's administration.

We hope you enjoy our concept.
The first (we think) research report ever to come with a choreography for some 200 people, is meant to highlight the cooperative nature of our research work at CeMM. The beehive of CeMM scientists and admin people, with the external adjunct teams, all moving in a coordinated dance. When one team hops, another reacts with a countermove. CeMM does indeed represent a corps de ballet, a chorus, a large music band. What next, a musical?

Science meets art.
Video recording with Nuno Maulide.


Dermatology


Loizou
Bergmaier

Skin/Dermatology

"I've Got You Under My Skin". Deep in the heart of CeMM's mission lies the commitment to reveal the molecular mechanisms underlying major diseases in humans with a view to improving diagnoses and developing targeted therapies with minimal side effects. Among its operating principles are collaboration and interdisciplinarity. Accordingly, CeMM formed exciting partnerships with the Children's Cancer Research Institute (CCRI), the Medical Universities of Vienna and Innsbruck, the Vienna University of Technology and the University of Vienna, shoring up expertise with adjunct principal investigators at these institutions.

While attributing diseases to the affected organs is helpful, it is not always sufficient. In fact, the largest human organ, the human skin, is involved in several – especially rare – diseases, and has proved highly worthwhile "getting under" in order to provide mechanistic insights into many illnesses.

CeMM has therefore expanded its original scope from cancer, immune disorders and infectious diseases to include dermatology with Adjunct Principal Investigator (PI) Georg Stary, as well as with Andreas Bergthaler's laboratory at CeMM examining the molecular basis of transmissible cancer in Tasmanian devils. Repair mechanisms in skin and other cancers are the research topic of the group of Joanna Loizou, who received a prestigious ERC Synergy Grant to further her studies.

Using the surface

The research projects of Georg Stary from the Department of Dermatology at the Medical University of Vienna, Co-Director of LBI-RUD, the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases, and Adjunct Principal Investigator at CeMM, focus on different aspects of host-pathogen interactions and the contribution of tissue-resident leukocytes to physiological and pathological immune responses. Currently, his group is studying the biology, longevity, turnover and function of tissue-resident leukocytes in peripheral tissue using the skin as an optimal and accessible organ on which to perform meaningful human experiments.

The skin is a widely-used paradigm to study regional immunity and the specialized functions of leukocyte subsets. In collaboration with research groups at CeMM and LBI-RUD, Georg Stary's laboratory is applying 'omics' technologies to explore the roles, relationships, and actions of the various types of molecules that make up these cells.

Sympathy for the devil

The immune system and its many molecular safety measures are responsible for rejecting and destroying any foreign tissue that enters the body. Therefore, apart from some rare cases such as the accidental transmission through a cut during surgery or after transplant of an affected organ, cancers are generally not transmissible.

In Tasmanian devils, the world's largest living carnivorous marsupial, however, a deadly facial tumor is spreading rapidly and has, over the last 20 years, killed around 90% of the wild population. Curiously, the cancer cells, which appear to derive from a single cell of origin, are transmitted from one Tasmanian devil to another by biting. The bitten animal's immune system fails to recognize the cells as foreign, and thus fails to eliminate them and prevent their growth.

Groups
Andreas Bergthaler, Joanna Loizou, Georg Stary

Location
CeMM, lab 6th floor

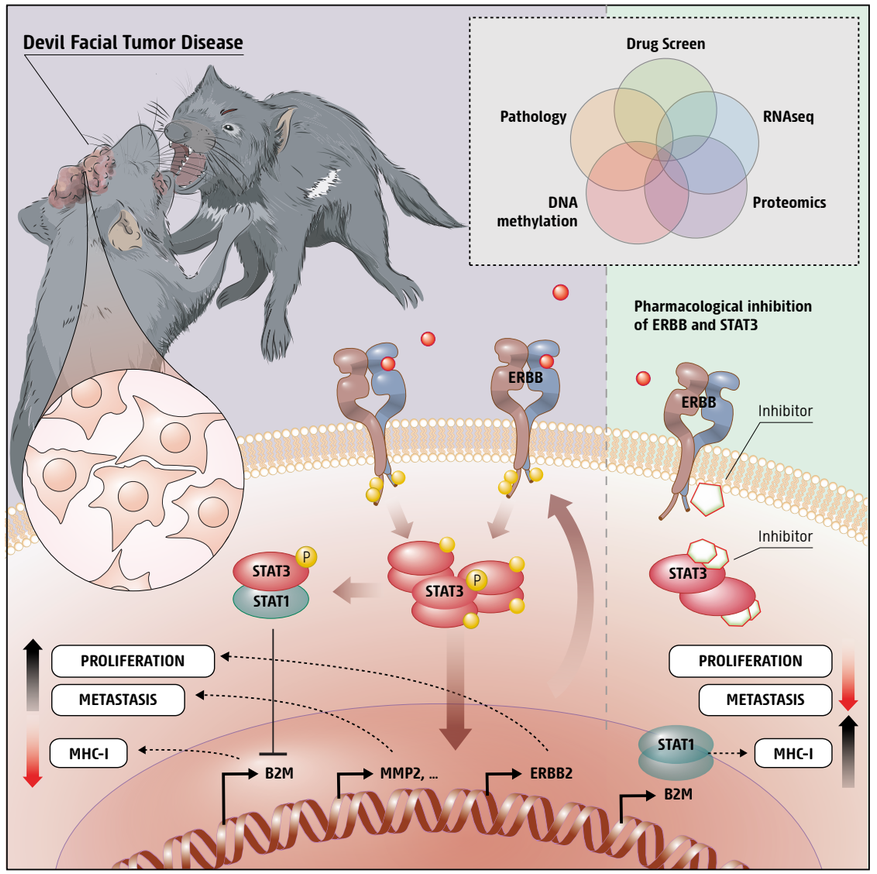


Fig. 1 Graphical abstract: Excessive activation of ERBB receptors and STAT3 proteins play a key role in the transmissibility of the Tasmanian devil's facial tumor, inhibition of ERBB receptors with a drug can selectively kill the cancer cells. Kosack et al., 2019, *Cancer Cell* 35, 1–5, 14 January 2019 © 2018 Published by Elsevier Inc.

By what means this cancer escapes the immune system of its otherwise healthy hosts has been a mystery since the discovery of this disease. Together with researchers from the Medical University of Vienna and the University of Veterinary Medicine in Vienna, and in collaboration with the Universities of Cambridge, Southampton, Toronto and Tasmania, Andreas Bergthaler's group has been able to reveal molecular mechanisms that are crucial for the transmissibility of the tumor.

Using pharmacological screening and an integrated systems-biology characterization, the scientists found that ErbB receptor molecules on the surface of the cancer cells show massively increased activity. These receptors trigger a biochemical chain reaction within the cells that eventually activates oncogenic transcription factor STAT3. The result is an extensive rebuild of the cell: The number of molecules serving as identification for the immune system are reduced; at the same time proliferation is accelerated and factors for metastasis of the tumor cells are produced. In further experiments in cell culture and xenograft mouse models, the researchers showed that chemically inhibiting ErbB receptors restored expression of MHC class I genes and inhibited tumor growth.

These results thus provide strong evidence for a central role of ErbB-STAT3 signaling in this tumor disease, the suppression of which to kill the cancer cells could contribute to efforts to save the Tasmanian devil from extinction.

Given that 99.1% of the Tasmanian devil's STAT3 are identical to human STAT3, and several genes that are activated by STAT3 in the animals are also active in human cancers, the findings also provide valuable insights on fundamental biological mechanisms of cancer development, cancer metastases and inflammatory processes in humans, and were published in the high-impact journal *Cancer Cell.*

References

Kosack L, Wingelhofer B, Popa A, Orlova A, Agerer B, Vilagos B, Majek P, Parapatics K, Lercher A, Ringler A, Klughammer J, Smyth M, Khamina K, Baazim H, de Araujo ED, Rosa DA, Park J, Tin G, Ahmar S, Gunning PT, Bock C, Siddle HV, Woods GM, Kubicek S, Murchison EP, Bennett KL, Moriggl R, Bergthaler A. The ERBB-STAT3 Axis Drives Tasmanian Devil Facial Tumor Disease. *Cancer Cell.* 2019 Jan 14; 35(1):125-139.e9.

Not just skin deep

Xeroderma pigmentosum (XP) is a rare genetic disease in which patients are extremely sensitive to ultraviolet (UV) rays from sunlight. This condition mostly affects the eyes and areas of skin exposed to the sun. Also known as "moon children", patients with XP develop inflammation upon exposure to tiny amounts of sunlight; rough-surfaced growths and eventually skin cancer often occur already in early childhood. The severe condition is caused by mutations in the genes for the nucleotide excision repair (NER) pathway – the only known mechanism that deals with UV-induced DNA damage in human cells. Although first described in 1874, xeroderma pigmentosum lacks a curative treatment, and patients can only be offered resources that provide protection from the sun.

In a study to discover compounds that allow xeroderma pigmentosum disease cells to survive UV treatment better, the group led by PI Joanna Loizou, together with collaborators from the Medical University of Vienna and the IRB Barcelona, found that the diabetes drug acetohexamide significantly improves the resilience of NER deficient cells against UV radiation *in vitro*. With several subsequent experiments the group was able to elucidate the underlying molecular mechanism: Aceto-hexamide leads to the degradation of the DNA repair enzyme MUTYH, triggering a hitherto unknown NER-independent mechanism for removing UV-induced DNA damage.

References

Mazouzi A, Battistini F, Moser SC, Ferreira da Silva J, Wiedner M, Owusu M, Lardeau CH, Ringler A, Weil B, Neesen J, Orozco M, Kubicek S, Loizou JI. Repair of UV-Induced DNA Damage Independent of Nucleotide Excision Repair Is Masked by MUTYH. *Mol Cell.* 2017 Nov 16;68(4):797-807.e7.

Successfully decoding the DNA repair mechanism since establishing her group at CeMM in 2011, Joanna Loizou's research has culminated in being awarded, together with Jacob Corn from ETH Zurich, Switzerland and Steve P. Jackson from The Gurdon Institute, University of Cambridge, UK, a prestigious ERC Synergy Grant for DNA damage response systems. In their project entitled "DNA Damage Response: Actionabilities, Maps and Mechanisms" (Acronym: DDREAMM), the three teams will provide major insights into human genome surveillance in multiple cell types, yield powerful tools to precisely control DNA repair outcomes, and speed up the development of new therapies for cancer and other diseases.

With funding of around €8.86 million starting in the first quarter of 2020, the scientists will devote the next six years to mapping and understanding how eukaryotic cells monitor and protect their genomes. They will use multidisciplinary approaches, including cutting-edge technologies in gene editing and chemical biology, to create deeply integrated genetic and physical maps of DNA repair pathways and interactions in several human cell types.

In this research project, each lab will play to its strengths while also assimilating expertise from the other labs. As the ERC Synergy Grant focuses on rapidly evolving scientific arenas, this international partnership allows the three teams to collectively embrace and exploit the very latest technological developments and scientific opportunities in ways that are more than additive, to tackle the fundamentally important question of how our genomes are maintained.

CeMM aims to unveil the molecular mechanisms underlying major diseases in humans, with a view to improving diagnoses and developing precision therapy with minimal side effects.


Boztug

Inflammation

"Light My Fire". When a fire is kindled, things start burning. If contained, as in a log or campfire, a blaze warms us; left unchecked it can turn into a conflagration and cause extensive damage. Not only wood is ignitable, our emotions may also become inflamed. Highly-charged emotions such as desire, dedication and passion for science, can make us feel like we are burning up. And fire that burns below the surface is notoriously difficult to put out. Inflammation is like a fire that lights up in our bodies. It is the normal response of our immune system to injuries and harmful things that enter our body. Immune cells quickly react to the damaged area to fix the problem. To do this, they use biochemical signaling pathways, which are activated by proteins or direct cell-cell contacts. The goal is to keep inflammation in check and not let the fire run wild.

In addition to protecting us against invading pathogens of all kinds, immune cells are responsible for monitoring tissue homeostasis and removing damaged cells. This wide and diverse range of tasks requires a vastly complex, yet highly organized biological network involving dozens of different immune cell types, many hundred different signaling molecules and countless biochemical reactions. Only the precise interaction of these factors guarantees a smooth and controlled functioning of the immune system.

Dysregulated immune responses allow a fire in the body to smolder unnoticed, causing damage to tissues, joints, and blood vessels and leading to a variety of diseases, including cancer, autoimmunity, and immune deficiency. Our knowledge of the underlying mechanisms of immunity, and ability to harness and manipulate the immune response, however, remains limited.

Collaborative efforts

For a better understanding of infection and immune disorders, greater cooperation between researchers and medical doctors from different institutions is needed. In response, CeMM has entered into research collaborations with physicians and universities in Austria and other parts of the world to explore the fundamental mechanisms of immunity.

These partnerships have, in 2019, led to discoveries of connections which modulate and fine-tune the immune response during infection and of an interaction between cancer cells and the immune system, and identified genetic causes for immune diseases as a way to uncover immune regulatory pathways. Further projects at CeMM are underway to develop a protein signaling complex into a future cancer drug target and to find new therapeutic options for liver inflammation.

Unusual suspects

Andreas Bergthaler's group is interested in how inflammatory processes are regulated and how the immune system responds to viral infections. In two recent studies, they discovered the inflammatory mediators CD8 T cells and antiviral cytokines type I interferons to be protagonists in metabolic processes occurring during infection.

In the first study, conducted with scientists from the University of Graz, the Medical University of Vienna and institutes in Germany, Switzerland and the USA, the team elucidated a novel mechanism of how chronic viral infection leads CD8 T cells to trigger a metabolic disorder called cachexia.

Cachexia affects a large proportion of cancer patients and those with chronic infections. The condition causes extreme loss of weight, body fat and muscle, which cannot be reversed by nutritional supplementation. This wasting aggravates the underlying disease and can lead to premature death, yet standards of care to prevent or alleviate cachexia remain as ill-defined as effective treatment remains elusive.

In recent years, studies using experimental models of cancer-associated cachexia have greatly helped us to understand how inflammation may trigger cachexia and the associated metabolic alterations. Secreted inflammatory factors were shown to be able to induce weight loss through either direct or indirect mechanisms that affect appetite and alter fat and muscle metabolism. In the context of infectious diseases, however, our knowledge of cachexia is lagging behind, including whether the same or different mechanisms of cachexia occur during infection and cancer.

Using a mouse model, Andreas Bergthaler's team was able to demonstrate that the weight loss induced by the viral infection could only partially be explained by reduced food intake. The scientists then showed that the infection caused a severe restructuring of adipose tissue causing lipid stores to be depleted. Rather than the suspected inflammatory mediators that usually play a role in infection, they found that CD8 T cells induced the morphological and molecular changes in the fat tissue. In order to trigger cachexia, the CD8 T cells required additional signals from antiviral cytokines type I interferons (IFN-1) that are needed to recognize the virus.

These findings provide much-needed insights into the molecular mechanisms underlying cachexia, and may stimulate the development of innovative therapeutic strategies. The study was published by the high-impact journal *Nature Immunology*.

References

Baazim H, Schweiger M, Moschinger M, Xu H, Scherer T, Popa A, Gallage S, Ali A, Khamina K, Kosack L, Vilagos B, Smyth M, Lercher A, Friske J, Merkler D, Aderem A, Helbich TH, Heikenwälder M, Lang PA, Zechner R, Bergthaler A. CD8(+) T cells induce cachexia during chronic viral infection. *Nat Immunol.* 2019 Jun;20(6):701-710.

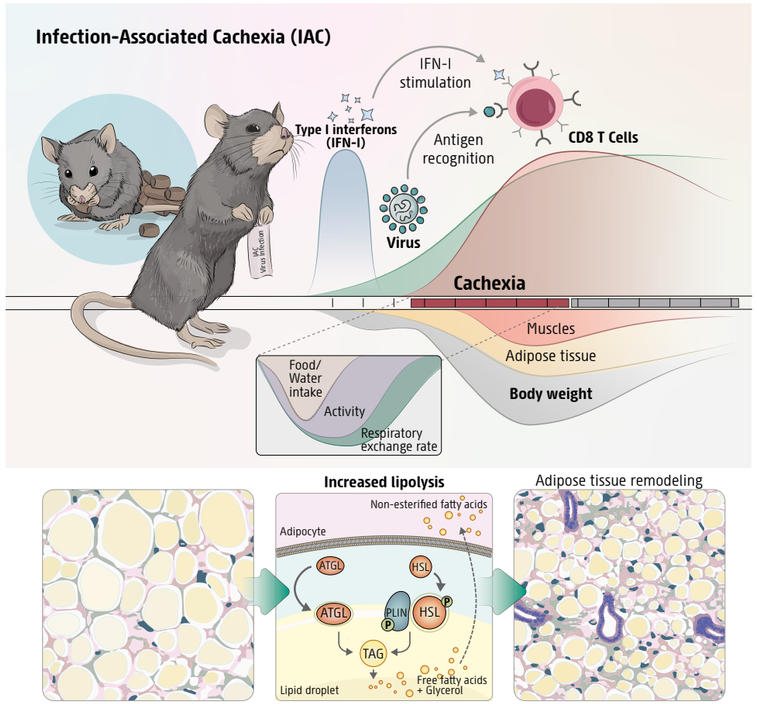


Fig. 2 Using a mouse model, Andreas Bergthaler's team was able to demonstrate that viral infection triggered weight loss and found that CD8 T cells induced the morphological and molecular changes in the fat tissue.

Groups
Kaan Boztug, Thomas Reiberger, Andreas Villunger

Location
CCRI/LBI-RUD

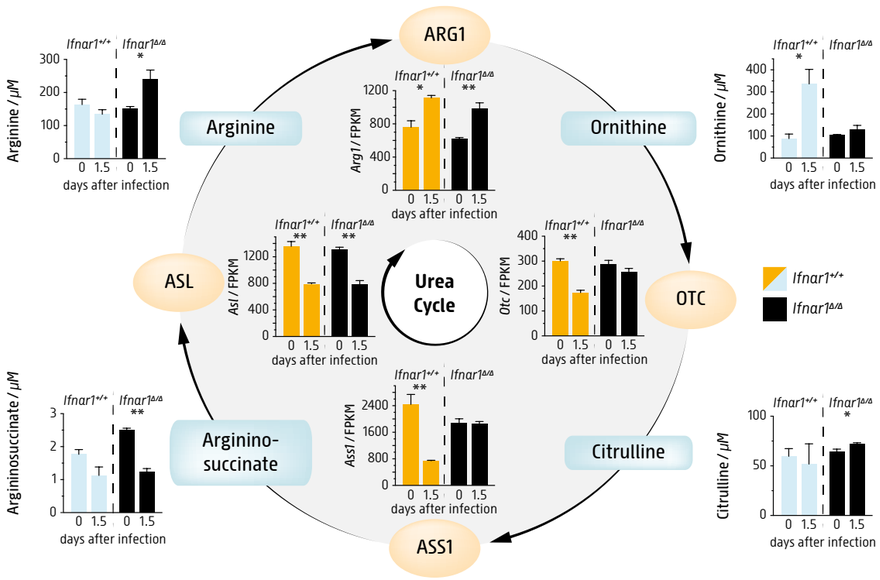


Fig. 3 The antiviral cytokine type I interferon counteracts viral infections but also reprograms liver metabolism. Critically, type I interferon stalls the urea cycle in hepatocytes to regulate serum metabolite levels that ultimately affect immune responses and tissue damage.

Previous studies in immunology and metabolism, or immunometabolism, have made groundbreaking discoveries of how the metabolic pathways of immune cells regulate their responses to pathogens and cancer. In the second collaboration exploring processes induced by viral infection, Andreas Bergthaler's team aimed to study the immunometabolic changes that occur in the whole organism during infection.

Together with researchers from the Medical University of Vienna, the University of Veterinary Medicine in Vienna (A), the Hanover Medical School (D), the Cantonal Hospital St. Gallen (CH) and the Chinese company Bio-Cancer Treatment International Ltd., the team found that the urea cycle, a central metabolic node, is disrupted by IFN-I during viral infection.

In a mouse model of lymphocytic choriomeningitis virus (LCMV), a benchmark model of chronic viral infection, the scientists observed the expected inflammatory changes, but also intriguing effects on hepatocyte metabolism. Hepatocytes, or liver cells, serve as an important immune signaling unit during infection. Many central metabolic pathways, among them the urea cycle, which is essential in removing toxic ammonia from the body, were found to be repressed upon infection. Surprisingly, the researchers identified the antiviral cytokine signaling pathway of IFN-I as a master regulator of the urea cycle. This resulted in altered blood concentrations of the amino acids arginine and ornithine. Subsequently removing the receptor for IFN-I on the surface of hepatocytes reversed these metabolic changes. The altered levels of arginine and ornithine were found to inhibit antiviral CD8 T-cell responses and to reduce liver damage.

Together, these results shed new light on how our immune system has evolved to regulate liver metabolism to adjust CD8 T-cell responses and reduce collateral tissue damage during infection. One day, such findings may be used to therapeutically interfere with the regulation of metabolic processes to modulate CD8 T-cell responses in infection, cancer and autoimmunity.

References

Lercher A*, Bhattacharya A*, Popa AM, Caldera M, Schlapansky MF, Baazim H, Agerer B, Gürtl B, Kosack L, Májek P, Brunner JS, Vitko D, Pinter T, Genger JW1, Orlova A, Pikor N, Reil D, Ozsvár-Kozma M, Kalinke U, Ludewig B, Moriggl R, Bennett KL, Menche J, Cheng PN, Schabbauer G, Trauner M, Klavins K, Bergthaler A. Type I Interferon Signaling Disrupts the Hepatic Urea Cycle and Alters Systemic Metabolism to Suppress T-Cell Function. *Immunity*. 2019 Nov 22. [Epub ahead of print] (*shared first authors)

Genetic igniters

When the immune system's ability to fight infectious disease and cancer is compromised or entirely absent, this is known as immunodeficiency. Inborn errors of the immune system are associated with or predispose patients to various complications, including infections, autoimmune disorders, and lymphomas and other cancers. Most cases of immunodeficiency are secondary, i.e. acquired due to extrinsic factors affecting a patient's immune system. Primary immunodeficiencies, on the other hand, are genetically determined and can be hereditary.

In a study led by the team of Kaan Boztug, Scientific Director of CCRI, St. Anna Children's Cancer Research Institute, Director of LBI-RUD, and Adjunct PI at CeMM, researchers from LBI-RUD, CeMM and the Medical University of Vienna together with scientists from the Universities of Leiden and Istanbul, have unveiled a hitherto unknown immune deficiency syndrome which is genetically determined.

Polymerase δ is an enzyme complex responsible for DNA replication, genome stabilization and cell cycle regulation. Impairment of its function leads to genomic instability, neurodevelopmental disorders and immunodeficiency. Organisms with severe disruption of these DNA polymerases are often not viable, which makes research difficult.

Studying two unrelated patients with developmental defects and combined immunodeficiency, the researchers detected biallelic germline mutations, i.e. gene mutations inherited from both parents, in one of the four subunits of polymerase δ: POLD1 or POLD2, respectively. In both cases, the mutation resulted in an immunodeficiency syndrome with recurrent respiratory infections, skin problems, and neurodevelopmental disorders.

Closer examination of the disease mechanisms revealed that the cell cycle was impaired in the lymphocytes of both patients. An increased number of copying errors during DNA replication led to DNA warning labels in the cell, thereby causing cell cycle dysfunction.

These findings unveil a hitherto unknown immune deficiency syndrome based on a reduced functionality of polymerase δ, as well as a previously undefined role of polymerase δ in neurodevelopment and lymphocyte biology.

The study also provides key information for other diseases such as childhood cancer: Unlike other immunodeficiency syndromes with a disruption of an immune-specific factor, the underlying disease mechanism was found to be a deficiency in a basic function of the cell. Although the deficiency particularly affected immune cells, the replication control mechanism of polymerase δ is relevant to the function of all cells.

Certain mutations in POLD1 are known to contribute to the emergence of the 'mutator phenotype', which contributes to genetic instability and thus to carcinogenesis. Accordingly, POLD1 is classified as a tier 1 cancer gene in the COSMIC database. Conversely, the inborn POLD1/2 mutations described in this study lead to a reduced intrinsic activity (the "actual task") of the polymerase δ, with a possibly increased tendency to develop cancer in the sense of a cancer predisposition syndrome.

References

Domínguez Conde C*, Petronczki ÖY*, Baris S*, Willmann KL*, Girardi E, Salzer E, Weitzer S, Ardy RC, Krolo A, Ijspeert H, Kiykim A, Karakoc-Aydiner E, Förster-Waldl E, Kager L, Pickl WF, Superti-Furga G, Martínez J, Loizou JI, Ozen A, van der Burg M, Boztug K. Polymerase δ deficiency causes syndromic immunodeficiency with replicative stress. *J Clin Invest*. 2019 Oct; 129(10):4194-4206. (*shared first authors)

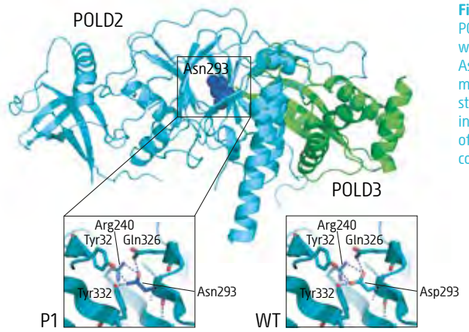


Fig. 4 Overview of the POLD2-POLD3 structure with the indicated position Asp293. The identified mutations affect the stability, interactions, and intrinsic enzymatic activity of the polymerase δ complex.

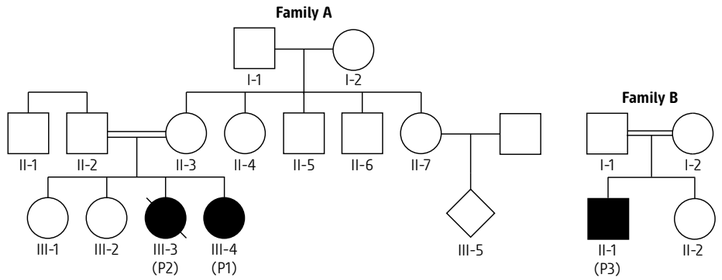


Fig. 5 Systemic autoimmunity in three patients from two families. The filled symbols in the pedigree of families A and B mark the affected patients (P).

Keeping the balance

Sometimes the cells of the immune system fail to distinguish between the body's own cells and those of invading pathogens. This is known as autoimmunity and results in inappropriate immune attacks on organs and tissues. Many human diseases are characterized by a multitude of autoimmune phenomena; however, the underlying mechanisms are often poorly understood.

Rather than using animal models of autoimmunity which are not always predictive of human responses to treatment, Kaan Boztug's team studies patients suffering from inborn errors of the immune system to identify core regulators of immune balance.

Partnering with colleagues from the USA, Sweden and the UK, the group identified a new rare disease and, in the process, a key factor in T-cell homeostasis. Using next generation sequencing on samples from a child suffering from severe autoimmunity affecting various organs, the researchers noticed a 'missense' mutation in the gene sequence encoding the protein DEF6 in T cells, causing an incorrect amino acid to be inserted into the protein. They subsequently identified a hitherto completely unknown mechanism by which DEF6 controls CTLA-4, a key regulatory protein on T cells, as the cause of the observed autoimmune symptoms in patients with DEF6 deficiency.

On the basis of these findings, the young patient was successfully treated with CTLA-4-Ig using a commercially available drug. Nina Serwas, then PhD student at CeMM, expects that this treatment may be effectively applied to other affected patients with this autoimmune disease.

CTLA-4 featured in studies on cancer treatments involving the inhibition of negative immune responses, which were awarded the 2018 Nobel Prize for Physiology or Medicine, and is being considered a promising point of attack for immunotherapies to treat cancer.

References

Serwas NK*, Hoeger B*, Ardy RC, Stulz SV, Sui Z, Memaran N, Meeths M, Krolo A, Yüce Petronczki Ö, Pfajfer L, Hou TZ, Halliday N, Santos-Valente E, Kalinichenko A, Kennedy A, Mace EM, Mukherjee M, Tesi B, Schrempf A, Pickl WF, Loizou JI, Kain R, Bidmon-Fliegenschnee B, Schickel JN, Glauzy S, Huemer J, Garncarz W, Salzer E, Pierides I, Bilic I, Thiel J, Priftakis P, Banerjee PP, Förster-Waldl E, Medgyesi D, Huber WD, Orange JS, Meffre E, Sansom DM, Bryceson YT, Altman A, Boztug K. Human DEF6 deficiency underlies an immunodeficiency syndrome with systemic autoimmunity and aberrant CTLA-4 homeostasis. *Nat Commun.* 2019 Oct 2;10(1):4555. (*shared first authors)

Smoke signals

Andreas Villunger, Head of the Division of Developmental Immunology at the Biocenter of the Medical University of Innsbruck explores basic mechanisms of immune cell development and general principles of cellular transformation. As an Adjunct PI at CeMM and LBI-RUD, his research focus is on the role of pro-apoptotic BH3-only proteins in lymphocyte transformation and anti-cancer treatment effects.

Cancer and many immune-related diseases have been shown to be caused by a failure to control apoptosis. Andreas Villunger demonstrated for the first time that cell death during radiotherapy can be pro-tumorigenic. More recently, 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. These studies have unveiled a so far overlooked function of the PIDDosome signaling platform in the activation of p53 in cells with extra centrosomes. This finding formed the basis for current ERC-funded studies into the role of the PIDDosome multi-protein complex in ploidy control during organogenesis and transformation aiming to develop the PIDDosome complex into a future drug target in disorders related to centrosome aberrations, including cancer and ageing.

References

Connolly P, Garcia-Carpio I, Villunger A. Cell Cycle Crosstalk with Caspases and Their Substrates. *Cold Spring Harb Perspect Biol.* 2019 Nov 14. pii: a036475. doi: 10.1101/cshperspect.a036475. [Epub ahead of print] PubMed PMID: 31727679.

Andreas Villunger's research team in Innsbruck is also looking into the role of steroid hormones, called glucocorticoids (GC), that are frequently prescribed to treat autoimmunity and certain types of cancer during inflammatory responses. Activation of the immune system increases systemic GC levels, which downregulate the immune response as part of a negative feedback loop. While CD4+ T cells are essential target cells affected by GC, it is not known whether these hormones exert their most important effects on CD4+ helper T cells, or on CD4+-Foxp3+ regulatory T cells (Treg cells), that prevent autoimmunity. His team's recent work suggests that GC instruct Treg cells to inhibit pro-inflammatory CD4+ T-cell expansion in a model of experimental colitis. If equally active in humans, this finding will provide a rationale to specifically target Foxp3+ Treg cells for the treatment of inflammatory bowel disease.

References

Rocamora-Reverte L, Tuzlak S, von Raffay L, Tisch M, Fiegl H, Drach M, Reichardt HM, Villunger A, Tischner D, Wiegers GJ. Glucocorticoid Receptor-Deficient Foxp3(+) Regulatory T Cells Fail to Control Experimental Inflammatory Bowel Disease. *Front Immunol.* 2019 Mar 18;10:472. doi: 10.3389/fimmu.2019.00472. eCollection 2019. PubMed PMID: 30936873.

Putting out liver fire

Liver cirrhosis is the consequence of inflammation, commonly resulting from immune-mediated liver injury. The hepatic immune system consists of predominant innate immunity, which plays an important role in the defense against invading pathogens and danger signals from the gut. However, repetitive or long lasting hepatic inflammation also drives liver fibrosis resulting in excessive amounts of scar tissue in the organ. Chronic inflammation of the liver may thus ultimately lead to cirrhosis. Currently, there are no effective therapies available to treat liver fibrosis in patients in whom the causative agent cannot be removed.

Liver fibrogenesis and inflammation are among the main research interests of Thomas Reiberger, from the Division of Gastroenterology and Hepatology at the Medical University of Vienna and Adjunct PI at CeMM and LBI-RUD. He conducted seminal studies for optimizing the role of non-selective betablocker therapy in patients with cirrhosis. His Hepatic Experimental Hemodynamic (HEPEX) laboratory at MedUni Vienna is focused on exploring novel treatment options for liver fibrosis and portal hypertension. Since liver inflammation is strongly linked to fibrogenesis, altered hepatic metabolism and abnormal angiogenesis, the molecular mechanisms orchestrating these central pathogenic processes in liver disease represent the main focus of his research. The changes of the hepatic vasculature are of key relevance to impaired organ perfusion, and the identification of the molecular signals driving these vascular abnormalities in the liver might lead to novel treatment options for portal hypertension.

References

Brusilovskaya K, Königshofer P, Schwabl P, Reiberger T. Vascular Targets for the Treatment of Portal Hypertension. *Semin Liver Dis.* 2019 Nov;39(4):483-501. Doi 10.1055/s-0039-1693115.

Experimental studies evaluate novel drugs, such as anti-angiogenic drugs, agonist of the farnesoid-X-receptor (FXR) and stimulators of the soluble guanylate cyclase. In 2019, Thomas Reiberger received the United European Gastroenterology (UEG) Rising Star Award for his research endeavors in understanding pathophysiology in order to identify novel therapeutic strategies for chronic liver diseases.

Thomas Reiberger also leads the Rare Liver Disease (RALID) program of the Ludwig-Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD) that aims to explore the molecular mechanisms of rare-liver diseases, such as alpha-1-antitrypsin deficiency (A1AD). As part of the RALID program, his group characterized patients with A1AD using several clinical non-invasive and invasive tests. In 2019, his lab contributed to a detailed characterization of liver fibrosis and metabolic alterations observed in A1AD patients harboring the PiZZ mutation.

References

Hamesch K, Mandorfer M, Pereira VM, Moeller LS, Pons M, Dolman GE, Richert MC, Schneider CV, Woditsch V, Voss J, Lindhauer C, Fromme M, Spivak I, Guldiken N, Zhou B, Arslanow A, Schaefer B, Zoller H, Aigner E, Reiberger T, Wetzel M, Siegmund B, Smoes C, Gaspar R, Maia L, Costa D, Bento-Miranda M, van Helden J, Yagmur E, Bzdok D, Stolk J, Gleier W, Knipel V, Windisch W, Mahadeva R, Bals R, Koczulla R, Barrecheguren M, Miravitlles M, Janciauskiene S, Stickel F, Lammert F, Liberal R, Genesca J, Griffiths WJ, Trauner M, Krag A, Trautwein C, Strnad P, European Alpha1-Liver Study Group. Liver Fibrosis and Metabolic Alterations in Adults With alpha-1-antitrypsin Deficiency Caused by the Pi*ZZ Mutation. *Gastroenterology.* 2019 Sep;157(3):705-719.e18.

Studying patients suffering from inborn errors of the immune system is key to identifying core regulators of immune balance.

Binder
Kralovics

Life

Facts

Heart/Blood

"Unchain My Heart". The heart is said to be the seat of our emotions. When we fall in love, we "give our hearts away". It no longer beats in our own chest but is only kept alive when joined to our beloved. Some, like Ray Charles, may even feel their heart belongs to the other entirely and when love ends, depend on them setting it free to feel whole again. Emotional situations may cause us to feel flutters in our chest and other physical symptoms such as chest tightness and a dull pain around where the literal heart is. Yet the figurative heart does not exist anatomically. The literal heart is a large, muscular organ that pumps blood through the blood vessels of the circulatory system. In circulating through the body, blood delivers essential substances like oxygen and nutrients to the body's cells.

Over half of our blood is plasma, whose main role it is to take nutrients, hormones, and proteins to the parts of the body that need it; the other half contains the blood cells: red blood cells, white blood cells and platelets. The red blood cells carry oxygen from the lungs, the white blood cells help to fight infection, and platelets are parts of cells the body uses for clotting.

All blood cells are produced in the bone marrow. They begin as immature cells called stem cells and clone themselves to become mature blood cells that leave the bone marrow and enter the bloodstream.

Joining forces against bone marrow disease

Mutations in the stem cells can cause excess numbers of mature blood cells to be produced. Overproduction of red and white blood cells and platelets can in turn lead to myeloproliferative neoplasia (MPN), a rare but malignant group of bone marrow diseases which may develop into acute life-threatening leukemia. MPN is currently undertreated, and new therapeutic approaches are urgently needed.

CeMM Adjunct Principal Investigator Robert Kralovics' team at the Department of Laboratory Medicine at the Medical University of Vienna works toward identifying MPN-associated mutations and other genetic factors that contribute to cancer progression. His team also investigates therapeutic interventions that could prevent clonal evolution and disease progression. In 2019, the group was involved in a collaborative study describing new immunotherapy targets for potential use in a personalized cancer vaccine.

Groups
Christoph Binder, Robert Kralovics

Location
Anna Spiegel Building

Stopping the overflow

Despite detailed knowledge of the disease mechanism of MPN, the only curative treatment currently available is stem cell transplantation – and only for a small subset of eligible patients. Recent advances in T-cell-based immunotherapy, however, raise hopes for targeted therapies sufficiently effective to eliminate MPN cells.

A key requirement for targeted immunotherapy is the identification of antigens that are present in tumor cells but absent in healthy cells. These antigens are mutated parts of proteins present in a patient's tumor cells. Traditional methods for neoantigen identification, however, are expensive and often insufficiently sensitive.

To address these challenges, Robert Kralovics' laboratory, joined by researchers from the Medical University of Vienna and the University of Pavia, established a novel RNA-based technique to systematically identify cancer antigens in individual MPN patients.

Performing RNA sequencing on tumor biopsies as a basis for target discovery is highly efficient. The method not only identifies targets that are expressed and therefore relevant but is also able to systematically detect various mutation classes, including fusions and splicing-related aberrations.

Using this cutting-edge technology, the scientists were able to demonstrate that especially patients with mutations in the splicing factor SF_3B_1 and CALR genes produce a variety of tumor-specific peptides. These altered peptides could serve as a blueprint for a therapeutic cancer vaccine.

The team generated a virtual peptide library from all the mutations detected and identified unique neoantigens in 62% of MPN patients. Further research will hopefully show that these tumor-specific antigens are capable of eliciting an immunogenic response and can therefore serve as valid targets for the T-cell-directed killing of cancer cells.

References

Schischlik F, Jäger R, Rosebrock F, Hug E, Schuster M, Holly R, Fuchs E, Milosevic Feenstra JD, Bogner E, Gisslinger B, Schalling M, Rumi E, Pietra D, Fischer G, Faé I, Vulliard L, Menche J, Haferlach T, Meggendorfer M, Stengel A, Bock C, Cazzola M, Gisslinger H, Kralovics R. Mutational landscape of the transcriptome offers putative targets for immunotherapy of myeloproliferative neoplasms. *Blood*. 2019 Jul 11;134(2):199-210.

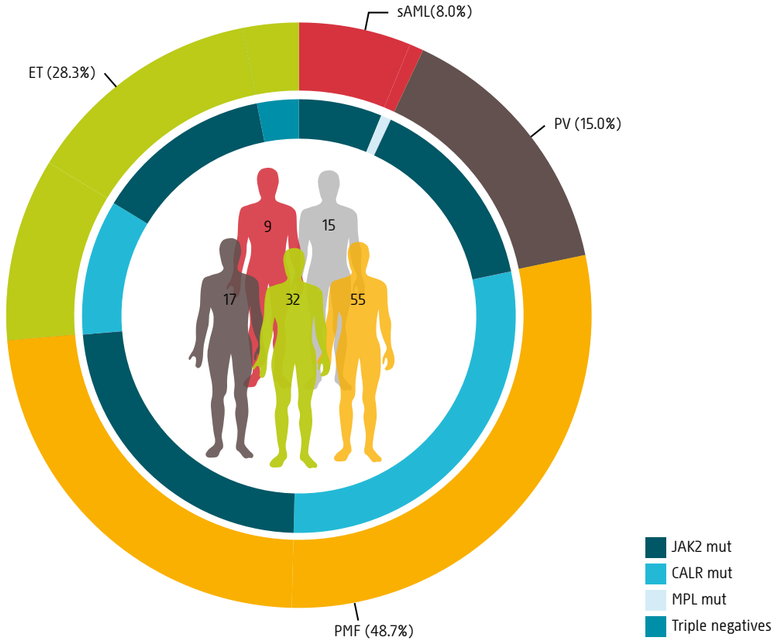


Fig. 6 The distribution of diagnosis in the MPN cohort is shown in the outer ring, the occurrence of the MPN driver mutation status in each diagnosis in the inner ring. At the center: number of patients by diagnosis. Healthy controls are in gray.

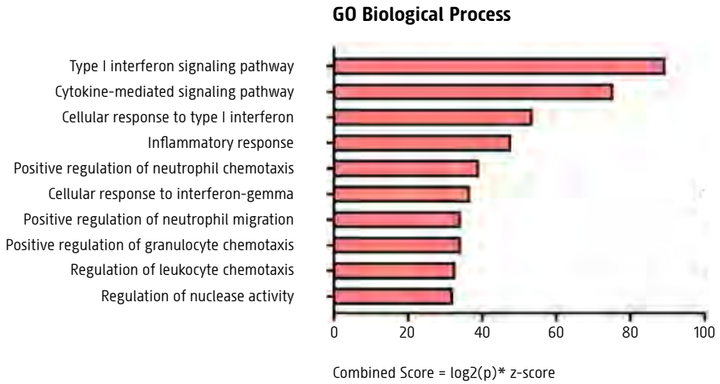


Fig. 7 Stressed mitochondria activate endothelial cells. These bar graphs show the 10 most enriched pathways based on the analysis of gene ontology (GO) biological processes and the Kyoto Encyclopedia of Genes and Genomes (KEGG).

Mutiny in the monocytes

White blood cells, or leucocytes, are part of the body's immune system, protecting us against illness and disease. There are many subtypes of leukocytes. They are found in the circulation, but routinely leave the bloodstream to fight infections and to perform their defensive functions in the body's tissues.

White blood cells are grouped into three major classes – lymphocytes, granulocytes, and monocytes – each of which carries out somewhat different functions. Monocytes, for example, move from the blood to sites of infection. Once they reach the tissues, they help to break down bacteria and kill infected host cells.

In collaboration with colleagues in Germany, Canada and the USA, Christoph Binder, Professor for Atherosclerosis Research, and members of his group at CeMM and the Medical University of Vienna investigated how monocytes react under stress. In so doing, they discovered a new mechanism by which endogenous mitochondria released from these monocytes become initiators of inflammation.

Monocytes shed parts of their cell membrane in the form of so-called microvesicles, which are capable of transmitting alarm signals to other cells. The scientists discovered that a subset of these microvesicles contains mitochondria. Normally mitochondria are an important component of cells and are known as cellular power plants. Under stress, however, these 'friendly' mitochondria were found to have an increased potential to trigger dangerous pro-inflammatory responses in recipient cells.

The researchers identified two factors that render these monocytic 'stressed mitochondria' dangerous: mitochondria-associated tumor necrosis factor (TNF, a messenger molecule of the immune system) and modified mitochondrial RNA. Via these two factors, 'stressed mitochondria' trigger TNF and Type 1 interferon (IFN) signaling pathways in recipient cells. Notably, these are two major signaling pathways in chronic inflammatory diseases.

These findings give rise to new potential therapeutic approaches targeting mitochondria and their release in cardiovascular disease and other inflammatory settings associated with type I IFN and TNF signaling.

Endogenous mitochondria released from stressed monocytes become initiators of inflammation.

References

Puhm F, Afonyushkin T, Resch U, Obermayer G, Rohde M, Penz T, Schuster M, Wagner G, Rendeiro AF, Melki I, Kaun C, Wojta J, Bock C, Jilma B, Mackman N, Boilard E, Binder CJ. Mitochondria Are a Subset of Extracellular Vesicles Released by Activated Monocytes and Induce Type I IFN and TNF Responses in Endothelial Cells. *Circ Res.* 2019 Jun;125(1):43-52.


Superti-Furga
Chemistry/Drugs


Winter
Kubicek
Chemistry/Drugs
Amanda
NG


Chemistry/Drugs
Maulide
Ce-M-M
SCIENTIST

Chemistry/Drugs

"Just Like A Pill." We take drugs to feel better. Some drugs have been developed to treat mental illnesses; others have been created to fight disease and infection. The intended effect comes from the drug altering the chemistry of our brain or body. After taking a pill, no one expects to feel worse. In interfering with our chemistry, however, there is always a risk of secondary effects occurring, which may be harmful. This can be the proverbial 'bad trip' when taking psychoactive drugs, or the mild to severe adverse side effects of medical treatment administered over a longer period.

When drugs are combined, for example, in treating cancer, things can become even more complicated. The interaction may cause an increase or decrease in one or both drugs' effect or a completely different effect than intended. Some drugs are simply not ideal for achieving the desired result, but the best we have at present, given our limited knowledge of certain diseases.

How can we improve this situation? A strategy increasingly being encouraged is to combine the experience, expertise and technologies of various players in the field of drug discovery and development.

Synergies towards improved therapies

In the past, drugs were often discovered either by isolating the active ingredient from traditional remedies or by serendipitous discovery, as with pencillin. Nowadays, in the post-genomic era, we have new methods and techniques on hand to understand the molecular and physiological mechanisms underlying disease and, based on this knowledge, we can develop drugs that target relevant molecules.

Until recently, the activities involved in gaining mechanistic insights into human disease, identifying therapeutic targets and developing effective treatment were usually conducted separately: Universities and research institutions studied biological malfunction and carried out some early-stage drug discovery, while drug candidate optimization and development was reserved for the pharmaceutical industry.

Lately, a paradigm shift has taken place though towards giving academic researchers a greater role in drug discovery. CeMM, already working in a highly collaborative and interdisciplinary manner, is happy to be part of this new model. Recent studies are making significant headway in targeting hitherto 'undruggable' proteins, and also finding ways to use existing drugs in new ways.

Groups
Stefan Kubicek, Nuno Maulide, Giulio Superti-Furga, Miriam Unterlass, Georg Winter

Location
University of Vienna, PLACEBO lab CeMM

Building a better immunosuppressive drug

Immunosuppressant drugs are drugs that inhibit the activity of the immune system. Some of these drugs are used after organ transplants to prevent rejection of the new organ, others are used to treat autoimmune disease.

Currently used immunosuppressants not only cause severe adverse reactions, but also have considerable limitations. The discovery of new immunosuppressants with a distinct mode of action is thus urgently needed to make immunosuppressive therapy safer and more effective.

In 2003, in pursuit of novel immunosuppressants acting on antigen-presenting cells (APC), researchers from a Japanese chemical company isolated three natural products – FR252921, FR252922, and FR256523 – from the microorganism *Pseudomonas fluorescens*, also referred to as FR molecules (Fig. 8). These highly complex natural products were found to have highly potent immunosuppressive properties.

Not long ago, efforts to recreate the synthesis of FR molecules in the laboratory were unsuccessful because of the Achilles heel of the molecule, the macrocycle, which has three consecutive double bonds. This year, the team around Nuno Maulide, Professor for Organic Synthesis at the University of Vienna and Adjunct PI at CeMM, overcame this obstacle by developing a novel chemical reaction that allows highly efficient synthesis of these macrocycles from simple starting materials. Yong Chen from Maulide's group at the Institute of Organic Chemistry compares the strategy to a Trojan horse, in which the intricate double bonds are hidden in a 'sealed' form so they can later be released and take effect.

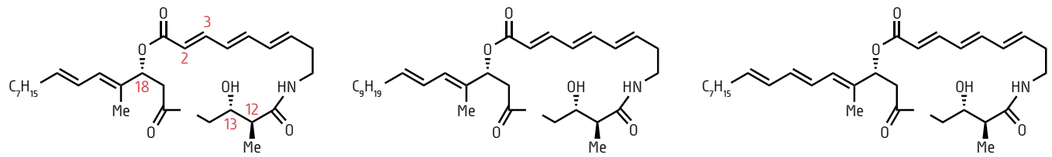
To achieve this, the researchers first installed a smaller ring, composed of only four carbons that masks the double bonds of the natural product (Fig. 8). This approach leads to a very short synthesis pathway of FR molecules. The lab can now produce several grams of the natural product; natural occurrence provides at most a few milligrams. This is a great advance, and what is more, the molecules are indistinguishable from those isolated from *Pseudomonas fluorescens*.

Since establishing this method, the researchers have created a whole range of analogs. Several of these variants are almost 100 times more potent than the natural product, and thus may become promising candidates for new and improved immunosuppressive therapy.

References

Chen Y, Coussanes G, Souris C, Aillard P, Kaldre D, Runggatscher K, Kubicek S, Di Mauro G, Maryasin B, Maulide N. A Domino 10-Step Total Synthesis of FR252921 and Its Analogues, Complex Macrocyclic Immunosuppressants. *J Am Chem Soc.* 2019 Sep;141(35):13772-13777.

Fig. 8 FR molecules, natural products with promising immunosuppressive effects. Credit: © University of Vienna/Maulide Group



Mutations of the BAF complex are found in about every fifth human cancer.

Contributing to targeted cancer therapy

Targeted therapy has been regarded as the biggest success in the treatment of cancer in the past few decades and as a cornerstone of personalized medicine. Instead of killing dividing cells like in chemotherapy, targeted therapy interferes with specific molecules needed for the development of cancer.

Some of these molecules are chromatin remodelers, enzymes which use adenosine triphosphate (ATP) to move or evict cell nucleosomes when a cell needs to alter the accessibility of its DNA to respond to signals or to DNA damage.

One chromatin remodeling complex is the BAF complex, mutations of which are found in about every fifth human cancer. Thus far, our knowledge of how BAF mutations are involved in cancer development has been limited, hence no therapies are available to treat such cancers. Typically, the genetic aberrations are loss-of-function mutations. These result in cancer cells lacking a specific BAF subunit protein, rendering it difficult to develop a drug against something that is not there.

Taking up the challenge, Stefan Kubicek's team at CeMM, supported by the Christian Doppler Laboratory for Chemical Epigenetics, in collaboration with Boehringer Ingelheim, set out to discover how to target BAF mutant cells and thus contribute to a potential cure.

Using 22 isogenic cell lines that differ only in that each lacks a different BAF subunit, the team characterized the consequences of loss of a single subunit for complex composition, chromatin accessibility and transcription. The group identified preferential BAF complex configurations, which can be altered when single subunits are lost. Furthermore, they discovered intense crosstalk between these subunits, so that, depending on the lost gene, other BAF subunits are incorporated with higher or lower frequency.

Although the original mutation results in the loss of one BAF subunit, this data indicates that the cancer-promoting properties might be conferred by aberrant functions of the remaining BAF complexes. And in turn, such aberrant functions might be druggable.

To test whether BAF mutant cancers indeed become addicted to the function of the remaining complexes, the team systematically depleted a second member of the BAF complexes in the cells that had already lost one subunit. Here they focused on three novel intra-complex synthetic lethalities, SMARCA4-ARID2, SMARCA4-ACTB, and SMARCC1-SMARCC2. The extensive systematic data on interaction proteomics, chromatin accessibility and transcription changes helped explain the molecular mechanism for these synthetic interactions (Fig. 9).

But would these novel targets hold up in relevant cancer cell lines beyond this cellular model system? Indeed, the researchers were able to verify this by demonstrating that, in a panel of 22 different cancer cell lines, in which the SMARCC1-SMARCC2 pair was particularly strong and conserved, cell lines with low SMARCC1 levels are extremely sensitive to loss of SMARCC2.

These findings thus provide not only deep molecular insight into the biochemical and epigenetic alterations after loss of a BAF subunit, but have also identified new possible targets for treating BAF mutant cancers.

References

Schick S, Rendeiro AF, Runggatscher K, Ringler A, Boidol B, Hinkel M, Májek P, Vulliard L, Penz T, Parapatics K, Schmidl C, Menche J, Boehmelt G, Petronczki M, Müller AC, Bock C, Kubicek S. Systematic characterization of BAF mutations provides insights into intracomplex synthetic lethalities in human cancers. *Nat Genet.* 2019 Sep; 51(9):1399-1410.

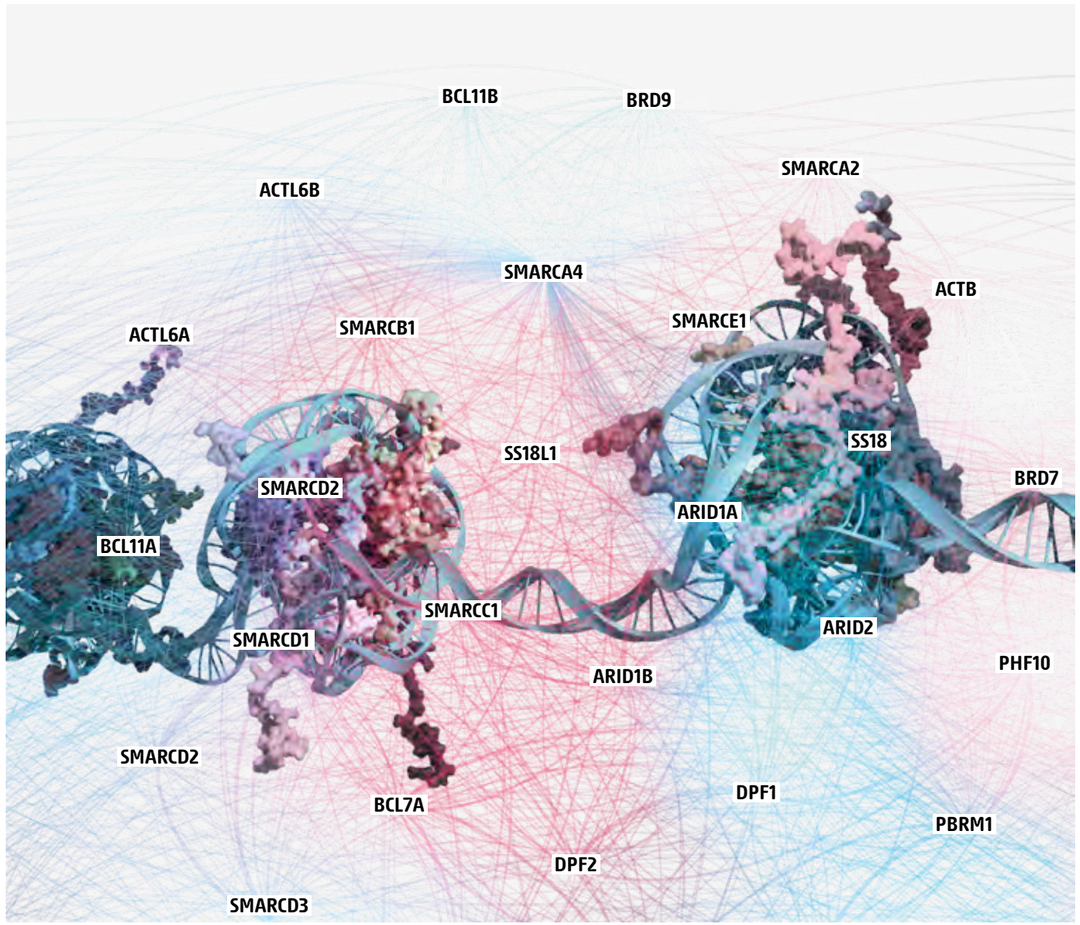


Fig. 9 Protein-protein interaction network between subunits of the chromatin-remodeling BAF complex. (Network: Loan Vulliard, artwork: Bobby Rajesh Malhotra)

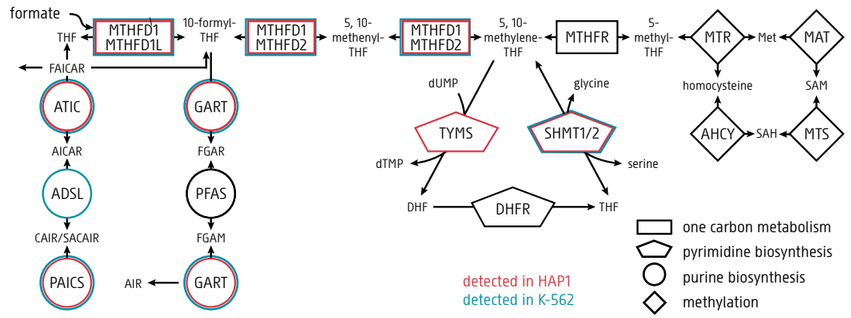


Fig. 10 Effects of MTHFD1 loss on nuclear metabolite composition. Representation of the folate pathway. Enzyme names are reported inside the geometric shapes, connecting the different metabolites.

Collaborating toward combination therapy

Another chromatin modifier under investigation in Stefan Kubicek's laboratory at CeMM is the histone acetyl reader bromodomain protein 4 (BRD4). Together with scientists from the Institute of Molecular Pathology (IMP) and the Medical University of Vienna, the team made a surprising discovery that could lead to novel approaches in combination therapy for BRD4-dependent tumors.

Epigenetic research has shown BRD4 to play a key role in cancer progression. To identify factors modulating its activity, Stefan Kubicek's group previously generated a cellular reporter system to monitor BRD4 inhibition. Recently, they have applied this model to systematically test whether loss of any of the approximately 23,000 human genes resembles BRD4 inhibition. Next generation sequencing converged on a single factor, methylenetetrahydrofolate dehydrogenase 1 (MTHFD1). MTHFD1 is an enzyme involved in folate metabolism, a process previously not associated with BRD4. Furthermore, MTHFD1 is located predominantly in the cytoplasm, while BRD4 resides in the nucleus.

A serendipitous meeting between Sara Sdelci, group leader at the Center for Genomic Regulation CRG Barcelona, then postdoctoral fellow at CeMM, and Philipp Rathert from Johannes Zuber's lab at IMP confirmed this finding. Philipp Rathert, coincidentally also working on BRD4, had generated data showing that MTHFD1 also physically binds to BRD4. Subsequent experiments at CeMM showed that the small portion of the MTHFD1 protein found in the nucleus interacts with BRD4. This interaction recruits MTHFD1 to the DNA, where the enzyme contributes to gene regulation.

In oncology, monotherapy with a single chemical agent is rarely successful due to the development of drug resistance. Antifolates, substances that inhibit the folate cycle, have been used for more than 70 years in cancer therapy and against diseases such as rheumatoid arthritis. The study results indicate that antifolates can be combined with BRD4 inhibitors to more effectively combat tumors. They may also help to stratify patients to ensure therapy success. In the best case, based on these findings, patients can also be selected who, because of their folic acid level and their genetics, respond particularly well to BRD4 inhibitors.

References

Sdelci S, Rendeiro AF, Rathert P, You W, Lin JG, Ringler A, Hofstätter G, Moll HP, Gürtl B, Farlik M, Schick S, Klepsch F, Oldach M, Buphamalai P, Schischlik F, Májek P, Parapatics K, Schmidl C, Schuster M, Penz T, Buckley DL, Hudecz O, Imre R, Wang SY, Maric HM, Kralovics R, Bennett KL, Müller AC, Mechtler K, Menche J, Bradner JE, Winter GE, Klavins K, Casanova E, Bock C, Zuber J, Kubicek S. MTHFD1 interaction with BRD4 links folate metabolism to transcriptional regulation *Nat Genet.* 2019 Jun;51(6):990-998.

Exploring combination therapies for leukemia

Scientists are increasingly exploring combination therapies, and leukemia is one of the first cancers where combination therapies have been explored and used. Treatment for chronic lymphocytic leukemia (CCL), the most common of blood cancers, involves drugs that inhibit proteins essential for the proliferation of immune cells. One of these drugs is ibrutinib. Ibrutinib breaks the circle of rampant cell proliferation and allows even patients with high-risk CLL to survive for many years. However, patients must take the drug every day, often endure severe side effects, and may develop drug resistance over time.

To improve CCL treatment toward higher efficacy and fewer adverse reactions, drug combinations are needed that exploit ibrutinib-induced vulnerabilities in leukemia cells with the aim of hitting the cells hard enough to eventually obviate treatment.

To speed up the search for promising drug combinations, scientists from three research groups at CeMM – Christoph Bock, Stefan Kubicek and Giulio Superti-Furga – and researchers from the Medical University of Vienna developed a method that can effectively sift through a large number of possibilities and identify and prioritize drug combinations that have true potential.

Combining epigenetic analysis using ATAC-seq (a method to assess genome-wide chromatin accessibility) with comprehensive testing of single-cell drug sensitivity, the researchers were able to identify characteristic epigenetic changes in leukemia cells for patients undergoing ibrutinib treatment. High-throughput imaging allowed them to single out drug sensitivities specific for these leukemia cells and not for healthy cells from the same patient. All experiments were done on primary samples collected from patients before and during ibrutinib treatment, which enabled systematic analysis of ibrutinib-induced vulnerabilities.

Given the availability of matched patient samples before and after induction of targeted therapy, this strategy is readily transferable to other cancers, providing a widely applicable tool for the systematic discovery and rational development of drug combinations in precision oncology.

References

Schmidl C, Vladimer GI, Rendeiro AF, Schnabl S, Krausgruber T, Taubert C, Krall N, Pemovska T, Araghi M, Snijder B, Hubmann R, Ringler A, Runggatscher K, Demirtas D, de la Fuente OL, Hilgarth M, Skrabs C, Porpaczy E, Gruber M, Hoermann G, Kubicek S, Staber PB, Shehata M, Superti-Furga G, Jäger U, Bock C. Combined chemosensitivity and chromatin profiling prioritizes drug combinations in CLL. *Nat Chem Biol.* 2019 Mar; 15(3):232-240.

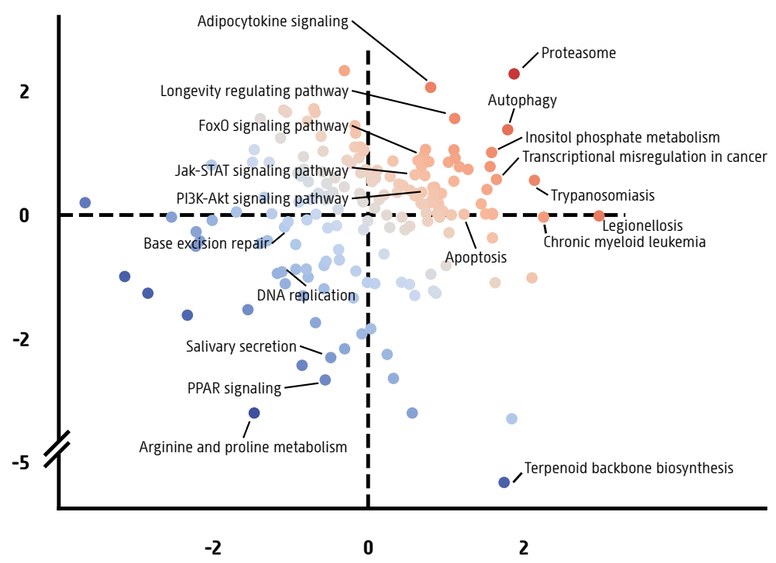


Fig. 11 Integrative analysis of differential chromatin accessibility (x-axis) and differential cell-selective chemosensitivity (y-axis) at the pathway level.

Drugging the undruggable

Conceptionally different new therapies to treat cancer are also on the rise. Because traditional drugs mostly function as inhibitors by binding to accessible pockets in disease-relevant proteins, only ~20% of all proteins are chemically addressable. This leaves some of the most relevant targets inaccessible to therapeutic development. The concept of chemically targeting proteins for their degradation promises to overcome this limitation.

Targeted protein degradation is based on small molecules, known as "degraders", which induce protein degradation by redirecting ubiquitin E3 ligases toward the protein to be eliminated. In other words, utilizing the cell's ubiquitin-proteasome system (UPS), the body's natural way of seeking out and destroying damaged proteins.

Until now, targeted protein degradation has been mostly studied from a structural perspective, while mechanisms determining the cellular response to small molecule degraders remain largely unknown. Seeking to fill this gap, Georg Winter's team conducted resistance screens on degraders of clinically relevant proteins that hijack different ubiquitin E3 ligases, to identify central UPS regulators essential for degrader efficacy (Fig. 12).

When these proteins are perturbed, ubiquitin E3 ligases lose their ability to flexibly assemble and disassemble in response to cellular needs. Instead, they start tagging themselves for destruction in a process called auto-degradation. As a consequence, the tested degrader drugs fail to destabilize their target proteins and are ineffective in blocking cancer cell growth.

Now that degraders are entering the clinic, understanding potential resistance mechanisms may inform on ways to overcome them. The modulator gene networks identified can serve as biomarkers to support patient stratification but also inform on fundamental aspects of the regulation and dynamics of the protein degradation machinery.

References

Mayor-Ruiz C, Jaeger MG, Bauer S, Brand M, Sin C, Hanzl A, Mueller AC, Menche J, Winter GE. Plasticity of the Cullin-RING Ligase Repertoire Shapes Sensitivity to Ligand-Induced Protein Degradation. *Mol Cell*. 2019 Aug;75(4):849-858.e8.

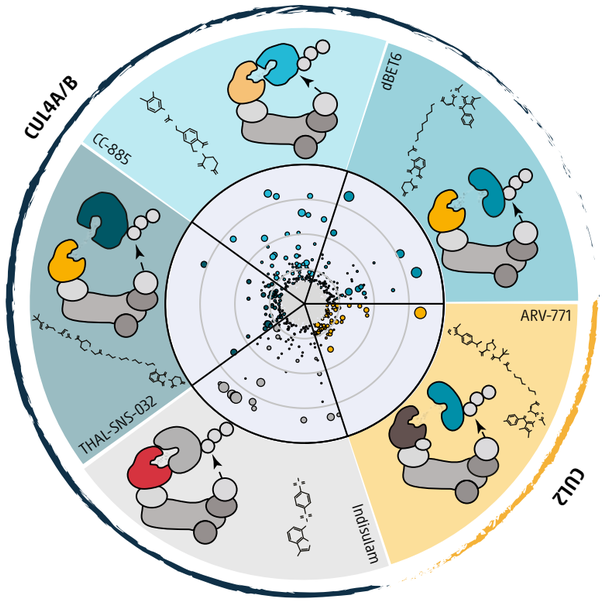


Fig. 12 Chemical structures of the screened degraders, hijacked ubiquitin E3 ligases, and targets. Results of the resistance screens are represented as circles in the middle.

In a 5-year project entitled "Glue2Degrade: Therapeutic Hijacking of E3 Ligases", Georg Winter now plans to chemically hijack many new E3 ligases in an unprecedented manner. For this ambitious undertaking, he has received a large Starting Grant of the European Research Council (ERC), one of the most prestigious sources of science funding in Europe. Building on the hypothesis that small molecules that can induce TDP are much more prevalent than currently anticipated, Georg Winter aims to identify "molecular glues", which degrade proteins by inducing cooperative protein binding to E3 ubiquitin ligases. This research is not only expected to deliver a fundamental understanding of the mechanisms governing cellular protein degradation but also novel therapeutic strategies to target otherwise undruggable proteins.

Expanding the druggable space

In the field of TDP, CeMM is furthermore proud to announce the start of a 3-year collaboration between the research groups of Georg Winter, Giulio Superti-Furga and Stefan Kubicek and scientists from Pfizer's Medicine Design organization in the USA to explore a combination of technologies aimed at expanding the druggable proteome. Combining the know-how, experimental and analytical pipelines and state-of-the-art proteomics facility at CeMM and the Pfizer team's strong background in medicinal chemistry and chemical biology, this partnership aims to scout new corners of the "ligandable" proteome followed by pharmacologic control over selected cellular proteins, including some hitherto deemed as poorly druggable.

This teamwork will allow the researchers at CeMM to apply some of the most powerful contemporary technologies in chemical biology at a scale beyond most academic research.

Developing chemical biology tools

An alternative to developing new drugs *de novo,* a time-consuming and expensive process, is to find new targets for existing drugs or drug combinations. To achieve this in an efficient manner, CeMM has created a comprehensive library of representative molecules and can screen these compounds and their combinations for their effect in various biological settings.

Fluorescent dyes, which are used daily in cell biology research, allow screening for new drugs and are often used in clinical diagnostics. Chemical fluorophores to a cell biologist are like colors to a painter. The project "3C Cellular Color Chart", winner of a Life Science Grant for Chemical Biology awarded by the Vienna Science and Technology Fund (WWTF) in 2017, combines the chemical-synthetic expertise of Adjunct PI Miriam Unterlass from the Institute of Materials Chemistry of the Vienna University of Technology with Stefan Kubicek's and Giulio Superti-Furga's experience in high-throughput automated microscopy and experimental discovery of the specificity of chemical substances for biological structures.

With the aim of expanding the color palette currently available, the team tested thousands of chemical substances in cells and identified around 200 new fluorescent substances that specifically stain cells. Based on these structures, they have generated derivatives with modified emission wavelengths and fluorescence yield by introducing push-pull effects, the extension of conjugated systems, and the positioning of supramolecular building blocks. They have also changed the biological binding affinity of the substances by altering their size, architecture and charge. Iterative synthesis and biological testing should soon allow researchers to identify the molecules with the best properties, properties, which would elucidate biological mechanisms in minute detail.


Lung/Brain
Knapp
Nagy

Lung/Brain

"Every Breath You Take". To breathe is to live. The first thing we do when we are born is to inhale, and the last thing we do when we die is to exhale. Breathing allows our body to obtain the energy it needs to sustain itself and its activities. It provides the oxygen necessary for metabolism and removes its by-product carbon dioxide. Breathing also affects our motor control and posture and is important for physiological and emotional regulation. And lastly, breathing influences homeostatic functions in other systems, such as our autonomic nervous system, circulatory system and chemical regulation.

Groups
Sylvia Knapp,
Vanja Nagy

Location
AKH/
MedUni Vienna

Fighting for breath

In normal lungs, the cells of the alveoli produce a thin, runny mucus that coats the surface of the airways. This mucus traps dust, germs, and any other foreign particles entering the airways as we inhale. Tiny hairs or cilia on the surface of the bronchi sweep the mucus and foreign particles upward into the larger air passages and then up to the throat where they can be swallowed or coughed up.

Cystic fibrosis (CF), a progressive genetic disease, causes the mucus in the lungs to become so thick and sticky that it captures the germs, with the trapped bacteria causing recurrent or chronic lung infections and in turn inflammation, respiratory failure and other complications. Over time, CF limits the ability to breathe, and most people with CF have a shorter-than-average life expectancy.

Treatment for CF is usually initiated only when the patient presents with acute infection, and is targeted to the most abundant, cultivable bacteria. Pathogen control is not easily achieved, however, and the microbiota may remain persistent despite the use of various treatment regimens. Over time, plastic changes can occur in the microbial metabolism, as recently reported. In the deep mucus, for example, the low availability of oxygen limits ATP production for survival, and competition for alternative terminal electron acceptors such as phenazines, nitrate, and fumarate drives metabolic adaptations.

In an editorial on CF in the *American Journal of Respiratory Cell and Molecular Biology*, Sylvia Knapp, Professor for Infection Biology at the Medical University of Vienna and her team at CeMM, emphasizes the need to identify predictable metabolic shifts during pathogen adaptation. This will help to exploit microbial metabolic requirements as therapeutic targets to prevent exacerbations, and to develop early-onset markers for disease aggravation. Reviewing a study that indicates that the substantial change in central carbon metabolism and overproduction of fumarate in CF is key to understanding its dynamics, the authors suggest expanded clinical investigations that will further our knowledge of microbial metabolic processes and provide relevant molecular triggers as promising drug targets that they are eager to explore.

References

Widder S, Knapp S. Microbial Metabolites in Cystic Fibrosis: A Target for Future Therapy? *Am J Respir Cell Mol Biol.* 2019; 61(2):132-133.

In addition to breathing, movement is essential to living long, healthy lives. Our bodies are designed to move. We feel better when we do some form of exercise, be it low impact like walking or more intense like running, than when we sit long hours at our desks or on the couch.

Like breathing, moving our bodies improves blood and oxygen flow which has positive effects on our bodily health and mental well-being. On top of increasing and maintaining our muscular strength, cardiovascular fitness and emotional health, physical movement also happens to be crucial for learning, cognition, attention and memory. Studies have shown that exercise improves the ability to concentrate and can even boost brain regeneration.

In early childhood, movement is vital for development, improving bone health, weight status cognitive function. Most babies take their first steps between 9 and 12 months of age and are walking well by around 15 months. Walking allows children to explore the world around them and prepares them for independence. A lack of movement at a young age can impede the experiential learning process.

Moving forward

Walking becomes difficult in a group of inherited neurodevelopmental disorders called spastic paraplegia that share the primary symptom of progressive muscle tightness (spasticity) and weakness of the leg and hip muscles. In around 10% of cases, lower limb spasticity and weakness may be accompanied by other neurological symptoms such as peripheral nerve impairment, muscle atrophy and intellectual impairment.

The research group led by Vanja Nagy, Adjunct Principal Investigator at CeMM and Key Researcher at the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD), works to identify novel genes underlying rare neurodevelopmental disorders and to decode their regulatory network. This group employs behavioral studies, imaging and molecular/biochemical assays in animal models to study various genetic mutations and their effects on human pathology.

In a truly international research project, Vanja Nagy and colleagues from institutes in Austria, Canada, Germany, New Zealand, Sweden, Turkey, the UK, and the USA, revealed two novel genetic mutations associated with spastic paraplegia and psychomotor retardation with or without seizures (SPPRS).

Using sequencing, the researchers identified two biallelic mutations in the HACE1 gene, p.Q209* and p.R332*, in three children from two unrelated families with severe intellectual disability, developmental delay and inability to sit or speak by the age of 5 years – symptoms similar to previously reported cases of SPPRS. They then demonstrated in a mouse model that a deficiency in HACE1 results in several clinical features of SPPRS, including locomotion and learning deficiencies, a decreased number of synapses, and structural and behavioral neuropathological features that resemble those in patients with the disorder.

Furthermore, they showed a marked upregulation of RAC1 levels throughout the mutant mouse brain and elevated ROS levels. These findings were confirmed in SPPRS patient-derived fibroblasts in which active RAC1 abundance, downstream signaling components, ROS production, and cellular migration are likewise dysregulated, all indicative of a hyperactive RAC1 pathway.

These results suggest that RAC1 is a key factor underlining neuronal pathology in HACE1-deficient patients and are a step forward toward understanding the pathogenic mechanism behind SPPRS.

References

Nagy V, Hollstein R, Pai TP, Herde MK, Buphamalai P, Moeseneder P, Lenartowicz E, Kavirayani A, Korenke GC, Kozieradzki I, Nitsch R, Cicvaric A, Monje Quiroga FJ, Deardorff MA, Bedoukian EC, Li Y, Yigit G, Menche J, Perçin EF, Wollnik B, Henneberger C, Kaiser FJ, Penninger JM. HACE1 deficiency leads to structural and functional neurodevelopmental defects. *Neurol Genet.* 2019 Apr 29;5(3):e330.

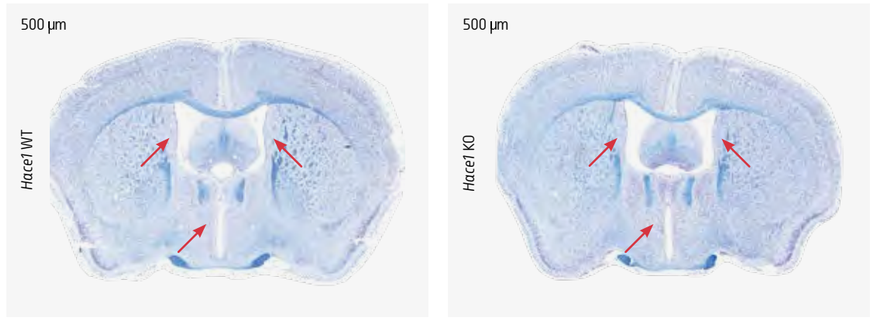


Fig. 13 LFB-CV-stained coronal sections of whole Hace1 WT and KO adult mouse brains. Ventriculomegaly (red arrows) is evident in the KO brain as compared with the WT littermate. This structural phenotype is also evident in HACE1-deficient patients. Scale bar 500 µm.


Menche
ck
Networks
Administration

Networks

"The Scientist". No man/woman is an island but needs to be part of a community in order to thrive. Being connected with others in relationships is necessary for sharing resources and for communication. Social networks help us find jobs, homes, friends, and mates. Social support and interaction are also critical for our health and well-being. We simply do not do well when we are alone and isolated. Teamwork in the workplace not only builds trust and establishes strong relationships, it also fosters creativity and learning. It maximizes shared knowledge and helps people learn new skills. Collaborating on projects creates an enthusiasm for learning that solitary work usually lacks. Being able to share discoveries with others makes work exciting and promotes both individual and team knowledge.

Disciplines are also more successful when they work together. Combining two or more disciplines and their respective methods offers fresh perspectives and ways to overcome the limitations of the methodologies of one field. In doing so, interdisciplinary work allows researchers to solve scientific questions and puzzles beyond the scope of a single specialty.

With this in mind, CeMM liaises researchers from different fields such as biology, medicine, chemistry, computer science, and physics. When colleagues and partners outside of our teams get together, share ideas, methodologies, and technologies, the results are fascinating. Our unique mode of super-cooperation helps to make significant progress in translational research.

Networks mapping

One such successful interdisciplinary collaboration has been a study in which researchers from CeMM and St. Anna Children's Cancer Research Institute (CCRI) and physicians at St. Anna Children's Hospital and the Vienna General Hospital were able to make a significant step forward in understanding an enigmatic disease.

Langerhans cell histiocytosis (LCH) is a rare disease affecting primarily young children. It is caused by myeloid immune cells that aggregate into lesions, leading to tissue damage and other complications. LCH is typically classified as a pediatric cancer because of uncontrolled cell growth in different parts of the body, but it also has features of an autoimmune disease, as LCH lesions attract immune cells and show characteristic tissue inflammation.

Groups
Christoph Bock,
Anita Ender,
Jörg Menche

Location
CeMM
Time Capsule

LCH symptoms can range from mild to serious. While some patients recover without treatment, others require intensive chemotherapy and suffer from long-term consequences, or may even succumb to the disease. LCH is difficult to diagnose: Skin involvement in babies with LCH can appear as a diaper rash, whereas bone involvement can be mistaken as sarcoma in an X-ray image. In its most aggressive form, LCH presents as a leukemia-like disease and leads to organ failure. These diverse manifestations and enormous clinical differences in disease severity continue to puzzle physicians and scientists around the world.

Observing LCH lesions under the microscope, Caroline Hutter, pediatric oncologist at St. Anna Children's Hospital and Principal Investigator at CCRI, noticed striking heterogeneity among LCH cells. A collaboration comprising experimental and computational researchers from CCRI and CeMM, as well as medical doctors from St. Anna Children's Hospital and the Vienna General Hospital was formed to investigate this diversity in full molecular detail.

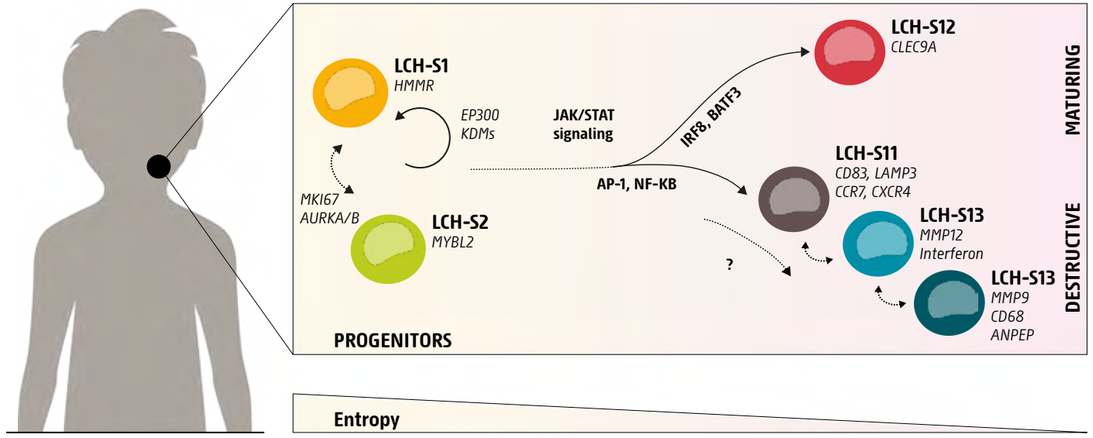
Using single-cell RNA sequencing and analysis done by Christoph Bock's group at CeMM, the interdisciplinary team investigated the molecular profiles of LCH lesions and developed a comprehensive map of cellular heterogeneity in LCH. These analyses identified multiple LCH cell subtypes that indicate a developmental trajectory in LCH lesions. One of these subtypes comprised actively dividing cells, which appear to give rise to the other LCH cell subtypes. In further experiments, the team unraveled the molecular pathways that are active in different branches of this unexpected developmental hierarchy, which corroborated an interplay of developmental, immunological, and oncogenic mechanisms in LCH.

These important insights may help devise better ways of distinguishing severe from less severe cases of LCH and potentially open up new treatment options.

References

Halbritter F, Farlik M, Schwentner R, Jug G, Fortelny N, Schnöller T, Pisa H, Schuster LC, Reinprecht A, Czech T, Gojo J, Holter W, Minkov M, Bauer WM, Simonitsch-Klupp I, Bock C, Hutter C. Epigenomics and Single-Cell Sequencing Define a Developmental Hierarchy in Langerhans Cell Histiocytosis. *Cancer Discov.* 2019 Oct; 9(10):1406-1421.

Fig. 14 Speculative model of the LCH developmental hierarchy and underlying regulatory mechanisms.



To avoid adverse reactions, and to develop beneficial combinations of drug-associated perturbations, we first need to understand how different perturbations interact.

Mapping networks

Just like interpersonal or communication networks, our body's function also relies on inter- and intracellular interactions. Cell-cell interactions allow cells to communicate with each other in response to environmental changes. Stimuli also cause direct or indirect interactions to take place among the proteins and genes within a cell to elicit particular biological consequences. This complex molecular network is referred to as the interactome.

Many diseases, rather than being a consequence of a single mutant gene, can be viewed as perturbations of this intricate system, driving it away from equilibrium. Likewise, drug therapy can be applied to perturb the human interactome with the aim of restoring the system.

Understanding the combined effect of independent perturbations is at the core of many fundamental, as well as practical challenges in current biology and medicine. Combination therapies using two or more drugs, for example, offer promising new treatment approaches for diseases including cancer. At the same time, interactions between drugs may induce unexpected side effects. To avoid such adverse reactions and to develop beneficial combinations of drug-associated perturbations, we first need to understand how different perturbations interact.

Over the last decade, numerous studies have revealed a close relationship between the structure of the interactome and the functional organization of the molecular machinery within the cell. This has opened exciting opportunities for using network-based approaches to investigate the foundations of both healthy and disease states.

Following this trend, Jörg Menche's group at CeMM developed a novel mathematical framework for accurately mapping out how different perturbations of the interactome influence each other.

This work offers a first general approach to quantify with precision how drugs interact, based on a mathematical model that considers their high-dimensional effects. Analyzing over 30,000 drug combinations applied to cell lines, the team identified a perturbation network of 242 drugs and 1,832 interactions. Their research revealed that the position of targets of a given drug within the interactome is not random but rather localized within drug modules. These locations were found to be linked to the specific cell morphological changes induced by the respective treatments, making morphology screens a valuable resource to study drug interactions.

Furthermore, the group identified various factors that contribute to the emergence of such interactions. Most notably, the distance between two drug modules on the interactome was found to be predictive of different types of interactions: the further away, the less likely an interaction.

In comparison with previous methods, which characterize interactions only as synergistic or antagonistic, the team reports that the new methodology can distinguish 12 distinct interaction types as well as reveal the direction of an interaction.

With this study, Jörg Menche's group provides the first comprehensive and complete description of any outcome that might arise from combining two drug perturbations. Moreover, the introduced framework can be used to address other key challenges, such as dissecting the combined impact of genetic variations or predicting the effect of a drug on a particular disease phenotype.

References

Caldera M, Müller F, Kaltenbrunner I, Licciardello MP, Lardeau CH, Kubicek S, Menche J. Mapping the perturbome network of cellular perturbations. *Nat Commun.* 2019 Nov 13;10(1):5140.

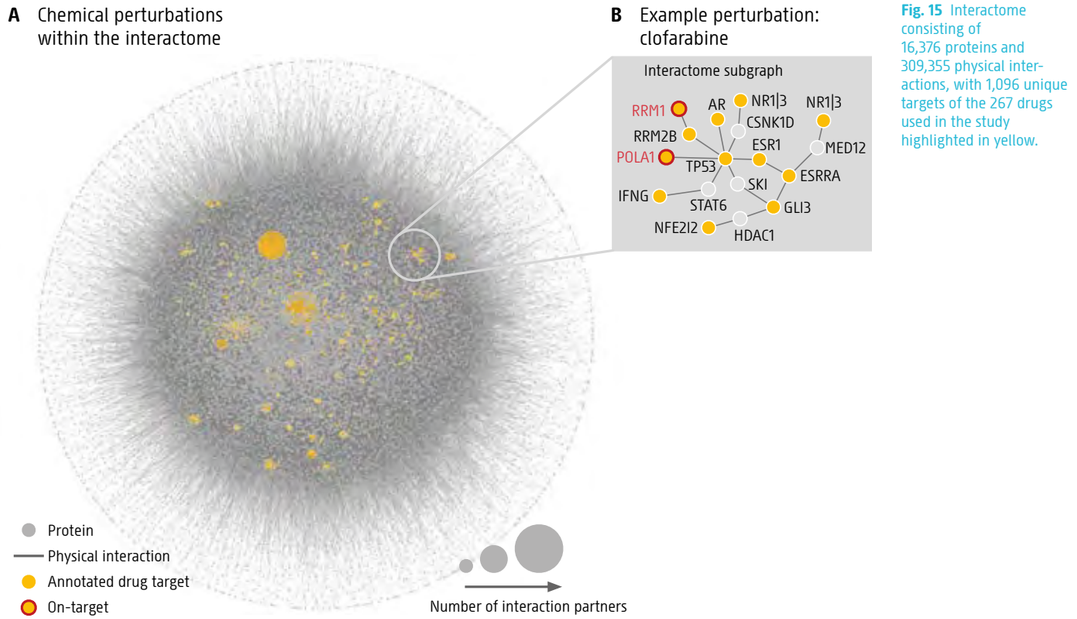


Fig. 15 Interactome consisting of 16,376 proteins and 309,355 physical interactions, with 1,096 unique targets of the 267 drugs used in the study highlighted in yellow.

Projects and Facilities

The RESOLUTE Consortium – Research Empowerment on Solute Carriers

Managing the access to resources: a key problem in biology

To drive advances in medicine, we think it is key to identify the biological questions that are still largely unresolved. Breakthroughs in scientific understanding of fundamental issues are usually the triggers of medical innovation down the line. This has been the case for cell cycle, cell death, cell signaling, autophagy and many other processes. How a cell acquires the nutrients and building blocks it requires to thrive, duplicate, differentiate and, generally, exert its function within the organ and organism that harbors it, is a fundamental question. This question has not been addressed yet in a satisfactory way, and most genes that encode transmembrane proteins thought to transport chemical matter across biological membranes are not characterized functionally. That is, we do not know what they do. Just as importantly, we do not know how their activity may be regulated in concert and by what general principles. We set out to try to address these questions by beginning to study one specific class of genes and their products: the large class of SLC proteins.

Solute carrier transporters

How the uptake of nutrients, vitamins, microelements, xenobiotics and drugs from the environment occurs and how these chemical substances distribute in the cells, is still not fully understood. Molecular transporters are proteins located in cellular membranes that control essential physiological functions, including nutrient uptake, ion transport and waste removal, so they could be seen as 'gatekeepers' of the cell. Solute carriers (SLCs) are the largest family of molecular transporters, with 446 members arranged into 65 sub-families. SLCs are vital for maintaining homeostasis in the body and in individual cells, and genetic polymorphisms on these proteins are associated with several diseases, such as amyotrophic lateral sclerosis (ALS), Alzheimer's disease, schizophrenia, diabetes and several types of cancer. Furthermore, SLCs can function as drug targets, as well as constitute paths for drug absorption into specific organs.

Despite their physiological and medical relevance, SLCs are relatively understudied and a large proportion of these membrane proteins are still considered 'orphans' in terms of substrate specificity (the nature of the transported molecule) and function (their precise role in cellular homeostasis). Consequently, there is an urgent need to 'unlock' the SLC family of transporters, in terms of specificity and regulation, which will increase the number of SLCs considered 'druggable' and hence, lead to new opportunities for therapies against human diseases.

Mission and work plan

The RESOLUTE consortium is a public-private research partnership funded by the Innovative Medicines Initiative (IMI) with 13 partners from academia and the pharmaceutical industry. Established in July 2018 for a duration of 5 years, the mission of RESOLUTE is to intensify worldwide research on SLCs and to establish them as a novel target class for medical research. Academic partners are interested in identifying the biochemical and biological functions and determining the ligand specificity of each family member, whereas the pharmaceutical industry seeks to integrate this information with available disease association data in order to identify SLCs that would merit a full drug discovery campaign. This synergy also comes into play because the pharmaceutical companies command a set of assays and technologies that are useful for the academic challenge of assigning a function to each SLC transporter.

RESOLUTE will tackle its mission in two ways:
1. by empowering the scientific community with novel research tools, protocols, and databases, as well as
2. by carrying out a systematic functional study of SLCs employing state-of-the-art 'omics' techniques and transport assays.

In this way, RESOLUTE will become an example of how a relatively understudied and biochemically demanding group of proteins can be 'unlocked' for research and development in a public-private partnership. Through the coupling of an inclusive, 'open-access ethos' to the results, techniques and reagents with the highest-possible quality of research output, RESOLUTE expects to accelerate the pace of research in the field of SLCs for both the global benefit of basic academic research and applied research in biotech and pharmaceutical companies.

Time plan

In the first 18 months, RESOLUTE released 443 DNA sequences of SLCs optimized to increase expression of SLC proteins in human cells, providing a reliable tool to facilitate the study of these proteins in cellular systems. The reagent collection is publicly available via Addgene, an open-access plasmid repository, and many more plasmid reagents will be added to the collection in 2020.

Additionally, RESOLUTE is exploring several approaches to produce highly-specific protein binders for SLCs, which are powerful but scarce biological tools. Currently new binders are being generated for 10 SLCs with medical relevance and they will be validated in a panel of RESOLUTE cell lines. RESOLUTE expects to generate binders for at least 30 SLCs by 2023 and to make them available at no cost to the scientific community from 2021 onwards.

RESOLUTE selected a set of six adherent human cancer cell lines cumulatively covering the expression of ~80% of all SLCs, based on a publicly-available dataset. These cell lines were characterized in terms of the transcriptome, the proteome and the abundance of major metabolites, and results were deposited in the RESOLUTE web portal in January 2020. Genetically-modified versions of these cell lines are being generated by the RESOLUTE consortium. To date, 440 SLC-overexpressing (OE) cell lines and 90 SLC-knockout (KO) cell lines were produced and will be deposited in an open-access cell repository from 2021. Furthermore, 100 KO and 100 OE cell lines per year will be released, until reaching a total number of 400 SLC-KO, 400 SLC-OE (in KO background) and 446 SLC-OE (in wildtype background) cell lines by 2023. For functional studies of SLCs, different approaches will be used to determine the transcriptome, ionome, proteome, metabolome and outcome of transport assays for the SLC-KO and SLC-OE cells. Furthermore, RESOLUTE's ambitious goal is to integrate this data as a fundamental principle to deorphanize and functionalize poorly characterized SLCs. These results will be released both as datasets or as scientific publications from 2020.

Moreover, to provide the research community with accessible SLC knowledge, the RESOLUTE web portal was created, a reference hub for research on solute carriers, which contains two main data resources: the RESOLUTE public database and the RESOLUTE knowledge base. On one hand, the RESOLUTE knowledge base displays compiled, connected and integrated public domain data on SLCs from multiple sources, allowing researchers to get an overview on the current knowledge on human SLC transporters. On the other hand, the RESOLUTE database provides access to data produced and released by the RESOLUTE consortium. The database will be continuously expanded with new datasets and reagents.

Communication and events

A valuable aspect in RESOLUTE is to establish and maintain a robust communication among all partners. We regularly coordinate and report the project's progress and discuss datasets before their public release. In addition to the monthly internal newsletters, regular teleconferences and face-to-face meetings, we are especially proud of our RESOLUTE consortium meetings, celebrated twice a year. In 2019, we had the opportunity to meet in Krems an der Donau near Vienna (Austria) and Bresso near Milan (Italy).

More than 65 participants coming from all over Europe and the US joined the RESOLUTE meeting in Krems an der Donau in June 2019. The event was a great chance to review the status of the RESOLUTE project right before completing the first year.

Updates from several of the RESOLUTE ongoing projects, a 'data integration workshop', and presentations of strategies to develop protein binders for SLCs by external collaborators were part of the RESOLUTE meeting program at Bresso in November 2019.

RESOLUTE

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 and EFPIA are responsible for any use that may be made of the information contained therein.

The RESOLUTE meeting in Krems an der Donau (June 2019) was attended by more than 65 participants from all over Europe and the US. It provided a great opportunity to review the status of the RESOLUTE project right before completing its first year. The meeting featured more than 30 young researchers presenting their progress in the generation of reagents, data and transport assays for SLCs. Additionally, we developed strategies to tackle the challenges of RESOLUTE's second year. Participants also enjoyed the excellent weather as well as the cultural amenities in the beautiful vineyards of the Wachau area.

The RESOLUTE meeting in Bresso (November 2019) was hosted by Axxam at OpenZone and attracted an audience of over 70 people. The first day of the meeting kicked off with presentations on updates from several of the RESOLUTE ongoing projects. The second day was dedicated to a 'data integration workshop', where participants discussed insights and tools to extract knowledge from the combination of diverse data types generated in the RESOLUTE project. The workshop included keynote talks by Avner Schlessinger (Mount Sinai, USA), Rob Russell and Francesco Raimondi (BioQuant, Germany), and Patrick Aloy (IRB, Spain), as well as by EFPIA representatives and CeMM scientists (Enrico Girardi and Eva Meixner). On the last day, external RESOLUTE collaborators presented several strategies to develop protein binders for SLCs.

Medical impact of RESOLUTE research

The scientific advances expected from RESOLUTE will impact both basic research and drug discovery. Furthermore, due to the 'open-access ethos' of the results, techniques and reagents developed within the RESOLUTE consortium, it is anticipated that these will all be used beyond the project's scope, in pharmaceutical companies and SMEs, for the creation of drug discovery projects. These campaigns will positively impact the goal of personalized medicine and will ultimately lead to new medicines for the benefit of patients.

The vision we have for RESOLUTE is to have started a worldwide matchmaking game. There are a limited number of SLC transporters and a limited number of metabolites and natural exogenous chemical molecules relevant for human physiology (such such as key evolutionary phytochemicals). In this matchmaking game, RESOLUTE intends to create enough tools and enough initial 'matchmaking' relationships to motivate the rest of the research community to engage and contribute. Solving the remaining mysteries of this key interface between the environment and the human biological system would represent a tremendous intellectual achievement and undoubtedly empower medicine and pharmacology with the knowledge to integrate metabolism, nutrition, drug uptake and drug action with physiology. We can't wait. Help us!

References

1. Hediger, MA. et al. The ABCs of membrane transporters in health and disease (SLC series): introduction. *Mol Aspects Med* 34, 95-107. (2013).
2. Cesar-Razquin, A. et al. A Call for Systematic Research on Solute Carriers. *Cell* 162, 478-487. (2015).
3. Lin, L. et al. SLC transporters as therapeutic targets: emerging opportunities. *Nat Rev Drug Discov* 14, 543-560. (2015).
4. Wang, W. et al. The Druggability of Solute Carriers. *J Med Chem*. 9b01237. (2019).
5. Klijn, C. et al. A comprehensive transcriptional portrait of human cancer cell lines. *Nat Biotechnol 33,* 306-312. (2015).

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

Obituary

We mourn the passing of Daniel Lackner, who left us in August 2019 after a serious illness at the age of 41. CeMM and the RESOLUTE community have lost an extraordinary researcher, colleague and friend.

Daniel performed his undergraduate studies in biology and genetics at the MFPL in Vienna. For his graduate work, he moved to the Wellcome Sanger Institute, in Hinxton, UK, where he used genomic approaches to study gene expression regulation in fission yeast. After obtaining his PhD from the University of Cambridge, he decided to do his postdoctoral work at the Salk Institute for Biological Studies in San Diego, USA. There, he studied telomere biology and aging with a focus on large-scale approaches. After returning to Austria in 2015, he joined the biotech company Horizon Discovery, where he led a team to generate human knockout cell lines using CRISPR/Cas9, before he started his new role as RESOLUTE Scientific Project Manager in the group of Giulio Superti-Furga at CeMM in 2018.

Daniel had played an essential role in setting up the scientific and organizational framework of the IMI-funded EU project. He quickly became the face and the driving force behind the international team of scientists across different nations. He was highly respected for his scientific expertise, his dedicated and diligent working style, and his ability to successfully build bridges between academia and industry, by connecting scientists with different backgrounds and expectations to work together toward a common overarching goal.

From the very beginning, Daniel was very open about his disease and his courageous and exhausting fight against a rare tumor. Daniel was a true scientist at heart and a role model in many ways. His intellectual rigor and his supportive as well as humorous attitude contributed positively to CeMM's culture and the success of the RESOLUTE project.

Daniel died far too early. Our thoughts and deepest sympathy are with his family. We miss him dearly.

Daniel Lackner
9 September 1977 –
31 August 2019

Research Collaboration on Targeted Protein Degradation with Pfizer Inc.

In November 2019, CeMM and Pfizer Inc. started a three-year research collaboration to explore a combination of technologies directed at expanding the druggable proteome. CeMM Principal Investigators Georg Winter (project coordinator), Giulio Superti-Furga and Stefan Kubicek, in collaboration with researchers from Pfizer's Medicine Design organization based in Cambridge, USA, will aim to explore a discovery strategy that combines parallel, efficient ligand identification with focused degradation of individual targets.

Traditionally, CeMM has pursued chemical proteomics approaches in the laboratories of Giulio Superti-Furga and Stefan Kubicek. These endeavors have resulted in a series of high-impact publications over the last decade. Project coordinator Georg Winter joined CeMM after postdoctoral research with Jay Bradner at the Dana Farber Cancer Center in Boston focusing on the field of protein degradation. Accordingly, significant expertise as well as experimental and analytical pipelines are available at CeMM, including a proteomics facility headed by André Müller with state of the art instrumentation and trained personnel.

Working closely with the Pfizer team, which supplies a strong background in medicinal chemistry and chemical biology, the main goal of the partnership is to scout new corners of the "ligandable" proteome followed by achieving pharmacologic control of selected cellular proteins, including some hitherto deemed as poorly druggable.

Both partners are very optimistic about the interplay and the impact of the collective effort. Charlotte Allerton, Senior Vice President and Head of Medicine Design, Pfizer, considers the collaboration to have the potential to further build capabilities in chemical biology and medicinal chemistry and to open up areas of target space that have historically been challenging. For Georg Winter and the team at CeMM, this collaboration will allow the application of some of the most powerful contemporary technologies in chemical biology at a scale beyond most academic research. Together, the teams at CeMM and Pfizer hope to inspire future efforts in drug discovery.

From left to right
CeMM project team:
Stefan Kubicek,
Georg Winter,
André Müller,
Giulio Superti-Furga

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 the deputy heads Thomas Winkler-Penz and Michael Schuster as well as 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 bioinformatic 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 (Pro-Met-)
Pro-Met- 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: *www.cemm.at/research/facilities*

Principal Investigators

Andreas Bergthaler

Viruses, Inflammation, Systemic Immunometabolism and the Devil

Andreas Bergthaler, born in 1977, studied veterinary medicine at the University of Veterinary Medicine in Vienna. For his graduate studies he joined the Institute of Experimental Immunology at the ETH and University of Zurich (Profs. Hans Hengartner and Nobel Laureate Rolf Zinkernagel). After postdoctoral work 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 inflammatory diseases. To this end, the Bergthaler laboratory studies viral infections in mouse models using an integrative approach of virology, immunology, pathology and systems biology. A particular focus rests on the metabolic-inflammatory disease of cachexia and the impact of liver metabolism on systemic immune responses and pathology. The Bergthaler laboratory is also interested in the mechanisms of transmissible cancers in the marsupial Tasmanian devil and why the immune system does not reject transmitted cancer cells. Together, this work may provide innovative insights into cancer and pave the way for novel therapeutic avenues for inflammatory and infectious diseases. 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 company Hookipa Pharma (Nasdaq: Hook), which develops immunotherapies against infectious and malignant diseases.

Main Research Interests

+ Chronic viral infections
+ Immunopathologies
+ Systemic immunometabolism
+ Cachexia
+ Transmissible cancers
+ Evolutionary dynamics of virus-host interactions

Relevant/Important Publications

Lercher A*, Bhattacharya A* et al. Type I interferon signaling disrupts the hepatic urea cycle and alters systemic metabolism to suppress T-cell function. *Immunity*. 2019 Dec 17;51(6): 1074-1087.e9.

Baazim H et al. CD8(+) T-cells induce cachexia during chronic viral infection. *Nature Immunology*. 2019 Jun;20(6):701-710.

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.e9. PMID: 30645971.

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). His recent work has focused on the identification and characterization of mitochondrial extracellular vesicles (Puhm et al., C2019). He has won numerous prestigious fellowships and awards and has authored >130 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 immunity as therapy for cardiovascular diseases

Relevant/Important Publications

Puhm F*, Afonyushkin T*, et al. Mitochondria are a subset of extracellular vesicles released by activated monocytes and induce type I IFN and TNF responses in endothelial cells. *Circ Res*. 2019;125 (1), 43-52.

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.

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

Christoph Bock

Cancer Epigenetics and Genome Technology

Christoph Bock joined CeMM as Principal Investigator in 2012. He pursues interdisciplinary research aimed at understanding the epigenetic and gene-regulatory basis of cancer, and advancing precision medicine with genomics technology. His research group combines experimental biology (high-throughput sequencing, epigenetics, CRISPR screening, synthetic biology) with computer science (bioinformatics, machine learning, artificial intelligence). He is also a guest professor at the Medical University of Vienna, scientific coordinator of the Biomedical Sequencing Facility at CeMM, and group leader at the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases. He coordinates an EU Horizon 2020 project on the single-cell analysis of human organoids as a contribution to the Human Cell Atlas. Christoph Bock is an elected member of the Young Academy of the Austrian Academy of Sciences and has received 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

+ Technology. High-throughput sequencing and genome editing
+ Bioinformatics. Algorithms for inferring epigenetic cell states
+ Epigenetics. Mapping epigenetic heterogeneity in cancer cells
+ Machine learning. Interpretable deep learning for biomedicine
+ Cell engineering. Designing CAR T cells for cancer therapy

Relevant/Important Publications

Rendeiro AF*, Krausgruber T* et al. Chromatin mapping and single-cell immune profiling defines the temporal dynamics of ibrutinib drug response in chronic lymphocytic leukemia. *Nature Communications*. 2020;11:577.

Schmidl C*, Vladimer GI*, Rendeiro AF*, Schnabl S* et al. Combined chemosensitivity and chromatin profiling prioritizes drug combinations in CLL. *Nature Chemical Biology*. 2019;15:232-240.

Halbritter F*, Farlik M* et al. Epigenomics and single-cell sequencing define a developmental hierarchy in Langerhans cell histiocytosis. *Cancer Discovery*. 2019;9:1406-1421.

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

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

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 interplay 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.

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 postdoctoral 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. Stefan Kubicek has also headed 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 working on metabolic enzymes in the cell's nucleus and 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
+ Chromatin remodeling in cancer development and progression
+ Role of chromatin in the specification of pancreatic cell types

Relevant/Important Publications

Schick et al. Systematic characterization of BAF mutations provides insights into intracomplex synthetic lethalities in human cancers. *Nat Genet*. 2019; 51(9):1399-1410.

Sdelci et al. MTHFD1 interaction with BRD4 links folate metabolism to transcriptional regulation. *Nat Genet*. 2019;51(6):990-998.

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.

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

+ Maintenance of genome stability in health and disease
+ 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

Owusu M, et al. Mapping the human kinome in response to DNA damage. *Cell Rep*. 2019; Jan 15;26(3):555-563.e6.

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.

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
+ Interactions between drugs and genes
+ Virtual reality approaches for visualizing and exploring large datasets

Relevant/Important Publications

Caldera M, et al. Mapping the perturbome network of cellular perturbations. *Nat Comm*. 2019;10:5140.

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

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.

Giulio Superti-Furga

Membrane Transporters and Drug Action

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 has been a member of the Scientific Council of the European Research Council (ERC) in 2017, 2018 and 2019. He completed his studies at the University of Zurich, Genentech and IMP/Vienna. He was a postdoctoral 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 six years, he has focused on unlocking the human "transportome" for medicine and drug discovery, trying to deorphanize 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 (IMI) 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 in immunity and cancer
+ 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 phenotypic 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
+ Gene control in cancer
+ E3 ubiquitin ligase regulation

Relevant/Important Publications

Mayor-Ruiz C, et al. Plasticity of the cullin-RING ligase repertoire shapes sensitivity to ligand-induced protein degradation. *Mol Cell*. 2019 Aug 22;75(4):849-858.e8.

Brand M, et al. Homolog-Selective Degradation as a Strategy to Probe the Function of CDK6 in AML. *Cell Chemical Biology*. 2019 Feb 21;26(2):300-306.e9.

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.

Adjunct Principal Investigators

Kaan Boztug

Genetics of Malignant and Immune System Disorders

Kaan Boztug, born in 1977, joined CeMM as PI 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 postdoctoral 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 patho-mechanisms of rare disorders of hematopoiesis and immunity. In 2019, he took over the agendas of Scientific Director at St. Anna Children's Cancer Research Institute (CCRI). He 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. He received an ERC Starting Grant in 2012 and an ERC Consolidator Grant in 2018. In 2019, Kaan Boztug was awarded the Johann Wilhelm Ritter von Mannagetta Prize for Medicine of the OeAW.

Main Research Interests

+ Genetics and molecular pathomechanisms of rare inherited disorders of hematopoiesis and immunity
+ Pediatric precision oncology
+ Molecular dissection of shared mechanisms underlying immune dysregulation and pediatric cancer
+ Systems biology and network medicine for rare and undiagnosed diseases

Relevant/Important Publications

Somekh I*, Thian M*, et al. CD137 deficiency causes immune dysregulation with predisposition to lymphomagenesis. *Blood*. 2019; 134(18):1510-1516

Domínguez Conde C*, Petronczki ÖY*, Baris S*, Willmann KL*, et al. Polymerase δ deficiency causes syndromic immunodeficiency with replicative stress. *J Clin Invest*. 2019; 129(10):4194-4206.

Serwas NK*, Hoeger B*, et al. Human DEF6 deficiency underlies an immunodeficiency syndrome with systemic autoimmunity and aberrant CTLA-4 homeostasis. *Nat Commun*. 2019; 10(1):4555.

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.

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. René 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 signaling. *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.

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

Schischlik F, et al. Mutational landscape of the transcriptome offers putative targets for immunotherapy of myeloproliferative neoplasms. *Blood*. 2019 Jul 11;134(2):199-210.

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 myelopro-liferative 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 myelo-proliferative disorders. *N Engl J Med*. 2005;352(17):1779-90.

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 and is currently Head of the Institute of Organic Chemistry. 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 also leads the Christian Doppler-Laboratory for Entropy-Oriented Drug Design 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
+ Design of new chemical probes in close collaboration with computational methods

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, 11, 329-334.

Chen Y, et al. A Domino 10-Step Total Synthesis of FR252921 and Its Analogues, Complex Macrocyclic Immunosuppressants. *Journal of the American Chemical Society*. 2019, 141, 13772-13777.

Kaiser D, et al. A general acid-mediated hydroaminomethylation of unactivated alkenes and alkynes. *Angewandte Chemie International Edition* 2019, 58, 14639-14643. *Angewandte Chemie*. 2019, 131, 14781-14785.

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.

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 neuro-science 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 utilizes NGS technology to identify novel causative genes that underlie undiagnosed rare neurodevelopmental disorders, with a focus on intellectual disability and epilepsy. 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 trans-differentiated patient neurons. This year, in close collaboration with Jörg Menche's team, the group employed a network-based approach generated from known intellectual disability genes to identify common molecular pathways and the most likely novel causative genes that will be functionally validated in a cellular system. Together, these 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

+ Whole-exome sequencing of undiagnosed neurodevelopmental disorders
+ Cellular and molecular basis of rare neurodevelopmental diseases
+ Preclinical phenotyping of rare neuropathologies
+ Basic molecular mechanisms underlining synaptic plasticity

Relevant/Important Publications

Desiderio S*, Vermeieren S*, et al. Prdm12 directs nociceptive sensory neuron development by regulating the expression of the NGF receptor TrkA. *Cell Rep*. 2019 Mar 26;26(13):3522-3536.e5.

Nagy V#, et al. HACE1 deficiency leads to structural and functional neurodevelopmental defects. *NeurolGenet*. 2019; 5(3). Co-corresponding author.

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

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

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, 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 postdoctoral fellowship in the United States from 2012 to 2015, Thomas Reiberger joined the Faculty at the Division of Gastroenterology and Hepatology at the Medical University of Vienna. Thomas conducted seminal studies for optimizing the role of non-selective betablocker therapy in cirrhotic patients with 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. In his role as the coordinator of the Rare Liver Disease (RALID) Center of the European Reference Network (ERN) at the Medical University of Vienna, he complements the mission of the LBI-RUD with translational research supported by the RALID center.

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 and has since been named Co-Director of LBI-RUD. 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.

Main Research Interests

+ Host-pathogen interactions
+ Tissue-resident leukocytes in peripheral tissue
+ Skin immune cells as target for chronic viral infections
+ 3D models of the skin to study complex interactions of immune and non-immune cells
+ Rare skin diseases

Relevant/Important Publications

Stary G, et al. A mucosal vaccine against Chlamydia trachomatis generates two waves of protective memory T cells. *Science*. 2015;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 polyimide/silica 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 of Innsbruck, Austria, where he heads the Division of Developmental Immunology at the MUI Biocenter. He joined CeMM in November 2018 as an Adjunct PI aiming to develop PIDDosom inhibitors. He studied biology at the Universities of Salzburg and Innsbruck, completed his PhD and early postdoctoral 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 and became a full professor in 2009. 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, such as polyploidy. His work is funded by the Austrian Science Fund (FWF) and the European Research Council (ERC).

Main Research Interests

+ BCL2 family proteins in tissue homeostasis
+ DNA damage & checkpoint signaling
+ Cell cycle – cell death crosstalk
+ The PIDDosome in polyploidization control

Relevant/Important Publications

Sladky VC, et al. E2F-Family Members Engage the PIDDosome to Limit Hepatocyte Ploidy in Liver Development and Regeneration. *Dev Cell*. 2020 Jan 13. pii: S1534-5807(19)31039-1. doi: 10.1016/j.devcel.2019.12.016.

Haschka MD, et al. MARCH5-dependent degradation of MCL1/NOXA complexes defines susceptibility to antimitotic drug treatment. *Cell Death Differ*. 2020 Feb 3. doi: 10.1038/s41418-020-0503-6.

Connolly P, et al. Cell-Cycle Cross Talk with Caspases and Their Substrates. *Cold Spring Harb Perspect Biol*. 2019 Nov 14. pii: a036475. doi: 10.1101/cshperspect.a036475.

Schuler F, et al. Checkpoint kinase 1 is essential for fetal and adult hematopoiesis. *EMBO Rep*. 2019. Aug;20(8):e47026. doi: 10.15252/embr.201847026.

Schuler F, et al. Checkpoint kinase 1 is essential for normal B cell development and lymphomagenesis. *Nat Commun*. 2017 Nov 22;8(1):1697. doi: 10.1038/s41467-017-01850-4.

Front row
from left to right
Andreas Villunger,
Joanna Loizou,
Sylvia Knapp,
Giulio Superti-Furga,
Anita Ender,
Jörg Menche,
Christoph Bock,
Miriam Unterlass

Back row
from left to right
Robert Kralovics,
Thomas Reiberger,
Georg Winter,
Andreas Bergthaler,
Kaan Boztug,
Georg Stary,
Stefan Kubicek,
Christoph Binder

Scientific Advisory Board

SAB members:
Dr. Janet Kelso,
Prof. Dr. Hidde Ploegh,
Prof. Dr. Carl-Henrik Heldin,
Prof. Dr. Emmanuelle Charpentier,
Prof. Dr. Richard Flavell

In scientific and strategic questions, CeMM and its stakeholders – the mother organization Austrian Academy of Sciences and the strategic partner Medical University of Vienna – are advised by a board of international top scientists that covers a broad range of expertise and has experience in managing research organizations and evaluation processes. Every 18 months, CeMM's Scientific Advisory Board members visit the institute to provide feedback on ongoing projects, to discuss future research plans with CeMM faculty, postdoctoral fellows and PhD students and to provide CeMM management with recommendations on strategy, recruitment, contract extensions as well as technology transfer and commercialization opportunities.

In 2019, there was a turnover of Scientific Advisory Board members. We would like to especially thank David Livingston, Deputy Director of the Dana-Farber/Harvard Cancer Center, Boston, USA, for being an energetic, demanding and inspiring Chair of the CeMM SAB for many years, and James "Jim" Griffin, also a long-term SAB member from the Dana-Farber/Harvard Cancer Center, Boston, USA. Both have supported the institute as SAB members since its inception and should be getting the credit for many important decisions that guided the institute through its critical early years of growth, which was key to CeMM's success. We are grateful for their continued insistence that we embrace the responsibility and the rare opportunity associated with CeMM's special location in the middle of one of Europe's largest medical campuses – and at a time of great mobility of talent in the region – with no fear or hesitation. Their lively interactions with our researchers and students were an invaluable source of inspiration and motivation, contributing greatly to creating the basis for the shared ambition of research excellence and training quality, which was necessary to establish CeMM as an international top research institute in the life sciences.

We were also happy to welcome a new member of the Scientific Advisory Board at our last SAB meeting in May 2019: Emmanuelle Charpentier, Director of the Max Planck Institute for Infection Biology, Berlin, DE. Likewise, we are thankful to Carl-Henrik Heldin, Director of the Ludwig Institute for Cancer Research, Uppsala University, and Chairman of the Board of the Nobel Foundation, SE, for taking up the role as new Chair of the CeMM SAB.

Please find below an excerpt (general part) of the 2019 report of the Scientific Advisory Board:
On May 19-22, 2019, five members of the Scientific Advisory Board (SAB) of the Research Center for Molecular Medicine (CeMM; Emmanuelle Charpentier, Richard Flavell, Carl- Henrik Heldin (chair), Janet Kelso and Hidde Ploegh), met on CeMM's premises in Vienna. Before the meeting, the SAB had received from the CeMM Director, Giulio Superti-Furga, a summary of the activities at CeMM since the last SAB visit two years ago, as well as the CVs, lists of publications and research plans of the PIs at CeMM. On the evening of May 19, the SAB met privately with Giulio Superti-Furga and the Administrative Director, Anita Ender, and was given a presentation of past, present and planned activities at CeMM. During the following two days, 30 PhD students and postdocs from the different groups of CeMM presented their projects to the SAB. The SAB also listened to presentations by the five newly appointed Adjunct PIs, and presentations on the Virtual Reality Platform and Business Opportunities and Technology Transfer at CeMM. In addition, individual SAB members met with postdocs and PhD students over lunch, and also met privately with each one of the PIs and some of the Adjunct PIs. In the morning of May 22, the SAB presented its impressions and recommendations to CeMM's Director, Administrative Director and PIs, as well as to representatives of the Austrian Academy of Sciences.

CeMM is now 12 years of age since the publication of its first research report. Under its strong and visionary leadership, CeMM has developed into an outstanding institute for molecular medicine. The fact that CeMM is located close to one of the largest hospitals in Europe makes it a perfect place for high-level translational research. Elaborate and successful branding efforts have contributed to making CeMM well known nationally and internationally. CeMM is truly international, with staff from 46 nations. The staff shows strong commitment to and engagement in their projects, as well as to CeMM as an institute. CeMM is characterized by extensive collaborations between the different groups, and a noticeable team spirit has been established.

The success of CeMM manifests itself in several ways. The scientific productivity has been outstanding, with a steady output of high-quality publications in leading journals. Several landmark discoveries have been published recently, including reports on somatic mutations of calreticulin in myeloproliferative neoplasms (New England Journal of Medicine), that CD55 deficiency is related to early-onset protein-losing enteropathy and thrombosis (New England Journal of Medicine), that the ubiquitin ligase LZTR1 regulates Ras ubiquitination (Science), that artemisinins target GABAA receptors and impair cell identity (Cell), that viral immune modulators perturb the human molecular network by common and unique strategies (Nature), on the structural basis for viral 5'-PPP-RNA recognition by human IFIT proteins (Nature), on the stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy (Nature), and that SLC38A9 is a component of the lysosomal amino acid sensing machinery that controls mTORC1 (Nature). All these reports, and several other CeMM publications, have had a significant impact in their respective fields of research.

Another sign of the success of CeMM is the success of PIs in bringing in external grant support. As an example, no fewer than 10 ERC grants have been awarded to CeMM scientists. In addition, the institute has been extraordinary successful in recruiting excellent staff at all levels, including PIs, postdocs, PhD students, and technical and administrative personnel.

Having reached a mature stage, CeMM now faces turnover among its group leaders. As another sign of CeMM's quality, the PIs who left left have found prestigious positions elsewhere. Thus, Robert Kralovics has moved to the Faculty of the Medical University of Vienna, where Sylvia Knapp and Christoph Binder are located. Kaan Boztug has been appointed Director of the Children's Cancer Research Institute (CCRI) of the St. Anna Children's Hospital. Of crucial and immediate importance for CeMM is the recruitment of new excellent international PIs with complementary expertise, who can contribute to the strong research program at CeMM.

Since entering the building in 2010/2011, CeMM has operated on a flat budget from the Austrian Academy of Sciences. Given its outstanding scientific performance and the fact that CeMM now needs to recruit additional excellent new PIs (which will require attractive startup packages to be successful), the SAB strongly supports an increase in budget for CeMM from the Academy.

Given that the evidence of CeMM's contribution to helping establish precision medicine in Austria is now beyond doubt, and given the systemic effect that CeMM is having through its trained alumni and the different spin-off institutes/biotech companies it has created, CeMM should become a national priority.

Prof. Dr. Carl-Henrik Heldin (CHAIR)
Director, Ludwig Institute for Cancer Research, Uppsala University, SE
Chairman, Board of the Nobel Foundation, SE

Prof. Dr. Emmanuelle Charpentier
Director, Max Planck Institute for Infection Biology, Berlin, DE

Prof. Dr. Richard Flavell
Chairman, Section of Immunobiology, Yale University School of Medicine, New Haven, USA

Dr. Janet Kelso
Group Leader Bioinformatics, Max Planck Institute for Evolutionary Anthropology, Leipzig, DE

Prof. Dr. Hidde Ploegh
Member, Whitehead Institute for Biomedical Research, Cambridge, USA

For more information on the Scientific Advisory Board of CeMM, please visit the CeMM website: *www.cemm.oeaw.ac.at/about/advisory-board*

SAB members with CeMM faculty, postdocs and students on the CeMM terrace

Training at CeMM

CeMM International PhD Program in Molecular Technologies and Systems Medicine

Since the founding of the CeMM PhD program in 2006, CeMM has had the pleasure of welcoming over 100 international and enthusiastic students through its doors to start their CeMM journeys.

In 2019, five PhD students successfully graduated from the CeMM PhD program: **Thea Gorki** (Knapp group), **Fiorella Schischlik** (Kralovics group), **Adrian Cesar-Razquin** (Superti-Furga group), **Florian Puhm** (Binder group), **Lydia Robinson-Garcia** (Loizou group).

Through these journeys of scientific and personal development, each of these students has made a lasting contribution to CeMM and the program, and we are very proud of every one of them. It is always a bittersweet moment when students complete their PhD studies and move on to the next exciting step in their journey, which 62 students have done over the past 13 years. Each one of them will continue to spread the CeMM spirit of kindness wherever they go.

Every year, CeMM seeks new students to join our international PhD program, particularly those excited to work in an environment of free-minded scientific creativity and to translate their findings with a view to impacting medical practice and healthcare. In order to identify the best candidates, CeMM has established a multi-step selection process, building up to a final three-day selection in Vienna. In 2019, over 700 candidates from around the world applied to the program. After navigating the review of applications, a round of video interviews and finally dazzling the faculty at the selection event, the successful candidates are offered a four-year scholarship, which covers university fees, work-related travel, salary and health insurance. Giulio Superti-Furga, Scientific Director and CEO of the Research Center for Molecular Medicine of the Austrian Academy of Sciences and Professor of Medical Systems Biology at the Medical University of Vienna, is the Dean of the PhD program and is responsible for all student affairs.

While the end result is the confirmation of a PhD by the Medical University of Vienna, the ultimate 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 three 'modes': collecting, connecting and contributing, together with an efficient onboarding/offboarding process.. These modes are intended to guide the students through scientific excellence in data generation and validation to responsible and professional scientific citizenship.

Introductory Program

In 2019, 12 new PhD students, from 8 different countries, joined CeMM. 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 faculty introduces themselves and their research topics in detail. A special treat, representing the high point of the introductory lecture series, was a lecture/concert given by Nuno Maulide, which probed the inter-connections between science and music and the patterns contained therein.

From left to right
The 2019 PhD student representatives:
Loan Vulliard (Jörg Menche group),
Michael Caldera (Jörg Menche group),
Christina Schüller (Robert Kralovics group),
Peter Traxler (Christoph Bock group),
Jakob-Wendelin Genger (Andreas Bergthaler group)

To complement faculty on relevant subjects that are not covered by their expertise, additional speakers from the Medical University of Vienna and beyond give expert talks, thus anchoring the program in the wider context. The introductory program capitalizes on the dynamic arising from having a small group together for a month in a highly interactive, discussion-based environment. This not only allows the students to interact deeply with the entire faculty and to exercise their critical thinking but also strengthens the group dynamic, thus creating a strong support network for their time at CeMM.

The second phase of the introductory program is spent experiencing CeMM from a different perspective by means of a one-month lab rotation. This has proven to be an excellent introduction to the collaborative nature and strong sense of community that characterize CeMM, whilst also benefitting the students through exposure to new labs, people and techniques. Even though some combinations might be more unconventional than others, both students and faculty rise to the challenge and new insights can be gained on both sides.

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.

Supervision of doctoral candidates

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.

One of the main contributing factors behind a successful PhD thesis is the close supervision of an experienced PI. To ensure adequate mentoring and to provide students with the means by which they may receive this supervision, after completing the first six months of the program, students present their lab rotation project in addition to their PhD thesis concept to the entire faculty. This critical checkpoint ensures that all students have direction and focus from an early stage.

All students are given the opportunity to present their research findings and progress to the entire faculty and research community as part of CeMM's institute-wide seminars, held every Friday. All new students are added to a rolling cycle of speakers upon arriving at CeMM and give their initial presentation after approximately nine months and every nine months subsequently until the conclusion of their PhD studies. Following the Thesis Seminar, students receive detailed feedback and constructive praise and criticism regarding their presentation and presentation skills. Additionally, students regularly attend the in-house Hot Topics Journal Club, where they present a critical review of recently published scientific papers.

Visibility and dissemination

International visibility of the CeMM PhD program has been achieved and is continually enhanced by (i) a high scientific output, and (ii) well-trained CeMM graduates who succeed in obtaining top biomedical positions around the world.

Over the past 5 years, 2/3 of CeMM graduates have gone on to complete a postdoctoral position in academia, with other major destinations including research in industry and medical fields. This is testament to the PhD program preparing and enthusing students to continue pursuing their research questions.

In addition to these achievements, specific CeMM students were singled out for awards to recognize their particular achievement. Most recently, these have included:

+ In March 2019, both Elisabeth Salzer and Bernd Boidol won individual Johann Wilhelm Ritter von Mannagetta Advancement Awards from the Austrian Academy of Sciences for their excellent publications and PhD studies in the field of medical research.
+ In April 2019, Julia Pazmandi won the Falling Walls Lab Austria competition for her VR Holodeck project.
+ In May 2019, Michel Owusu was awarded the Wilhelm Auerswald Prize 2019 for the Best Doctoral Thesis at an Austrian Medical University.

Pre-ERC Postdoc Program

CeMM has an excellent track record of nurturing postdocs to become internationally successful principal investigators, professors, entrepreneurs, of which we are justifiably proud. Postdocs at CeMM benefit from the highly collaborative environment surrounded by the ideas, projects, resources, infrastructure, collaborations and mindset required for ground-breaking research. In-lab mentoring and supervision contribute greatly to developing the scientific leaders of the future.

CeMM's position at the heart of one of Europe's largest medical campuses provides the unique opportunity to engage in close interactions with physicians and clinical researchers. In order to strengthen these connections amongst the post-doctoral community at CeMM and those in the various departments of the Medical University of Vienna, the CeMM postdoc representatives organized and hosted a Postdoc Networking Day in November 2019, where around 40 postdocs were able to present their research and strengthen their networks.

CeMM postdocs regularly participate in training events across CeMM including the Friday Seminars, Scientific Illustration course, IP workshop and bioinformatics course.

They also benefit from opportunities within the EU-Life network, with two CeMM postdocs being selected to visit and give seminars as part of the EU-Life visiting postdoctoral seminar series commencing in 2020, a program designed to encourage and promote postdocs looking to transition to PI positions in the near future.

In 2019, CeMM conducted a postdoc call, culminating in an invite-only workshop event for future scientific leaders, and recruited a group of postdocs to enter the CeMM Pre-ERC Postdoc Program in Cellular, Molecular and Digital Medicine.

The postdoc program is designed to prepare postdoctoral researchers for a successful ERC Starting Grant or comparable grant application and for an independent research career in top research organizations in Europe and around the world.

It will kick off in 2020, and will bring selected candidates to CeMM for 3 to 6 years to address ambitious research questions in areas such as cancer, immunology, chemical biology, epigenetics, metabolism, and genomic medicine. Interdisciplinary research projects will focus on medically relevant problems, including disease mechanisms, modern therapeutics and diagnostic strategies. On top of this, postdocs will receive extensive career development and leadership training from the entire CeMM faculty and additional experts in a highly collaborative and supportive environment.

As always at CeMM, the postdocs will be free to explore ideas, go deep into the fundamentals, be interested in mechanisms and familiar with the translational process. However, they should also be armed with the necessary discipline and soft skills. The training program will therefore encompass project management, scientific writing, visual communication, entrepreneur-ship, leadership and data science, as well as offer opportunities to collaborate with industry (biotech/pharma) and to get involved in academic start-up/spin-off companies.

As postdocs progress through the program, they will receive more opportunities for teaching and providing supervision as well as special training for writing successful ERC Starting Grants as a 'ticket' to an outstanding academic career in Europe.

The new CeMM postdoc program is an extension rather than a replacement of our previous excellent training, and all postdocs, existing and new, will benefit from the increased focus.

From left to right
The 2019 postdoc representatives:
Andrea Majoros (Robert Kralovics group),
Philipp Starkl (Sylvia Knapp group),
Celine Sin (Jörg Menche group),
Ariel Bensimon (Giulio Superti-Furga group)

Retreats and a Scientific Recess

CeMM organizes its annual Scientific Recess with representatives of each research group and the adjunct laboratories as well as regular faculty retreats, and retreats with administrative team leaders. The themes and concepts of the annual recess and retreats have to play into the mission of CeMM, encourage CeMM members, faculty and team leaders to reflect on performances, new developments and future directions, and the outcome of the discussions is communicated to the entire institute. These types of meetings are usually held in a location outside of CeMM to foster out-of-the-box thinking. They are an opportunity and a forum at which to discuss strategic goals, to analyze and overcome existing challenges and to work on the improvement of processes. The overall goal is to empower group leaders, postdoctoral fellows and PhD students, technical personnel, administration and the scientific support team to provide the best possible results and services in order to contribute to excellent research and to research integrity at CeMM. It is also an important tool with which the directors motivate the different groups and individuals to support each other and the overall mission of CeMM, and to appreciate the benefit of being embedded within the strong, collaborative and corporate culture of CeMM.

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 a modern blend of 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.

CeMM's administration and scientific support team understands that an ever-improving technical, operational, educational, financial and ethical infrastructure is an essential and integral part of modern research operations. In fact, each and every aspect of CeMM's commitment to research excellence and its societal pact to advance medicine and healthcare has been, and constantly is, dependent on an administration and scientific support team that has the ambition to reach new levels of synergy with the experimental teams to create true innovation and world-class training in molecular medicine. Timely and effective services contribute to an atmosphere of mutual trust and respect, strengthen CeMM in its mandate to create value and credibility, and are necessary to stay competitive in this branch of innovation.

CeMM Scientific Recess 2019, Waidhofen an der Ybbs

From 18-20 February 2019, CeMM's annual Scientific Recess took place in Hotel Schloss an der Eisenstrasse, Waidhofen a.d. Ybbs, with about 60 representatives from the different research groups and our facilities in attendance. Thank you to the organizers Andreas Villunger and Christoph Binder and to all the participants from CeMM and the adjunct groups, who contributed to a successful meeting with lively discussions, their presentations and their new ideas. The overall topic of the 2019 Recess was to identify translational opportunities, agree on emerging topics and themes, and to look for new possibilities for interactions within CeMM. We also thank our special guests Michael Sixt, IST Austria, who gave an interesting talk about dendritic cell migration for immunity, and Markus Zeitlinger, MedUni Vienna, who presented an overview on clinical trial management.

From 25-26 November 2019, the Faculty Retreat and the Administrative Team Leaders Retreat took place at the same time in Refugium Hochstrass in Stössing. While the CeMM faculty discussed how chemistry and chemical biology as well as organoids can change, affect and accelerate CeMM's research, the administrative team leaders worked on SWOT analyses per support unit and on an update of the description of the functions and roles of all admin and scientific support units.

The growth of the institute, existing and new requirements in terms of service requests, constant legal, technical and scientific developments as well as the need to de-risk and professionalize certain areas all require a regular analysis of the status quo and a common effort towards the advancement of organizational, scientific and technical areas in CeMM. The willingness to constantly improve is one of the key assets of CeMM as a research center of excellence.

CeMM Alumni Network

CeMM has established an alumni network with the mission to connect, reconnect, value, exchange and share. The network offers a platform through which former CeMM members can stay in touch with each other and share their knowledge and expertise with current CeMM employees.

CeMM Alumni Board in CeMM Brain Lounge, May 2019

Treasure hunt with the cast from the company Nesterval.

The Alumni Kick-Off Event took place in Vienna on Sunday, 4 May 2019. Despite the cold and rainy weather, former and current CeMM members actively participated in a treasure hunt through Vienna, solving the criminal case around the disappearance of our Scientific Director. We thank the cast of the company *www.nesterval.at* for their great performance and the team of *www.stiftstpeter.at* for their warm hospitality during dinner.

On Monday, 6 May 2019, the program continued at CeMM. In a discussion round with the Alumni Board, alumni members and CeMMies, suggestions and ideas on how to further improve our institute and its network were collected. In the evening, many Alumni Network members joined the CeMM Karl Landsteiner Lecture held by Luke O'Neill, Trinity College Dublin, who gave a talk on the question "Will we cure all diseases by targeting inflammation?" After the talk and a cocktail reception, Luke O'Neill rocked the Haus der Industrie as lead singer and guitarist of his band "The Metabollix".

We thank the CeMM Alumni Board members for their voluntary support and dedication to setting up the CeMM Alumni Network: Ferran Fece de la Cruz, Adriana Goncalves, Tatjana Hirschmugl, Katrin Hörmann, Evren Karayel, Erika Schirghuber, Christopher Schliehe, Christian Schmidl.

The Cemm Alumni Network will have regular meetings and activities and invite former CeMM members to participate and stay connected with CeMM. Some of the benefits of joining the CeMM Alumni Network include:

+ Keeping in touch with CeMM and former colleagues
+ Reconnecting with other alumni
+ Participating in alumni-specific events
+ Sharing research knowledge with others and forming new collaborations
+ Sharing professional expertise as a mentor
+ Finding a mentor and enhancing your career

If you worked for CeMM in the past and would like to stay part of this community, please sign up for the CeMM Alumni Network: *www.cemm.at/alumni_registration*

Life at CeMM

"CeMM has it all: excellent scientists and breakthrough discoveries, professional administration, team spirit, a strong institutional identity, and a bit of healthy craziness that makes CeMM both outstanding and unique. As an active member of the EU-Life alliance, CeMM has been gaining even more recognition worldwide. As the newest addition to EU-Life, our institute is looking forward to collaborating with CeMM at multiple levels, as we share the same values and aspirations: to pioneer science that aims to make a difference for society."

Professor Marta Miączyńska, PhD
Director of the Institute
Head of Laboratory of Cell Biology
International Institute of Molecular and
Cell Biology in Warsaw

"What particularly impresses me at CeMM is the integration of the arts into research and a truly open mind to trans- and interdisciplinary impulses. The enormous scientific output of CeMM speaks for itself. My ride in the CeMM Brain Lounge was memorable for the amplitude of the topics covered and of interest to CeMM. Science is part of Viennese culture! In 2019, I was glad to be able to host a dinner with the members of the Scientific Advisory Board and stakeholders of CeMM at which I learned yet more about CeMM's outstanding research and interconnectedness within the scientific community in Vienna and worldwide. CeMM is a true and innovative ambassador for Vienna's best scientific cultural tradition."

Mag.ª Veronica Kaup-Hasler
Executive City Councillor for Cultural Affairs and Science, Vienna

“I was on the committee that appointed the CeMM Scientific Director many years ago and have since followed the evolution and destiny of CeMM with attentive eyes. It has developed as a wonderful place for technical and conceptual innovations aimed at medical translational research and as such enjoys a special, mutually beneficial relationship with the Medical University. I also cherish the dialogue with society on topics of great importance and through art projects.”

Prof. Dr. Markus Hengstschläger
Department Head
Center for Pathobiochemistry and Genetics,
Medical University of Vienna

"I have had the privilege to follow the evolution of CeMM from its – less than immaculate – conception some 20+ years ago. The appointment of a brilliant and flamboyant director was transformative: Recruitment of equally brilliant and dedicated researchers has created an institute, where success breeds success. The culture of CeMM can also be gauged by the quality of training, which PhD students obtain. Over the past 25 years, I have been an opponent in PhD defenses in the academic institutions of many different countries. Hence, I have a reference base for comparison, when I quiz CeMMies during their thesis defense. The conclusion is: CeMM PhD students stand out. They do not crack under pressure, because they both master their very field and have a command of what can be considered common knowledge in science. If you are a young scientist aiming high, consider CeMM as THE place to learn about basic science and translational medicine."

Prof. Dr. Michael Freissmuth
Department Head
Center for Physiology and Pharmacology,
Medical University of Vienna

Lectures, Symposia and Workshops

CeMM's lecture series are an integral part of its training/communication program. While providing a forum for scientific researchers to discuss highly specialized topics, the lectures also introduce current scientific research to the general public. The CeMM Landsteiner Lecture series in particular invites prominent scientists, whose molecular research is deemed to have a high impact on medicine, to address a mixed audience of scientists and laymen.

13th CeMM Landsteiner Lecture – Will We Cure all Diseases by Targeting Inflammation?

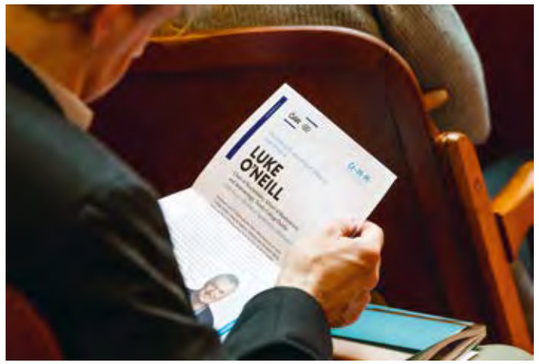
On 6 May 2019, Luke O'Neill, Chair of Biochemistry at Trinity College Dublin, thrilled an audience of around 350 experts and laypeople with his inspiring talk on inflammation and the urgent need for new treatments for major diseases. After a subsequent cocktail reception, Professor Luke O'Neill rocked the Haus der Industrie as lead singer and guitarist of his band "The Metabollix".

At the present time, only 500 treatment options are available for 7,000 distinct diseases. We are still unable to sufficiently treat illnesses with a social impact, such as neurodegenerative diseases, cancer, neuropsychiatric disorders, and several types of inflammatory disease. Clinicians and patients are anxiously waiting for scientific innovations or breakthroughs. Given the timeline of at least 10 years from discovery of a new, disease-causing molecular mechanism to the development of an effective drug, it is crucial that research improve our understanding of disease and its management.

After listing the five most significant medical discoveries, i.e. vaccines, penicillin (antibiotics), anesthetics, insulin and birth control, Luke O'Neill provided insights into his own research, which focuses on inflammation at the root of most diseases. In response to major trauma and injury, inflammation restores us to health, yet it can also – for largely unknown reasons – go rogue and induce a whole host of inflammatory diseases, which remain challenging to treat.

Comparing the inflammatory process and pathways to a domino game, Luke O'Neill described his studies as a quest for the first treatable domino. His bridging the gap between discovering NLRP3 as a main pathway for pathology in multiple inflammatory diseases to detecting effective small molecules demonstrates the value of basic research and its impact on drug discovery and development.

Reiterating his commitment to basic science, Luke raised hopes for the future with many new treatments on the horizon and the promise of funding and support through the responsible politicians and policymakers.



1st Vienna Symposium on Machine Learning in Medicine & Biology

(Bio)medicine consistently ranks among the areas in which machine learning will have the greatest impact. This challenging field requires dedicated technology to be applicable and acceptable in biomedical research and clinical practice. Supported by the Austrian Platform for Personalized Medicine, the "1st Vienna Symposium on Machine Learning in Medicine & Biology" took place at CeMM on 5 June 2019. Bursting at the seams, the event organized by Georg Langs (Medical University of Vienna) and Christoph Bock (CeMM), brought together the diverse community of Austrian researchers in this rapidly growing field.

The invited talks covered new methods and exciting applications of machine learning, including deep neural networks and interpretable AI, cancer and drug toxicity, the social dimension of machine learning and what machine learning can learn from the way our brains work. Finally, a keynote lecture by Thomas Lengauer (Max Planck Institute for Informatics & University of Cologne) demonstrated how machine learning can predict drug resistance in HIV and improve the treatment of patients with HIV in a precise/specific manner. Following the success of this first symposium, a follow-up event is planned in 2020.

2nd AustroMetabolism Workshop

On Wednesday, 9 October 2019, around 120 researchers from 15 institutions located all over Austria got together for the second time for the AustroMetabolism Workshop at the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences in Vienna.

Launched in 2017 by a joint initiative of the Medical University of Vienna, the University of Veterinary Medicine of Vienna, the University of Graz and CeMM, this interdisciplinary event provides a forum for Austrian basic and clinical researchers to discuss metabolic research. The gathering also aims to support the establishment of networks and the formation of scientific cooperation in the field. For a deeper understanding of metabolic processes in the human body, which is key to treating many diseases, the program included a diverse selection of scientific talks. In the 2019 workshop, contributions ranged from cell metabolism of cancer and immune cells, diabetes, obesity, fat and liver metabolism to the effect of food degradation by the intestinal microbiome on inflammatory bowel disease.

One of the many highlights of the event was a guest lecture by Matthias Tschöp, Scientific Director of the Helmholtz Center Munich, which engages over 2,300 employees. Matthias Tschöp is one of the world's leading researchers in the fight against obesity and type 2 diabetes and has developed several of what are known as poly-agonists that could revolutionize the treatment of these diseases. In addition, Pooja Jha, editor of *Nature Metabolism,* represented this renowned scientific journal, offering participants a fascinating glimpse behind the scenes of academic publishing. In turn, she was highly impressed by Austria's fertile and diverse research landscape.

Overview Seminars and Scientific Meetings in 2019

9 Jan 2019
Impromptu
Mirjam van der Burg
Associate Professor, Leiden University Medical Center, The Netherlands
"B-cell immunity in primary immunodeficiencies"

Qiang Pan-Hammarström
Professor of Clinical Immunology, Department of Biosciences and Nutrition, Karolinska Institute, Sweden
"Genetic landscape of hepatitis B virus-associated B cell lymphoma"
Host: Jörg Menche

17 Jan 2019
Impromptu
John Kuriyan
Professor, Departments of Chemistry and Molecular and Cell Biology, University of California, Berkeley; Investigator, Howard Hughes Medical Institute, USA
"Phosphorylation control in CamKII"
Host: Giulio Superti-Furga

21 Jan 2019
Impromptu
Dirk Trauner
Janice Cutler Chair in Chemistry and Adjunct Professor of Neuroscience and Physiology, New York University, USA
"Optical control of transport proteins"
Host: Giulio Superti-Furga

6 Feb 2019
Impromptu
Nicolas Thomä
FMI Basel, Switzerland
"The CRL4 ubiquitin ligase: at the intersection of genome stability and drug discovery"
Host: Georg Winter

4 Mar 2019
CeMM LBI-RUD
Impromptu
Thomas Berger
Director, Department of Neurology, Medical University of Vienna
"Current status and challenges in microbiome research in multiple sclerosis"
Host: Vanja Nagy

11 Mar 2019
CeMMinar
Mariano Barbacid
AXA-CNIO Professor of Molecular Oncology, Spanish National Cancer Research Center (CNIO)
"Precision Medicine: Targeting KRAS mutant lung and pancreatic cancers"
Host: Georg Winter

12 Apr 2019
Impromptu
Matteo Innacone
San Raffaele Scientific Institute, Head of Dynamics of Immune Responses, Italy
"In vivo imaging of anti-viral immune responses"
Host: Sylvia Knapp

24 Apr 2019
LBI-Rud/CeMM Special Seminar
Meral Ozguc
Molecular Genetics Diagnostic Laboratory, Faculty of Medicine Hacettepe, Ankara, Turkey
"Rare Diseases and Ethical Challenges"
Hosts: Christiane Druml/ Kaan Boztug

30 Apr 2019
Impromptu
Thomas Berger
Director, Department of Neurology, Medical University of Vienna, Austria
"Current status and challenges in microbiome research in multiple sclerosis"
Host: Vanja Nagy

3 May 2019
Impromptu
Markus Müllner
Chief Technology Officer, PhoreMost Ltd, Babraham Research Campus, United Kingdom
"Drugging the undrugged with protein interference"
Host: Georg Winter

6 May 2019
Landsteiner Lecture
Luke O'Neill
Professor of Biochemistry in the School of Biochemistry and Immunology at Trinity College Dublin; Co-Founder Opsona Therapeutics, Ireland
"Will we cure all diseases by targeting inflammation?"
Host: Giulio Superti-Furga

5 Jun 2019
1st Vienna Symposium on Machine Learning in Medicine & Biology
Organizers: Christoph Bock (CeMM) & Georg Langs (Medical University of Vienna)

8 Jul 2019
CeMMinar
Jacob Corn
Professor of Genome Biology, ETH Zurich, Switzerland
"Watching CRISPR genome editing at work in human cells"
Host: Joanna Loizou

11 Jul 2019
Impromptu
Fran Supek
ICREA Research Professor, IRB Barcelona, Spain
"Error-free and error-prone DNA repair shape mutation landscapes in human tumors"
Host: Joanna Loizou

27 Aug 2019
Impromptu
Lukas Mager
University of Calgary, Canada
"Harnessing the microbiota and immune system for the treatment of colorectal cancer"
Host: Andreas Bergthaler

9 Oct 2019
2nd AustroMetabolism Workshop
Organizers: Andreas Bergthaler (CeMM), Kristaps Klavins (CeMM), Richard Moriggl (University of Veterinary Medicine), Thomas Scherer (Medical University of Vienna), Martina Schweiger (University of Graz)

16 Oct 2019
CeMMinar
Elly Tanaka
IMP, Vienna
"Tissue regeneration"
Host: Giulio Superti-Furga

17 Oct 2019
Impromptu
Jörn Aldag
CEO Hookipa Biotech, Vienna
"How to run a successful biotech company"
Host: Giulio Superti-Furga

23 Oct 2019
Impromptu
Martin Brunner
Medical University of Vienna
"Introduction to clinical studies"
Host: Giulio Superti-Furga

24 Oct 2019
Impromptu
Seth Scanlon
Immunology Editor at *Science*
"Publishing in Science: an Inside Look"
Host: Andreas Bergthaler

21 Nov 2019
EU-Life Seminar
Dai Long Vu
Berlin Institute of Health, Max Delbrück Center of Molecular Medicines, Germany
"Bioanalytical method to study tryptophan metabolism in gut microbiota-host crosstalk"
Host: André Müller

2 Dec 2019
CeMMinar
Marcel Tijsterman
Leiden University, The Netherlands
"On worms, transgenic plants and breast cancer patients"
Host: Joanna Loizou

3 Dec 2019
Impromptu
Theodore Alexandrov
Head of Metabolomics Core Facility, EMBL Heidelberg, Germany
"Spatial metabolomics in tissues and single cells"
Host: Andreas Bergthaler

Outreach and Visits to CeMM

CeMM is involved in various scientific, cultural and educational projects with the aim of informing and enthusing children and adults for science. While art projects and social partnerships at CeMM are important tools for active dialogue with society, participation in outreach events like the KinderUni (Children's University) allows us to share our knowledge and engage with people directly. Over the years, CeMM has been honored by visits from decision-makers, opinion leaders and future scientists.

A highlight among the visits in 2019 was a scientific and cultural tour of CeMM by the MAK Art Society. The tour was organized to showcase the recent acquisition of Martin Walde's chair "Le Baron Noir" by the Museum of Applied Art. This piece was originally designed for the CeMM Time Capsule, one of our art projects which CeMM considers effective in actively engaging with society.

During their visit on 20 March 2019, the members of the Circle of Ambassador's Spouses Austria (CASA) were particularly interested in CeMM's research into societally important diseases such as immune disorders and infections, cancer and metabolic disorders.

VBCeMM summer school, a collaboration between CeMM and the Vienna Biocenter, takes place in July and August each year. This two-month course in a vibrant and culturally diverse atmosphere attracts talented students from around the world, who are interested in graduate studies in the life sciences. An active social calendar that was kicked off with a BBQ at CeMM on 9 July 2019 complements the scientific program. The summer school is generously sponsored by the Max Birnstiel Foundation. Successful applicants receive accommodation, a travel allowance and a stipend for the duration of the scholarship.

On 1 August 2019, CeMM hosted a visit from 25 Summer Academy fellows at the Studienstiftung des deutschen Volkes. With the support of Judith E. Unterlass, team leader at Evotec, they learned more about cancer drug research and the cutting-edge technologies at our institute. Lectures by the facility deputy heads Kristaps Klavins and Thomas Penz were followed by a riveting presentation of the Virtual Reality (VR) Holodeck project developed by Jörg Menche's group at CeMM.

Another event for lower grade pupils was the "Academics Comic Day" organized by the Austrian Academy of Sciences on 7 November 2019. In an interactive workshop, a team of CeMM Phd students and 3D artists introduced around 150 children to the complexity of the human body, explaining basic scientific concepts such as genes and their role in our body with virtual reality tools.

To inspire future scientific researchers, CeMM participated in the Children's University at the Austrian Academy of Sciences and at the Medical University of Vienna. In a workshop entitled "From the gene to the cell to the living organism", CeMM PhD students introduced the complex and intriguing world of human cells to children aged 10-12 while Christoph Bock explained the book of life and how to read it to 120 excited young students. CeMM thanks him and Christina Schüller, Michael Caldera, Jakob-Wendelin Genger and Peter Traxler for their enthusiasm in communicating science.

On 17 October 2019, CeMM hosted the opening symposium "THINKING DIGITAL HEALTH FORWARD – The future has already started" of the cooperation HEALTH.DigitalCity. Under the patronage of Professor Dr. Siegfried Meryn, this kick-off event attracted over 150 people from healthcare and IT, as well as thought leaders, decision-makers, managers, experts, politicians and the public to discuss how to advance digitalization in healthcare for the sake of the people concerned.

Social Events

Social events play an important role when it comes to maintaining the collaborative spirit within the CeMM community and beyond. A yearly outing at the beginning of the fall term, a Halloween party, organized by the PhD students during their first year and the festive Christmas party have a fixed place in our annual calendar.

Well prepared by dance workshops held at the institute, the CeMMies – as the employees call themselves – are regular and enthusiastic visitors of the Vienna Ball of Sciences. Organizing a summer party is almost a tradition. This year it was combined with the EMBL World Alumni Day. In 2019, we also had the pleasure of watching the first theater premiere by CeMM's Amateur Theater, CAT. CeMM's PhD students invited their colleagues from the Vienna Biocenter to a highly entertaining pub quiz and distinguished themselves as excellent event managers.

Vienna Science Ball
CeMM and LBI-RUD had a great time at the 5th Vienna Ball of Sciences which is THE highlight of the ball season for the scientific community. Thank you to the organizers: The Science Ball is a gas, it brings the mad crowd of researchers, creatives, innovators and future shapers together and inspires us all!

Summer Party and EMBL World Alumni Day
On Friday, 19 July 2019, CeMM hosted a summer party and barbecue. The event brought together the esteemed CeMM members, adjunct labs, collaboration partners and friends, as well as the Austrian EMBL alumni branch. Part of the program was dedicated to a – remote – celebration of the first EMBL World Alumni Day. The community also merrily celebrated that Adjunct PI Miriam Unterlass has become a professor at the Vienna University of Technology (TU Wien).

CeMM's Amateur Theater
The Imaginary Invalid, a comedy in three acts based on Molière's famous play, with interesting insights into 17th century medicine and plenty of humorous reinterpretations, was performed on 12 July 2019 in CeMM's Seminar Room. Super professionally staged by CeMM Postdoc Andrea Majoros and starring PhD and Postdoc Program Manager Matthew Spencer, the premiere was a huge success.

Outing
On 5 October 2019, CeMMies and adjunct members got together for an excursion and enjoyed a day full of interesting talks and social activities outside the institute. A special focus was on materials and material testing. Kicked off by talks of Miriam Unterlass, CeMM Adjunct PI and Assistant Professor at the TU Vienna, and Joachim Rajek, TÜV AUSTRIA General Manager, the program included an exciting visit to the TÜV Laboratories for mechanical testing of materials, components and structures. After an insightful morning and a typical Austrian lunch in Klostergasthaus Thallern, a wine rally at Freigut Thallern rounded out the day. Thank you to Joachim Rajek and his team for their hospitality!

Halloween Party
Every year, the CeMM Halloween Party is a showcase of creativity: not only did CeMM's new PhD students devote a lot of wit, imagination and passion for detail to its organization, but everyone at CeMM competed with ingenious costumes as they embarked on their "Space Odyssey to Alpha CeMMtauri".

VBCeMM Pub Quiz
On 26 November 2019, CeMM hosted the 4th VBCeMM event with over 60 PhD students from the Vienna Biocenter, the Gregor Mendel Institute (GMI), the Institute for Molecular Biology (IMBA), the Institute for Molecular Pathology (IMP), the Max Perutz Laboratories, and – for the first time – also from the Institute of Science and Technology (IST) Austria. In this edition, CeMM's PhD representatives organized a fun pub quiz to (successfully!) test the audience's general science knowledge.

Christmas Party
CeMM celebrated its Christmas Party 2019 at TMW – Technisches Museum Wien. Thank you to Eva Schweng and team, as well as the 2nd-year PhD students for their enthusiasm and hard work in preparing a welcoming and enjoyable event. The evening started with a "high-voltage demonstration" at the museum, a 30-minute show, which introduced our CeMMies to the world of electrical charges and currents, followed by a tasty buffet dinner. While kids could enjoy guided tours and a craft program, the adults amused themselves with a quiz show by the students and a performance featuring faculty members as Smurfs.

Vienna City Marathon
On 2 April 2019, 15 CeMM relay teams, together with colleagues from the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases and the Vienna Liver Study Groups, participated in the 36th Vienna City Marathon. Thank you to Lindsay Kosack who kindly organized this team challenge.

Hockey Events
On 22 March and again on 13 September 2019, the CeMMies were invited to a hockey experience at the ice rink, in Vienna's 21st district. No matter how good their skating skills were, everybody was invited to take part in "the probably most exhausting leisure activity of the year". It was great fun!

Prizes and Recognitions

We would like to highlight the following prizes and recognitions garnered by CeMM members in 2019.

Congratulations on the prestigious honors and awards:
Hatoon Baazim, Andreas Bergthaler, Christoph Bock, Bernd Boidol, Kaan Boztug, Joanna Loizou, Michel Owusu, Julia Pazmandi, Elisabeth Salzer, Sandra Schick, Georg Winter

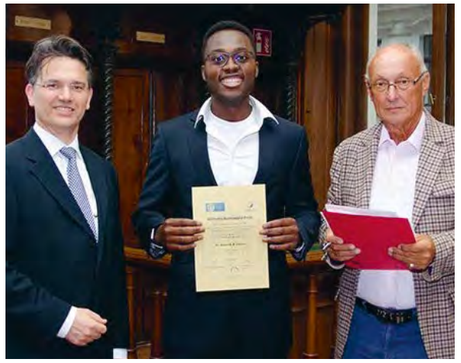
In October 2019, CeMM PI Joanna Loizou was the first female scientist in Austria to be awarded a European Research Council Synergy Grant under the Horizon 2020 funding program from the European Union. Her research collaborators are Steve Jackson, at Gurdon Institute, University of Cambridge, UK and Jacob Corn, at ETH Zurich. The collaborative project "DNA Damage Response: Actionabilities, Maps and Mechanisms" will focus on DNA repair mechanisms. Joanna Loizou's vision is to piece together the intricate puzzle that encompasses the human DNA damage response at the cellular level, hence providing a complete understanding of how such pathways go wrong in disease states, with a strong emphasis on cancer. Her long-standing expertise is embedded in investigating the cellular pathways that respond to DNA damage, to maintain genome stability and suppress disease. Joanna's important contributions within this field began during her PhD and continued during two postdoctoral positions in France and in the UK. In September 2011, Joanna established her independent group at CeMM, Vienna, Austria. The prestigious funding worth around €8.86 million for a period of six years, of which €2.95 million will go to Joanna Loizou's group, will help provide major insights into human genome surveillance and speed the development of new therapies for cancer and other diseases.

On 27 June 2019, CeMM PI Georg Winter received the Eppendorf Award for Young European Investigators. Georg Winter was awarded the €20,000 prize for his pioneering work of developing a method for targeting specific proteins for degradation. The winner of the prestigious prize is selected by an independent jury of scientists, who emphasized the importance of Georg Winter's work for the development of new therapies for cancer and other diseases of unmet need.

Every year the "Highly Cited Researchers" list provided by Clarivate Analytics recognizes the most influential researchers with highly cited papers that rank in the top 1% by citation in different scientific fields. This year, 44 researchers in the list are currently working in Austria. Among them is CeMM PI Christoph Bock, who has been included in the cross-field category, highlighting the interdisciplinary nature of his work. CeMM PI Andreas Bergthaler was nominated for "Austrian of the Year 2019" in the research category. Organized by the newspaper Die Presse, and in collaboration with the Austrian Broadcasting Corporation, ORF, the prize goes to individuals who made outstanding contributions in the relevant field.

For his outstanding achievements in the study of congenital immune system disorders, CeMM Adjunct PI Kaan Boztug received the Johann Wilhelm Ritter von Mannagetta Prize for Medicine from the Austrian Academy of Sciences. The prize, aimed at scientists under the age of 45 who are conducting research into immune system diseases for the first time, was first awarded in 2019. In addition to the Prize for Medicine, the ÖAW also granted two generous €4,000 funding awards by the Johann Wilhelm Ritter von Mannagetta Foundation, backdated for their PhD Studies at CeMM, to Elisabeth Salzer, postdoc at the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases, as well as to Bernd Boidol, postdoc at MedUni Vienna.

CeMM is especially proud of its PhD students and postdoctoral fellows who are not only an important pillar of research and first authors of key publications in the most prestigious magazines but have also successfully convinced strict juries with their talents and achievements. The following awards are illustrative of the many accomplishments of CeMMies: Michel Owusu received the Wilhelm Auerswald Prize 2019 for the best doctoral thesis at an Austrian Medical University. Julia Pazmandi won the Falling Walls Lab Austria Competition with a virtual reality project. Hatoon Baazim received the Karl Landsteiner Prize by the Austrian Society for Allergology and Immunology. Sandra Schick won the Life Science Research Award 2019 by the Austrian Association of Molecular Life Sciences and Biotechnology (ÖGMBT).



CeMM Facts

Facts

Co-Workers

48 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, Ireland, Israel, Italy, Jordan, Latvia, Lebanon, Macedonia, Mexico, Netherlands, New Zealand, Peru, Poland, Portugal, Romania, Russia, Saudi Arabia, Serbia, Singapore, Slovakia, Slovenia, Spain, Switzerland, Taiwan, Thailand, Tunisia, 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

Stefan Kubicek

Joanna Loizou

Jörg Menche

Giulio Superti-Furga

Georg Winter

Adjunct Principal Investigators

Kaan Boztug
LBI-RUD, CeRUD, CCRI

Thijn Brummelkamp
Netherlands Cancer Institute

Robert Kralovics
Medical University of Vienna

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 Ó Ríordáin
Head of Scientific Support

Michael Pilz
Head of IT Services

Eva Schweng
Head of Office, Event and PR Management

Sigrid Strodl
Head of Finance, Division Accounting and Special Projects

Kathrin Wiesendorfer
Head of Finance, Division Grants and 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 of Metabolomics Facility

Michael Schuster
Deputy Head of Biomedical Sequencing Facility (BSF)

Thomas Winkler-Penz
Deputy Head of Biomedical Sequencing Facility (BSF)

Postdoctoral Fellows

Taras Afonyushkin
Medical University of Vienna

Laura Antonio-Herrera
ERC CMIL

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, EU MSCA IF SingleCellAI

Nikolaus Fortelny
EMBO Long-Term Fellowship ALTF 241-2017

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Eugenia Iofinova WWTF NXT19-008

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Cleaning Staff

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Cleaning Staff

Nina Novotny
Purchaser

Anton Johann Peisser
Facility Manager

Peter Pelz
House Logistics

Sona Rettenbacherova
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Mate Sebök
Wash and Media Kitchen

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Peter Kotzan*
Purchaser

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Victoria Kulcsar-Mecsery
Accountant

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Martina Moreno
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LBI-RUD

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to Sylvia Knapp
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to Giulio Superti-Furga

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Te Fung Fiona Tseng*
Human Resources
Administrator

Lukas Weitz
Temporary Support
of Accounting

Cafeteria

Maximilian Bruder

Tuende Fuchs*

Magdalena Legierska

Janek Leszczynski

Walter Steinbrecher

graduated in 2019
° on parental leave
~ on education leave
* left CeMM in 2019
† sadly died in 2019

Legend of Grants

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

CCRI
St. Anna Children's Cancer
Research Institute

CeRUD
Vienna Center for Rare and
Undiagnosed Diseases

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 bio-
informatics 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"

EU MSCA IF ChemRAS
Marie Sklodowska-Curie
Individual Fellowship,
"Chemical probing
of transcriptional RAS
effectors-ChemRAS"

EU MSCA IF REAP
Marie Sklodowska-Curie
Individual Fellowship,
"Repair of DNA lesions induced
by platinum drugs – REAP"

EU MSCA IF SingleCellAI
Marie Sklodowska-Curie
Individual Fellowship,
"Deep-learning models of
CRISPR-engineered cells
define a rulebook of cellular
transdifferentiation –
SingleCellAI"

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

EU MSCA ITN INITIATE
Marie Sklodowska-Curie
Innovative Training Network,
"Innate-ImmunomeTabolIsm
as Antiviral TargEt – INITIATE"

EU MSCA ITN DohART-NET
Marie Sklodowska-Curie
Innovative Training Network,
"Periconceptional Program-
ming of Health Training
Network – DohART-NET"

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

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

FFG 874712
FFG Bridge "Innovating
strategies to prompt anti-
cancer immunity via targeted
protein degradation"

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 F7002
Special Research Program
"Systems-level analysis
of HDAC-dependent Th cell
plasticity"

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 P32125
Stand-Alone Project,
"Development of c-RAF
degraders to probe KRAS
mutant cancers"

FWF P31690
Stand-Alone Project,
"Chemical Dissection of the
Super Elongation Complex"

FWF P33024
Stand-Alone Project,
"Crosstalk between cellular
metabolism and DNA repair"

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

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

LBI-RUD
Ludwig Boltzmann Institute
for Rare and Undiagnosed
Diseases

Medical University of Vienna

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 DOC Fellowship 25271
Doctoral Fellowship Program
of the Austrian Academy
of Sciences

ÖAW DOC Fellowship 25524
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 Innovationsfonds
"Small Cell Collider: dissecting
the regulatory impact of
physical interactions between
single immune cells"

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 auto-
mated 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"

WWTF LS18-058
"Systems medicine analysis
of sarcoidosis by targeting
mTOR in a co-clinical trial in
patients and mice"

WWTF LS18-049
"Characterizing and targeting
the Ewing sarcoma micro-
environment to overcome
resistance to therapy"

WWTF LS18-111
"Ultra-high risk pediatric
cancer – combinatorial drivers
and therapeutic targets for
precision medicine"

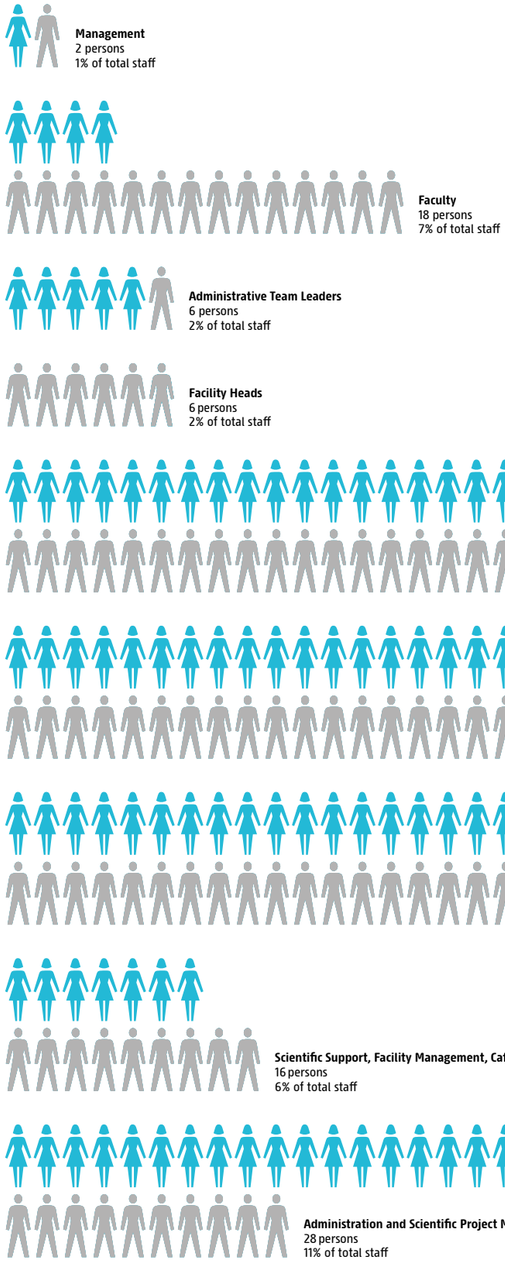
WWTF NXT19-008
NXT19-008 *"DataDiVR –*
A Virtual Reality Platform
for Biomedical Data Anlyses
in Clinical Practice"

Facts & Figures

Staff

Listed by number of persons per field of work. In the observation period, an average of 158 people not comprising Adjunct Principal Investigators, the colleagues from the Medical University of Vienna, and the LBI-RUD are equal to 144.78 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
18 persons
7% of total staff

Administrative Team Leaders
6 persons
2% of total staff

Facility Heads
6 persons
2% of total staff

Postdoctoral Fellows
48 persons
19% of total staff

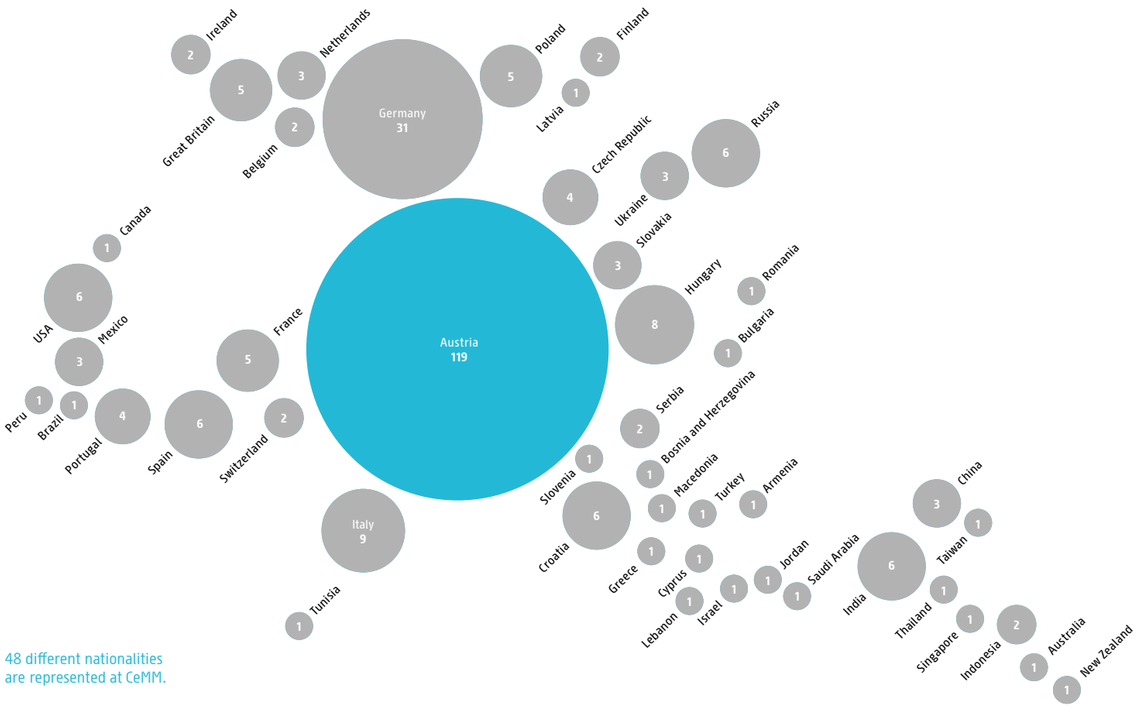
PhD Students
66 persons
26% of total staff

Technical Assistants and Computer Scientists
68 persons
26% of total staff

Scientific Support, Facility Management, Cafeteria
16 persons
6% of total staff

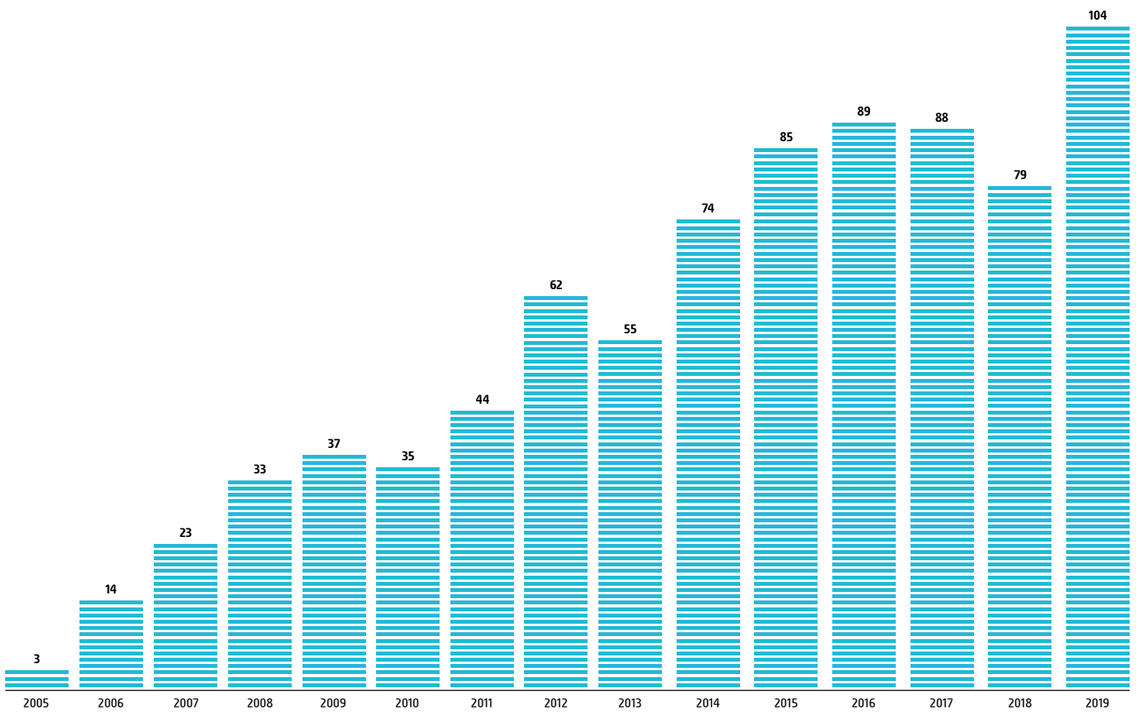
Administration and Scientific Project Management
28 persons
11% of total staff

Nationalities at CeMM

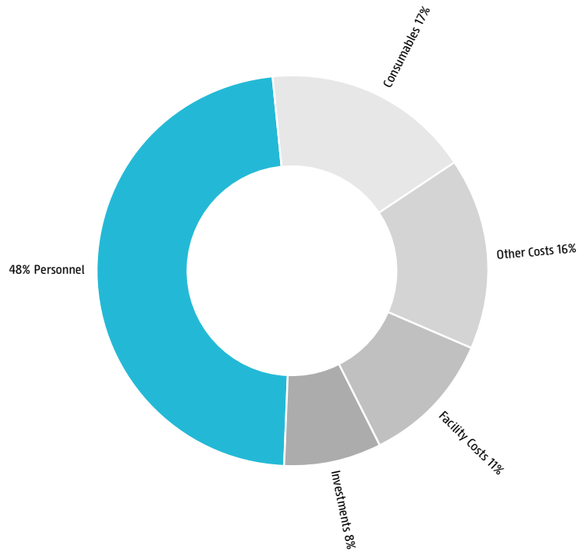


48 different nationalities
are represented at CeMM.

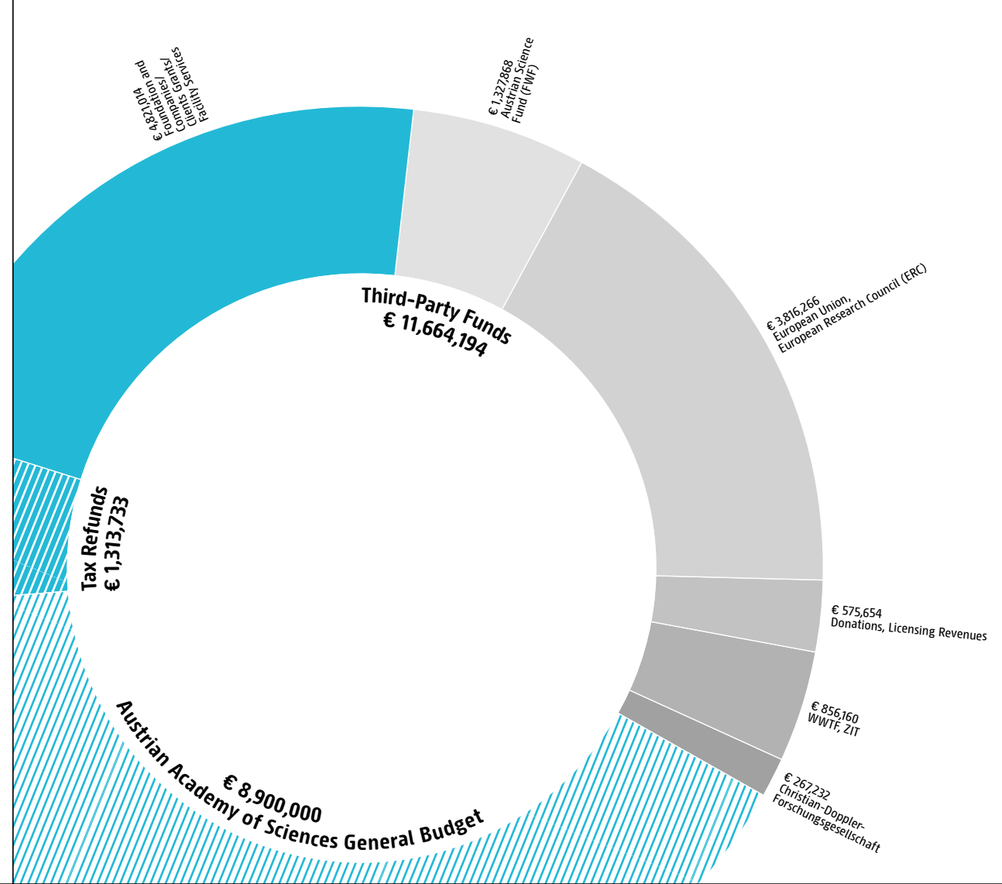
Publications



Expenses in 2019



Money Sources in 2019



Publications 2019

1. Adamopoulos A, Landskron L, Heidebrecht T, Tsakou F, Bleijerveld OB, Altelaar M, Nieuwenhuis J, Celie PHN, Brummelkamp TR, Perrakis A. **Crystal structure of the tubulin tyrosine carboxypeptidase complex VASH1-SVBP.** *Nat Struct Mol Biol.* 2019 Jul;26(7):567-570. doi: 10.1038/s41594-019-0254-6.

2. Andergassen D, Muckenhuber M, Bammer PC, Kulinski TM, Theussl HC, Shimizu T, Penninger JM, Pauler FM, Hudson QJ. **The Airn lncRNA does not require any DNA elements within its locus to silence distant imprinted genes.** *PLoS Genet.* 2019 Jul 22;15(7):e1008268. doi: 10.1371/journal.pgen.1008268.

3. Andersen L, Gülich AF, Alteneder M, Preglej T, Orola MJ, Dhele N, Stolz V, Schebesta A, Hamminger P, Hladik A, Floess S, Krausgruber T, Faux T, Andrabi SBA, Huehn J, Knapp S, Sparwasser T, Bock C, Laiho A, Elo LL, Rasool O, Lahesmaa R, Sakaguchi S, Ellmeier W. **The Transcription Factor MAZR/PATZ1 Regulates the Development of FOXP3+ Regulatory T Cells.** *Cell Rep.* 2019;29(13): 4447–4459.e6. doi:10.1016/j. celrep.2019.11.089.

4. Asslaber D, Wacht N, Leisch M, Qi Y, Maeding N, Hufnagl C, Jansko B, Zaborsky N, Villunger A, Hartmann TN, Greil R, Egle A. **BIRC3 Expression Predicts CLL Progression and Defines Treatment Sensitivity via Enhanced NF-κB Nuclear Translocation.** *Clin Cancer Res.* 2019 Mar 15;25(6):1901-1912. doi: 10.1158/1078-0432. CCR-18-1548. Epub 2018 Nov 28.

5. Baazim H, Schweiger M, Moschinger M, Xu H, Scherer T, Popa A, Gallage S, Ali A, Khamina K, Kosack L, Vilagos B, Smyth M, Lercher A, Friske J, Merkler D, Aderem A, Helbich TH, Heikenwälder M, Lang PA, Zechner R, Bergthaler A. **CD8+ T cells induce cachexia during chronic viral infection.** *Nat Immunol.* 2019;20(6):701–710. doi:10.1038/s41590-019-0397-y

6. Bagchi-Chakraborty J, Francis A, Bray T, Masters L, Tsiantoulas D, Nus M, Harrison J, Broekhuizen M, Leggat J, Clatworthy MR, Espéli M, Smith KGC, Binder CJ, Mallat Z, Sage AP. **B-Cell Fcγ Receptor IIb Modulates Atherosclerosis in Male and Female Mice by Controlling Adaptive Germinal Center and Innate B-1-Cell Responses.** *Arterioscler Thromb Vasc Biol.* 2019;39(7):1379–1389. doi:10.1161/ATVBAHA.118.312272.

7. Balligand T, Achouri Y, Pecquet C, Gaudray G, Colau D, Hug E, Rahmani Y, Stroobant V, Plo I, Vainchenker W, Kralovics R, Van den Eynde BJ, Defour JP, Constantinescu SN. **Knock-in of murine Calr del52 induces essential thrombocythemia with slow-rising dominance in mice and reveals key role of Calr exon 9 in cardiac development.** *Leukemia.* 2019 Aug 30. doi: 10.1038/s41375-019-0538-1.

8. Barthel FP, Johnson KC, Varn FS, Moskalik AD, Tanner G, Kocakavuk E, Anderson KJ, Abiola O, Aldape K, Alfaro KD, Alpar D, Amin SB, Ashley DM, Bandopadhayay P, Barnholtz-Sloan JS, Beroukhim R, Bock C, Brastianos PK, Brat DJ, Brodbelt AR, Bruns AF, Bulsara KR, Chakrabarty A, Chakravarti A, Chuang JH, Claus EB, Cochran EJ, Connelly J, Costello JF, Finocchiaro G, Fletcher MN, French PJ, Gan HK, Gilbert MR, Gould PV, Grimmer MR, Iavarone A, Ismail A, Jenkinson MD, Khasraw M, Kim H, Kouwenhoven MCM, LaViolette PS, Li M, Lichter P, Ligon KL, Lowman AK, Malta TM, Mazor T, McDonald KL, Molinaro AM, Nam DH, Nayyar N, Ng HK, Ngan CY, Niclou SP, Niers JM, Noushmehr H, Noorbakhsh J, Ormond DR, Park CK, Poisson LM, Rabadan R, Radlwimmer B, Rao G, Reifenberger G, Sa JK, Schuster M, Shaw BL, Short SC, Smitt PAS, Sloan AE, Smits M, Suzuki H, Tabatabai G, Van Meir EG, Watts C, Weller M, Wesseling P, Westerman BA, Widhalm G, Woehrer A, Yung WKA, Zadeh G, Huse JT, De Groot JF, Stead LF, Verhaak RGW; GLASS Consortium. Barthel FP, Johnson KC, Varn FS, et al. **Longitudinal molecular trajectories of diffuse glioma in adults.** *Nature.* 2019;576(7785):112–120. doi:10.1038/s41586-019-1775-1.

9. Bier J, Rao G, Payne K, Brigden H, French E, Pelham SJ, Lau A, Lenthall H, Edwards ESJ, Smart JM, Cole TS, Choo S, Joshi AY, Abraham RS, O'Sullivan M, Boztug K, Meyts I, Gray PE, Berglund LJ, Hsu P, Wong M, Holland SM, Notarangelo LD, Uzel G, Ma CS, Brink R, Tangye SG, Deenick EK. **Activating mutations in PIK3CD disrupt the differentiation and function of human and murine CD4+ T cells.** *J Allergy Clin Immunol.* 2019 Jul;144(1): 236-253. doi: 10.1016/j.jaci.2019.01.033.

10. Bonelli M, Dalwigk K, Platzer A, Olmos Calvo I, Hayer S, Niederreiter B, Holinka J, Sevelda F, Pap T, Steiner G, Superti-Furga G, Smolen JS, Kiener HP, Karonitsch T. **IRF1 is critical for the TNF-driven interferon response in rheumatoid fibroblast-like synoviocytes : JAKinibs suppress the interferon response in RA-FLSs.** *Exp Mol Med.* 2019 Jul 8;51(7):75. doi: 10.1038/s12276-019-0267-6.

11. Bösl K, Ianevski A, Than TT, Andersen PI, Kuivanen S, Teppor M, Zusinaite E, Dumpis U, Vitkauskiene A, Cox RJ, Kallio-Kokko H, Bergqvist A, Tenson T, Merits A, Oksenych V, Bjørås M, Anthonsen MW, Shum D, Kaarbø M, Vapalahti O, Windisch MP, Superti-Furga G, Snijder B, Kainov D, Kandasamy RK. **Common Nodes of Virus-Host Interaction Revealed Through an Integrated Network Analysis.** *Front Immunol.* 2019 Oct 4;10:2186. doi: 10.3389/fimmu.2019.02186.

12. Brand M, Winter GE. **Locus-Specific Knock-In of a Degradable Tag for Target Validation Studies.** *Methods Mol Biol.* 2019;1953:105-119. doi: 10.1007/978-1-4939-9145-7_7.

13. Brand M, Winter GE. **Stick it to E3s.** *Nat Chem Biol.* 2019 Jul;15(7):655-656. doi: 10.1038/s41589-019-0312-8.

14. Brandstetter B, Dalwigk K, Platzer A, Niederreiter B, Kartnig F, Fischer A, Vladimer GI, Byrne RA, Sevelda F, Holinka J, Pap T, Steiner G, Superti-Furga G, Smolen JS, Kiener HP, Karonitsch T. **FOXO3 is involved in the tumor necrosis factor-driven inflammatory response in fibroblast-like synoviocytes.** *Lab Invest.* 2019 May;99(5):648-658. doi: 10.1038/s41374-018-0184-7.

15. Buettner R, Nguyen LXT, Kumar B, Morales C, Liu C, Chen LS, Pemovska T, Synold TW, Palmer J, Thompson R, Li L, Hoang DH, Zhang B, Ghoda L, Kowolik C, Kontro M, Leitch C, Wennerberg K, Yu X, Chen CC, Horne D, Gandhi V, Pullarkat V, Marcucci G, Rosen S1. **8-chloro-adenosine activity in FLT3-ITD acute myeloid leukemia.** *J Cell Physiol.* 2019 Feb 15. doi: 10.1002/jcp.28294.

16. Cagdas D, Halaçlı SO, Tan Ç, Lo B, Çetinkaya PG, Esenboğa S, Karaatmaca B, Matthews H, Balcı-Hayta B, Arıkoğlu T, Ezgü F, Aladağ E, Saltık-Temizel İN, Demir H, Kuşkonmaz B, Okur V, Gümrük F, Göker H, Çetinkaya D, Boztuğ K, Lenardo M, Sanal Ö, Tezcan İ. **A Spectrum of Clinical Findings from ALPS to CVID: Several Novel LRBA Defects.** *J Clin Immunol.* 2019 Oct;39(7):726-738. doi: 10.1007/s10875-019-00677-6.

17. Caldera M, Müller F, Kaltenbrunner I, Licciardello MP, Lardeau CH, Kubicek S, Menche J. **Mapping the perturbome network of cellular perturbations.** *Nat Commun.* 2019 Nov 13;10(1):5140. doi: 10.1038/s41467-019-13058-9.

18. Calzoni E, Platt CD, Keles S, Kuehn HS, Beaussant-Cohen S, Zhang Y, Pazmandi J, Lanzi G, Pala F, Tahiat A, Artac H, Heredia RJ, Dmytrus J, Reisli I, Uygun V, Uygun D, Bingol A, Basaran E, Djenouhat K, Benhalla N, Bendahmane C, Emiroglu M, Kirchhausen T, Pasham M, Jones J, Wallace JG, Zheng L, Boisson B, Porta F, Rosenzweig SD, Su H, Giliani S, Lenardo M, Geha RS, Boztug K, Chou J, Notarangelo LD. **F-BAR domain only protein 1 (FCHO1) deficiency is a novel cause of combined immune deficiency in human subjects.** *J Allergy Clin Immunol.* 2019 Jun;143(6):2317-2321.e12. doi: 10.1016/j.jaci.2019.02.014.

19. Centa M, Jin H, Hofste L, Hellberg S, Busch A, Baumgartner R1, Verzaal NJ, Lind Enoksson S, Perisic Matic L, Boddul SV, Atzler D, Li DY, Sun C, Hansson GK, Ketelhuth DFJ, Hedin U, Wermeling F, Lutgens E, Binder CJ, Maegdesfessel L, Malin SG. **Germinal Center-Derived Antibodies Promote Atherosclerosis Plaque Size and Stability.** *Circulation.* 2019 May 21;139(21):2466-2482. doi: 10.1161/CIRCULATIONAHA.118.038534.

20. Chen Y, Coussanes G, Souris C, Aillard P, Kaldre D, Runggatscher K, Kubicek S, Di Mauro G, Maryasin B, Maulide N. **A Domino 10-Step Total Synthesis of FR252921 and Its Analogues, Complex Macrocyclic Immunosuppressants.** *J Am Chem Soc.* 2019 Sep 4;141(35): 13772-13777. doi: 10.1021/jacs.9b07185.

21. Chien J, Wolf FW, Grosche S, Yosef N, Garriga G, Mörck C. **The Enigmatic Canal-Associated Neurons Regulate Caenorhabditis elegans Larval Development Through a cAMP Signaling Pathway.** *Genetics.* 2019 Dec;213(4):1465-1478. doi: 10.1534/genetics.119.302628.

22. Clement M, Raffort J, Lareyre F, Tsiantoulas D, Newland S, Lu Y, Masters L, Harrison J, Saveljeva S, Ma MKL, Ozsvar-Kozma M, Lam BYH, Yeo GSH, Binder CJ, Kaser A, Mallat Z. **Impaired Autophagy in CD11b+ Dendritic Cells Expands CD4+ Regulatory T Cells and Limits Atherosclerosis in Mice.** *Circ Res.* 2019;125(11): 1019–1034. doi:10.1161/CIRCRESAHA.119.315248.

23. Conde CD, Petronczki ÖY, Baris S, Willmann KL, Girardi E, Salzer E, Weitzer S, Ardy RC, Krolo A, Ijspeert H, Kiykim A, Karakoc-Aydiner E, Förster-Waldl E, Kager L, Pickl WF, Superti-Furga G, Martínez J, Loizou JI, Ozen A, van der Burg M, Boztug K. **Polymerase δ deficiency causes syndromic immunodeficiency with replicative stress.** *J Clin Invest.* 2019 Oct 1;129(10):4194-4206. doi: 10.1172/JCI128903.

24. Connolly P, Garcia-Carpio I, Villunger A. **Cell-Cycle Cross Talk with Caspases and Their Substrates.** *Cold Spring Harb Perspect Biol.* 2019 Nov 14. pii: a036475. doi: 10.1101/cshperspect.a036475.

25. Di Giacomo AM, Covre A, Finotello F, Rieder D, Danielli R, Sigalotti L, Giannarelli D, Petitprez F, Lacroix L, Valente M, Cutaia O, Fazio C, Amato G, Lazzeri A, Monterisi S, Miracco C, Coral S, Anichini A, Bock C, Nemc A, Oganesian A, Lowder J, Azab M, Fridman WH, Sautès-Fridman C, Trajanoski Z, Maio M. **Guadecitabine Plus Ipilimumab in Unresectable Melanoma: The NIBIT-M4 Clinical Trial.** *Clin Cancer Res.* 2019;25(24):7351–7362. doi:10.1158/1078-0432. CCR-19-1335.

26. Doukas A, Karena E, Botou M, Papakostas K, Papadaki A, Tziouvara O, Xingi E, Frillingos S, Boleti H. **Heterologous expression of the mammalian sodium-nucleobase transporter rSNBT1 in Leishmania tarentolae.** *Biochim Biophys Acta Biomembr.* 2019 Sep 1;1861(9):1546-1557. doi: 10.1016/j.bbamem.2019.07.001.

27. Downes K, Megy K, Duarte D, Vries M, Gebhart J, Hofer S, Shamardina O, Deevi SVV, Stephens J, Mapeta R, Tuna S, Al Hasso N, Besser MW, Cooper N, Daugherty L, Gleadall N, Greene D, Haimel M, Martin H, Papadia S, Revel-Vilk S, Sivapalaratnam S, Symington E, Thomas W, Thys C, Tolios A, Penkett CJ; NIHR BioResource, Ouwehand WH, Abbs S, Laffan MA, Turro E, Simeoni I, Mumford AD, Henskens YMC, Pabinger I, Gomez K, Freson K. **Diagnostic high-throughput sequencing of 2,396 patients with bleeding, thrombotic, and platelet disorders.** *Blood.* 2019 Dec 5;134(23):2082-2091. doi: 10.1182/blood.2018891192.

28. Farmer JR, Foldvari Z, Ujhazi B, De Ravin SS, Chen K, Bleesing JJH, Schuetz C, Al-Herz W, Abraham RS, Joshi AY, Costa-Carvalho BT, Buchbinder D, Booth C, Reiff A, Ferguson PJ, Aghamohammadi A, Abolhassani H, Puck JM, Adeli M, Cancrini C, Palma P, Bertaina A, Locatelli F, Di Matteo G, Geha RS, Kanariou MG, Lycopoulou L, Tzanoudaki M, Sleasman JW, Parikh S, Pinero G, Fischer BM, Dbaibo G, Unal E, Patiroglu T, Karakukcu M, Al-Saad KK, Dilley MA, Pai SY, Dutmer CM, Gelfand EW, Geier CB, Eibl MM, Wolf HM, Henderson LA, Hazen MM, Bonfim C, Wolska-Kuśnierz B, Butte MJ, Hernandez JD, Nicholas SK, Stepensky P, Chandrakasan S, Miano M, Westermann-Clark E, Goda V, Kriván G, Holland SM, Fadugba O, Henrickson SE, Ozen A, Karakoc-Aydiner E, Baris S, Kiykim A, Bredius R, Hoeger B, Boztug K, Pashchenko O, Neven B, Moshous D, Villartay JP, Bousfiha AA, Hill HR, Notarangelo LD, Walter JE. **Outcomes and Treatment Strategies for Autoimmunity and Hyperinflammation in Patients with RAG Deficiency.** *J Allergy Clin Immunol Pract.* 2019 Jul - Aug;7(6): 1970-1985.e4. doi: 10.1016/j.jaip.2019.02.038.

29. Ferreira da Silva J, Salic S, Wiedner M, Datlinger P, Essletzbichler P, Hanzl A, Superti-Furga G, Bock C, Winter G, Loizou JI. **Genome-scale CRISPR screens are efficient in non-homologous end-joining deficient cells.** *Sci Rep.* 2019 Oct 31;9(1):15751. doi: 10.1038/s41598-019-52078-9.

30. Goncalves-Alves E, Saferding V, Schliehe C, Benson R, Kurowska-Stolarska M, Brunner JS, Puchner A, Podesser BK, Smolen JS, Redlich K, Bonelli M, Brewer J, Bergthaler A, Steiner G, Blüml S. **MicroRNA-155 Controls T Helper Cell Activation During Viral Infection.** *Front Immunol.* 2019;10:1367. Published 2019 Jun 13. doi:10.3389/fimmu.2019.01367-

31. Göschl L, Preglej T, Boucheron N, Saferding V, Müller L, Platzer A, Hirahara K, Shih H-Y, Backlund J, Matthias P, Niederreiter B, Hladik A, Kugler M, Gualdoni GA, Scheinecker C, Knapp S, Seiser C, Holmdahl R, Tillmann K, Plasenzotti R, Podesser B, Aletaha D, Smolen JS, Karonitsch T, Steiner G, Ellmeier W, Bonelli M. **Histone deacetylase 1 (HDAC1): A key player of T cell-mediated arthritis.** *J Autoimmun.* 2019;102379. doi:10.1016/j.jaut.2019.102379.

32. Göschl L, Winkler S, Dmytrus J, Heredia RJ, Lagler H, Ramharter M, Scheinecker C, Bonelli M, Schmetterer K, Pickl WF, Grabmeier-Pfistershammer K, Hershfield MS, Boztug K, Förster-Waldl E, Gualdoni GA. **Unreported Missense Mutation in the Dimerization Domain of ADA2 Leads to ADA2 Deficiency Associated with Severe Oral Ulcers and Neutropenia in a Female Somalian Patient-Addendum to the Genotype-Phenotype Puzzle.** *J Clin Immunol.* 2019 Nov 4. doi: 10.1007/s10875-019-00700-w.

33. Goyal G, Zheng J, Adam E, Steffes G, Jain M, Klavins K, Hummel T. **Sphingolipid-dependent Dscam sorting regulates axon segregation.** *Nat Commun.* 2019 Feb 18;10(1):813. doi: 10.1038/s41467-019-08765-2.

34. Griss J, Bauer W, Wagner C, Simon M, Chen M, Grabmeier-Pfistershammer K, Maurer-Granofszky M, Roka F, Penz T, Bock C, Zhang G, Herlyn M, Glatz K, Läubli H, Mertz KD, Petzelbauer P, Wiesner T, Hartl M, Pickl WF, Somasundaram R, Steinberger P, Wagner SN. **B cells sustain inflammation and predict response to immune checkpoint blockade in human melanoma.** *Nat Commun.* 2019;10(1):4186. Published 2019 Sep 13. doi:10.1038/s41467-019-12160-2.

35. Gruber M, Bozic I, Leshchiner I, Livitz D, Stevenson K, Rassenti L, Rosebrock D, Taylor-Weiner A, Olive O, Goyetche R, Fernandes SM, Sun J, Stewart C, Wong A, Cibulskis C, Zhang W, Reiter JG, Gerold JM, Gribben JG, Rai KR, Keating MJ, Brown JR, Neuberg D, Kipps TJ, Nowak MA, Getz G, Wu CJ. **Growth dynamics in naturally progressing chronic lymphocytic leukaemia.** *Nature.* 2019 Jun;570(7762):474-479. doi: 10.1038/s41586-019-1252-x.

36. Gusach A, Luginina A, Marin E, Brouillette RL, Besserer-Offroy É, Longpré JM, Ishchenko A, Popov P, Patel N, Fujimoto T, Maruyama T, Stauch B, Ergasheva M, Romanovskaia D, Stepko A, Kovalev K, Shevtsov M, Gordeliy V, Han GW, Katritch V, Borshchevskiy V, Sarret P, Mishin A, Cherezov V. **Structural basis of ligand selectivity and disease mutations in cysteinyl leukotriene receptors.** *Nat Commun.* 2019 Dec 6;10(1):5573. doi: 10.1038/s41467-019-13348-2.

37. Hacker K, Benke S, Agerer B, Scinicariello S, Budroni V, Versteeg GA. **A repetitive acidic region contributes to the extremely rapid degradation of the cell-context essential protein TRIM52.** *Sci Rep.* 2019 May 27;9(1):7901. doi: 10.1038/s41598-019-44359-0.

38. Halbritter F, Farlik M, Schwentner R, Jug G, Fortelny N, Schnöller T, Pisa H, Schuster LC, Reinprecht A, Czech T, Gojo J, Holter W, Minkov M, Bauer WM, Simonitsch-Klupp I, Bock C, Hutter C. **Epigenomics and Single-Cell Sequencing Define a Developmental Hierarchy in Langerhans Cell Histiocytosis.** *Cancer Discov.* 2019;9(10): 1406–1421. doi:10.1158/2159-8290.CD-19-0138.

39. Halbritter F, Farlik M, Schwentner R, Jug G, Fortelny N, Schnöller T, Pisa H, Schuster LC, Reinprecht A, Czech T, Gojo J, Holter W, Minkov M, Bauer W, Simonitsch-Klupp I, Bock C, Hutter C. **Epigenomics and Single-Cell Sequencing Define a Developmental Hierarchy in Langerhans Cell Histiocytosis.** *Cancer Discov.* 2019 Oct;9(10):1406-1421.doi: 10.1158/2159-8290. CD-19-0138.

40. Hamdane N, Jühling F, Crouchet E, El Saghire H, Thumann C, Oudot MA, Bandiera S, Saviano A, Ponsolles C, Roca Suarez AA, Li S, Fujiwara N, Ono A, Davidson I, Bardeesy N, Schmidl C, Bock C, Schuster C, Lupberger J, Habersetzer F, Doffoël M, Piardi T, Sommacale D, Imamura M, Uchida T, Ohdan H, Aikata H, Chayama K, Boldanova T, Pessaux P, Fuchs BC, Hoshida Y, Zeisel MB, Duong FHT, Baumert TF. **HCV-Induced Epigenetic Changes Associated With Liver Cancer Risk Persist After Sustained Virologic Response.** *Gastroenterology.* 2019;156(8):2313–2329.e7. doi:10.1053/j.gastro.2019.02.038.

41. Heijink AM, Talens F, Jae LT, van Gijn SE, Fehrmann RSN, Brummelkamp TR, van Vugt MATM. **BRCA2 deficiency instigates cGAS-mediated inflammatory signaling and confers sensitivity to tumor necrosis factor-alpha-mediated cytotoxicity.** *Nat Commun.* 2019 Jan 9;10(1):100. doi: 10.1038/s41467-018-07927-y.

42. Houben T, Magro Dos Reis I, Oligschlaeger Y, Steinbusch H, Gijbels MJJ, Hendrikx T, Binder CJ, Cassiman D, Westerterp M, Prickaerts J, Shiri-Sverdlov R. **Pneumococcal Immunization Reduces Neurological and Hepatic Symptoms in a Mouse Model for Niemann-Pick Type C1 Disease.** *Front Immunol.* 2019 Jan 7;9:3089. doi: 10.3389/fimmu.2018.03089. eCollection 2018.

43. Jia R, Kralovics R. **Progress in elucidation of molecular pathophysiology of myeloproliferative neoplasms and its application to therapeutic decisions.** *Int J Hematol.* 2019 Nov 18. doi: 10.1007/s12185-019-02778-9.

44. Katholnig K, Schütz B, Fritsch SD, Schörghofer D, Linke M, Sukhbaatar N, Matschinger JM, Unterleuthner D, Hirtl M, Lang M, Herac M, Spittler A, Bergthaler A, Schabbauer G, Bergmann M, Dolznig H, Hengstschläger M, Magnuson MA, Mikula M, Weichhart T. **Inactivation of mTORC2 in macrophages is a signature of colorectal cancer that promotes tumorigenesis.** *JCI Insight.* 2019;4(20): e124164. Published 2019 Oct 17. doi:10.1172/jci.insight.124164.

45. Ketelhuth DFJ, Lutgens E, Bäck M, Binder CJ, Van den Bossche J, Daniel C, Dumitriu IE, Hoefer I, Libby P, O'Neill L, Weber C, Evans PC. **Immunometabolism and atherosclerosis: perspectives and clinical significance: a position paper from the Working Group on Atherosclerosis and Vascular Biology of the European Society of Cardiology.** *Cardiovasc Res.* 2019;115(9):1385–1392. doi:10.1093/cvr/cvz166.

46. Kiss MG, Ozsvár-Kozma M, Porsch F, Göderle L, Papac-Miličević N, Bartolini-Gritti B, Tsiantoulas D, Pickering MC, Binder CJ. **Complement Factor H Modulates Splenic B Cell Development and Limits Autoantibody Production.** *Front Immunol.* 2019; 10:1607. Published 2019 Jul 11. doi:10.3389/fimmu.2019.01607.

47. Klufa J, Bauer T, Hanson B, Herbold C, Starkl P, Lichtenberger B, Srutkova D, Schulz D, Vujic I, Mohr T, Rappersberger K, Bodenmiller B, Kozakova H, Knapp S, Loy A, Sibilia M. Klufa J, Bauer T, Hanson B, et al. **Hair eruption initiates and commensal skin microbiota aggravate adverse events of anti-EGFR therapy.** *Sci Transl Med.* 2019;11(522):eaax2693. doi:10.1126/scitranslmed.aax2693.

48. Kocacik Uygun DF, Uygun V, Daloğlu H, Öztürkmen S, Karasu G, Reisli İ, Sayar E, Yüksekkaya HA, Glocker EO, Boztuğ K, Yeşilipek A. **Hematopoietic Stem Cell Transplantation From Unrelated Donors in 2 Cases of Interleukin-10 Receptor Deficiency: Is Surgery Not a Requirement?** *J Pediatr Hematol Oncol.* 2019 Jan;41(1): 64-66. doi: 10.1097/MPH.0000000000001165.

49. Korchynska S, Krassnitzer M, Malenczyk K, Prasad RB, Tretiakov EO, Rehman S, Cinquina V, Gernedl V, Farlik M, Petersen J, Hannes S, Schachenhofer J, Reisinger SN, Zambon A, Asplund O, Artner I, Keimpema E, Lubec G, Mulder J, Bock C, Pollak DD, Romanov RA, Pifl C, Groop L, Hökfelt TG, Harkany T. **Life-long impairment of glucose homeostasis upon prenatal exposure to psychostimulants** [published online ahead of print, 2019 Nov 21]. *EMBO J.* 2019;e100882. doi:10.15252/embj.2018100882.

50. Kosack L, Wingelhofer B, Popa A, Orlova A, Agerer B, Vilagos B, Majek P, Parapatics K, Lercher A, Ringler A, Klughammer J, Smyth M, Khamina K, Baazim H, de Araujo ED, Rosa DA, Park J, Tin G, Ahmar S, Gunning PT, Bock C, Siddle HV, Woods GM, Kubicek S, Murchison EP, Bennett KL, Moriggl R, Bergthaler A. **The ERBB-STAT3 Axis Drives Tasmanian Devil Facial Tumor Disease.** *Cancer Cell.* 2019;35(1):125–139.e9. doi:10.1016/j.ccell.2018.11.018.

51. Kral-Pointner JB, Schrottmaier WC, Salzmann M, Mussbacher M, Schmidt GJ, Moser B, Heber S, Birnecker B, Paar H, Zellner M, Knapp S, Assinger A, Schabbauer G. **Platelet PI3K Modulates Innate Leukocyte Extravasation during Acid-Induced Acute Lung Inflammation.** *Thromb Haemost.* 2019;19(10):1642–1654. doi:10.1055/s-0039-1693693.

52. Kutluğ Ş, Boztuğ K, Yıldıran A. **Development of multiple gallstones in a child with lipopolysaccharide-responsive beige-like anchor protein mutation.** *Cent Eur J Immunol.* 2019;44(3):332-335. doi: 10.5114/ceji.2019.89613.

53. Lee NJ, Clarke IM, Zengin A, Enriquez RF, Nagy V, Penninger JM, Baldock PA, Herzog H. **RANK deletion in neuropeptide Y neurones attenuates oestrogen deficiency-related bone loss.** *J Neuroendocrinol.* 2019 Feb;31(2):e12687. doi: 10.1111/jne.12687.

54. Lercher A, Bhattacharya A, Popa AM, Caldera M, Schlapansky MF, Baazim H, Agerer B, Gürtl B, Kosack L, Májek P, Brunner JS, Vitko D, Pinter T, Genger JW, Orlova A, Pikor N, Reil D, Ozsvár-Kozma M, Kalinke U, Ludewig B, Moriggl R, Bennett KL, Menche J, Cheng PN, Schabbauer G, Trauner M, Klavins K, Bergthaler A. **Type I Interferon Signaling Disrupts the Hepatic Urea Cycle and Alters Systemic Metabolism to Suppress T Cell Function.** *Immunity.* 2019;51(6):1074–1087.e9. doi:10.1016/j.immuni.2019.10.014.

55. Maurer B, Nivarthi H, Wingelhofer B, Pham HTT, Schlederer M, Suske T, Grausenburger R, Schiefer AI, Prchal-Murphy M, Chen D, Winkler S, Merkel O, Kornauth C, Hofbauer M, Hochgatterer B, Hoermann G, Hoelbl-Kovacic A, Prochazkova J, Lobello C, Cumaraswamy AA, Latzka J, Kitzwögerer M, Chott A, Janikova A, Pospíšilova Š, Loizou JI, Kubicek S, Valent P, Kolbe T, Grebien F, Kenner L, Gunning PT, Kralovics R, Herling M, Müller M, Rülicke T, Sexl V, Moriggl R. **High activation of STAT5A drives peripheral T-cell lymphoma and leukemia.** *Haematologica.* 2019 May 23. pii: haematol.2019.216986. doi: 10.3324/haematol.2019.216986.

56. Mayor-Ruiz C, Jaeger MG, Bauer S, Brand M, Sin C, Hanzl A, Mueller AC, Menche J, Winter GE. **Plasticity of the Cullin-RING Ligase Repertoire Shapes Sensitivity to Ligand-Induced Protein Degradation.** *Mol Cell.* 2019 Aug 22;75(4):849-858.e8. doi: 10.1016/j.molcel.2019.07.013.

57. Mayor-Ruiz C, Winter GE. **Identification and characterization of cancer vulnerabilities via targeted protein degradation.** *Drug Discov Today Technol.* 2019 Apr;31:81-90. doi: 10.1016/j.ddtec.2018.12.003.

58. McAlpine CS, Kiss MG, Rattik S, He S, Vassalli A, Valet C, Anzai A, Chan CT, Mindur JE, Kahles F, Poller WC, Frodermann V, Fenn AM, Gregory AF, Halle L, Iwamoto Y, Hoyer FF, Binder CJ, Libby P, Tafti M, Scammell TE, Nahrendorf M, Swirski FK. **Sleep modulates haematopoiesis and protects against atherosclerosis.** *Nature.* 2019 Feb;566(7744): 383-387. doi: 10.1038/s41586-019-0948-2.

59. Mezzadra R, de Bruijn M, Jae LT, Gomez-Eerland R, Duursma A, Scheeren FA, Brummelkamp TR, Schumacher TN. **SLFN11 can sensitize tumor cells towards IFN-γ-mediated T cell killing.** *PLoS One.* 2019 Feb 12;14(2):e0212053. doi: 10.1371/journal.pone.0212053.

60. Mian AA, Baumann I, Liebermann M, Grebien F, Superti-Furga G, Ruthardt M, Ottmann OG, Hantschel O. **The phosphatase UBASH3B/Sts-1 is a negative regulator of Bcr-Abl kinase activity and leukemogenesis.** *Leukemia.* 2019 Sep;33(9): 2319-2323. doi: 10.1038/s41375-019-0468-y.

61. Miragaia RJ, Gomes T, Chomka A, Jardine L, Riedel A, Hegazy AN, Whibley N, Tucci A, Chen X, Lindeman I, Emerton G, Krausgruber T, Shields J, Haniffa M, Powrie F, Teichmann SA. **Single-Cell Transcriptomics of Regulatory T Cells Reveals Trajectories of Tissue Adaptation.** *Immunity.* 2019 Feb 19;50(2): 493-504.e7. doi: 10.1016/j.immuni.2019.01.001.

62. Moik F, Riedl JM, Winder T, Terbuch A, Rossmann CH, Szkandera J, Bauernhofer T, Kasparek AK, Schaberl-Moser R, Reicher A, Prinz F, Pichler M, Stöger H, Stotz M, Gerger A, Posch F. **Benefit of second-line systemic chemotherapy for advanced biliary tract cancer: a propensity score analysis.** *Sci Rep.* 2019 Apr 3;9(1):5548. doi: 10.1038/s41598-019-42069-1.

63. Moskovskich A, Goldmann U, Kartnig F, Lindinger S, Konecka J, Fiume G, Girardi E, Superti-Furga G. **The transporters SLC35A1 and SLC30A1 play opposite roles in cell survival upon VSV virus infection.** *Sci Rep.* 2019 Jul 18;9(1): 10471. doi: 10.1038/s41598-019-46952-9.

64. Muller A, Gasch J, Albring KF, Aberger F, Nivarthi H, Khemeri M, Moriggl R, Friedrich KH. **Interplay of transcription factors STAT3, STAT1 and AP-1 mediates activity of the matrix metalloproteinase-1 promoter in colorectal carcinoma cells.** *Neoplasma.* 2019 May 23; 66(3):357-366. doi: 10.4149/neo_2018_180731N560.

65. Müller F, Scherer M, Assenov Y, Lutsik P, Walter J, Lengauer T, Bock C. **RnBeads 2.0: comprehensive analysis of DNA methylation data.** *Genome Biol.* 2019;20(1):55. Published 2019 Mar 14. doi:10.1186/s13059-019-1664-9.

66. Nagy V, Hollstein R, Pai TP, Herde MK, Buphamalai P, Moeseneder P, Lenartowicz E, Kavirayani A, Korenke GC, Kozieradzki I, Nitsch R, Cicvaric A, Monje Quiroga FJ, Deardorff MA, Bedoukian EC, Li Y, Yigit G, Menche J, Perçin EF, Wollnik B, Henneberger C, Kaiser FJ, Penninger JM. **HACE1 deficiency leads to structural and functional neurodevelopmental defects.** *Neurol Genet.* 2019 Apr 29;5(3): e330. doi: 10.1212/NXG.0000000000000330.

67. Owusu M, Bannauer P, Ferreira da Silva J, Mourikis TP, Jones A, Májek P, Caldera M, Wiedner M, Lardeau CH, Mueller AC, Menche J, Kubicek S, Ciccarelli FD, Loizou JI. **Mapping the Human Kinome in Response to DNA Damage.** *Cell Rep.* 2019 Jan 15;26(3):555-563.e6. doi: 10.1016/j.celrep.2018.12.087.

68. Patra V, Strobl J, Gruber-Wackernagel A, Vieyra-Garcia P, Stary G, Wolf P. **CD11b+ cells markedly express the itch cytokine interleukin-31 in polymorphic light eruption.** *Br J Dermatol.* 2019 Nov;181(5):1079-1081. doi: 10.1111/bjd.18092. Epub 2019 Jul 21.

69. Pazmandi J, Kalinichenko A, Ardy RC, Boztug K. **Early-onset inflammatory bowel disease as a model disease to identify key regulators of immune homeostasis mechanisms.** *Immunol Rev.* 2019 Jan;287(1):162-185. doi: 10.1111/imr.12726.

70. Pecquet C, Chachoua I, Roy A, Balligand T, Vertenoeil G, Leroy E, Albu RI, Defour JP, Nivarthi H, Hug E, Xu E, Ould-Amer Y, Mouton C, Colau D, Vertommen D, Shwe MM, Marty C, Plo I, Vainchenker W, Kralovics R, Constantinescu SN. **Calreticulin mutants as oncogenic rogue chaperones for TpoR and traffic-defective pathogenic TpoR mutants.** *Blood.* 2019 Jun 20; 133(25):2669-2681. doi: 10.1182/blood-2018-09-874578.

71. Piper CJM, Rosser EC, Oleinika K, Nistala K, Krausgruber T, Rendeiro AF, Banos A, Drozdov I, Villa M, Thomson S, Xanthou G, Bock C, Stockinger B, Mauri C. **Aryl Hydrocarbon Receptor Contributes to the Transcriptional Program of IL-10-Producing Regulatory B Cells.** *Cell Rep.* 2019;29(7): 1878–1892.e7. doi:10.1016/j.celrep.2019.10.018.

72. Porsch F, Binder CJ. **Impact of B-Cell-Targeted Therapies on Cardiovascular Disease.** *Arterioscler Thromb Vasc Biol.* 2019;39(9):1705–1714. doi: 10.1161/ATVBAHA.119.311996.

73. Puhm F, Afonyushkin T, Resch U, Obermayer G, Rohde M, Penz T, Schuster M, Wagner G, Rendeiro AF, Melki I, Kaun C, Wojta J, Bock C, Jilma B, Mackman N, Boilard E, Binder CJ. **Mitochondria Are a Subset of Extracellular Vesicles Released by Activated Monocytes and Induce Type I IFN and TNF Responses in Endothelial Cells.** *Circ Res.* 2019; 125(1):43–52. doi:10.1161/CIRCRESAHA.118.314601.

74. Robinson-Garcia L, Ferreira da Silva J, Loizou JI. **Synthetic Lethal Interactions for Kinase Deficiencies to DNA Damage Chemotherapeutics.** *Cancer Res.* 2019 Nov 15;79(22):5693-5698. doi: 10.1158/0008-5472.CAN-19-1364.

75. Rocamora-Reverte L, Tuzlak S, von Raffay L, Tisch M, Fiegl H, Drach M, Reichardt HM, Villunger A, Tischner D, Wiegers GJ. **Glucocorticoid Receptor-Deficient Foxp3+ Regulatory T Cells Fail to Control Experimental Inflammatory Bowel Disease.** *Front Immunol.* 2019 Mar 18;10:472. doi: 10.3389/fimmu.2019.00472.

76. Scalise M, Galluccio M, Pochini L, Cosco J, Trotta M, Rebsamen M, Superti-Furga G, Indiveri C. **Insights into the transport side of the human SLC38A9 transceptor.** *Biochim Biophys Acta Biomembr.* 2019 Sep 1;1861(9): 1558-1567. doi: 10.1016/j.bbamem.2019.07.006.

77. Schick S, Rendeiro AF, Runggatscher K, Ringler A, Boidol B, Hinkel M, Májek P, Vulliard L, Penz T, Parapatics K, Schmidl C, Menche J, Boehmelt G, Petronczki M, Müller AC, Bock C, Kubicek S. **Systematic characterization of BAF mutations provides insights into intracomplex synthetic lethalities in human cancers.** *Nat Genet.* 2019;51(9):1399–1410. doi: 10.1038/s41588-019-0477-9.

78. Schiefer AI, Salzer E, Füreder A, Szepfalusi Z, Müller-Sacherer T, Huber WD, Michel-Behnke I, Lawitschka A, Pichler H, Mann G, Hutter C, Simonitsch-Klupp I, Attarbaschi A. **PD-L1 and PD1 expression in post-transplantation lymphoproliferative disease (PTLD) of childhood and adolescence: An inter- and intra-individual descriptive study covering the whole spectrum of PTLD categories.** *Cancer Med.* 2019 Aug;8(10):4656-4668. doi: 10.1002/cam4.2394.

79. Schischlik F, Jäger R, Rosebrock F, Hug E, Schuster M, Holly R, Fuchs E, Milosevic Feenstra JD, Bogner E, Gisslinger B, Schalling M, Rumi E, Pietra D, Fischer G, Faé I, Vulliard L, Menche J, Haferlach T, Meggendorfer M, Stengel A, Bock C, Cazzola M, Gisslinger H, Kralovics R. **Mutational landscape of the transcriptome offers putative targets for immunotherapy of myeloproliferative neoplasms.** *Blood.* 2019;134(2):199–210. doi:10.1182/blood.2019000519.

80. Schmidl C, Vladimer GI, Rendeiro AF, Schnabl S, Krausgruber T, Taubert C, Krall N, Pemovska T, Araghi M, Snijder B, Hubmann R, Ringler A, Runggatscher K, Demirtas D, de la Fuente OL, Hilgarth M, Skrabs C, Porpaczy E, Gruber M, Hoermann G, Kubicek S, Staber PB, Shehata M, Superti-Furga G, Jäger U, Bock C. **Combined chemosensitivity and chromatin profiling prioritizes drug combinations in CLL.** *Nat Chem Biol.* 2019;15(3):232–240. doi:10.1038/s41589-018-0205-2.

81. Schoeler K, Aufschnaiter A, Messner S, Derudder E, Herzog S, Villunger A, Rajewsky K, Labi V. **TET enzymes control antibody production and shape the mutational landscape in germinal centre B cells.** *FEBS J.* 2019 Sep;286(18):3566-3581. doi: 10.1111/febs.14934.

82. Schoeler K, Jakic B, Heppke J, Soratroi C, Aufschnaiter A, Hermann-Kleiter N, Villunger A, Labi V. **CHK1 dosage in germinal center B cells controls humoral immunity.** *Cell Death Differ.* 2019 Dec;26(12):2551-2567. doi: 10.1038/s41418-019-0318-5.

83. Schuler F, Afreen S, Manzl C, Häcker G, Erlacher M, Villunger A. **Checkpoint kinase 1 is essential for fetal and adult hematopoiesis.** *EMBO Rep.* 2019 Aug;20(8):e47026. doi: 10.15252/embr.201847026.

84. Sdelci S, Rendeiro AF, Rathert P, You W, Lin JG, Ringler A, Hofstätter G, Moll HP, Gürtl B, Farlik M, Schick S, Klepsch F, Oldach M, Buphamalai P, Schischlik F, Májek P, Parapatics K, Schmidl C, Schuster M, Penz T, Buckley DL, Hudecz O, Imre R, Wang SY, Maric HM, Kralovics R, Bennett KL, Müller AC, Mechtler K, Menche J, Bradner JE, Winter GE, Klavins K, Casanova E, Bock C, Zuber J, Kubicek S. **MTHFD1 interaction with BRD4 links folate metabolism to transcriptional regulation.** *Nat Genet.* 2019;51(6):990–998. doi:10.1038/s41588-019-0413-z.

85. Semmler G, Simbrunner B, Scheiner B, Schwabl P, Paternostro R, Bucsics T, Stättermayer AF, Bauer D, Pinter M, Ferenci P, Trauner M, Mandorfer M, Reiberger T. **Impact of farnesoid X receptor single nucleotide polymorphisms on hepatic decompensation and mortality in cirrhotic patients with portal hypertension.** *J Gastroenterol Hepatol.* 2019 Dec;34(12):2164-2172. doi: 10.1111/jgh.14700.

86. Serhan N, Basso L, Sibilano R, Petitfils C, Meixiong J, Bonnart C, Reber LL, Marichal T, Starkl P, Cenac N, Dong X, Tsai M, Galli SJ, Gaudenzio N. **House dust mites activate nociceptor-mast cell clusters to drive type 2 skin inflammation.** *Nat Immunol.* 2019 Nov;20(11):1435-1443. doi: 10.1038/s41590-019-0493-z.

87. Serwas NK, Hoeger B, Ardy RC, Stulz SV, Sui Z, Memaran N, Meeths M, Krolo A, Yüce Petronczki Ö, Pfajfer L, Hou TZ, Halliday N, Santos-Valente E, Kalinichenko A, Kennedy A, Mace EM, Mukherjee M, Tesi B, Schrempf A, Pickl WF, Loizou JI, Kain R, Bidmon-Fliegenschnee B, Schickel JN, Glauzy S, Huemer J, Garncarz W, Salzer E, Pierides I, Bilic I, Thiel J, Priftakis P, Banerjee PP, Förster-Waldl E, Medgyesi D, Huber WD, Orange JS, Meffre E, Sansom DM, Bryceson YT, Altman A, Boztug K. **Human DEF6 deficiency underlies an immunodeficiency syndrome with systemic autoimmunity and aberrant CTLA-4 homeostasis.** *Nat Commun.* 2019 Jul 15;10(1):3106. doi: 10.1038/s41467-019-10812-x.

88. Shabani M, Aleyasin S, Kashef S, Zoghi S, Deswarte C, Casanova JL, Bustamante J, Rezaei N. **A Novel Recessive Mutation of Interferon-γ Receptor 1 in a Patient with Mycobacterium tuberculosis in Bone Marrow Aspirate.** *J Clin Immunol.* 2019 Feb;9(2):127-130. doi: 10.1007/s10875-019-00595-7.

89. Shahin T, Aschenbrenner D, Cagdas D, Bal SK, Conde CD, Garncarz W, Medgyesi D, Schwerd T, Karaatmaca B, Cetinkaya PG, Esenboga S, Twigg SRF, Cant A, Wilkie AOM, Tezcan I, Uhlig HH, Boztug K. **Selective loss of function variants in IL6ST cause Hyper-IgE syndrome with distinct impairments of T-cell phenotype and function.** *Haematologica.* 2019 Mar;104(3):609-621. doi: 10.3324/haematol.2018.194233.

90. Simonović N, Witalisz-Siepracka A, Meissl K, Lassnig C, Reichart U, Kolbe T, Farlik M, Bock C, Sexl V, Müller M, Strobl B. **NK Cells Require Cell-Extrinsic and -Intrinsic TYK2 for Full Functionality in Tumor Surveillance and Antibacterial Immunity.** *J Immunol.* 2019;202(6):1724–1734. doi:10.4049/jimmunol.1701649.

91. Singh DD, Hawkins RD, Lahesmaa R, Tripathi SK. **CRISPR/Cas9 guided genome and epigenome engineering and its therapeutic applications in immune mediated diseases.** *Semin Cell Dev Biol.* 2019 Dec;96:32-43. doi: 10.1016/j.semcdb.2019.05.007.

92. Skucha A, Ebner J, Grebien F. **Roles of SETD2 in Leukemia-Transcription, DNA-Damage, and Beyond.** *Int J Mol Sci.* 2019 Feb 27;20(5). pii: E1029. doi: 10.3390/ijms20051029.

93. Soldatov R, Kaucka M, Kastriti ME, Petersen J, Chontorotzea T, Englmaier L, Akkuratova N, Yang Y, Häring M, Dyachuk V, Bock C, Farlik M, Piacentino ML, Boismoreau F, Hilscher MM, Yokota C, Qian X, Nilsson M, Bronner ME, Croci L, Hsiao WY, Guertin DA, Brunet JF, Consalez GG, Ernfors P, Fried K, Kharchenko PV, Adameyko I. **Spatiotemporal structure of cell fate decisions in murine neural crest.** *Science.* 2019;364(6444):eaas9536. doi:10.1126/science.aas9536.

94. Somekh I, Thian M, Medgyesi D, Gülez N, Magg T, Gallón Duque A, Stauber T, Lev A, Genel F, Unal E, Simon AJ, Lee YN, Kalinichenko A, Dmytrus J, Kraakman MJ, Schiby G, Rohlfs M, Jacobson JM, Özer E, Akcal Ö, Conca R, Patiroglu T, Karakukcu M, Ozcan A, Shahin T, Appella E, Tatematsu M, Martinez-Jaramillo C, Chinn IK, Orange JS, Trujillo-Vargas CM, Franco JL, Hauck F, Somech R, Klein C, Boztug K. **CD137 deficiency causes immune dysregulation with predisposition to lymphomagenesis.** *Blood.* 2019 Oct 31;134(18):1510-1516. doi: 10.1182/blood.2019000644.

95. Spencer S, Köstel Bal S, Egner W, Lango Allen H, Raza SI, Ma CA, Gürel M, Zhang Y, Sun G, Sabroe RA, Greene D, Rae W, Shahin T, Kania K, Ardy RC, Thian M, Staples E, Pecchia-Bekkum A, Worrall WPM, Stephens J, Brown M, Tuna S, York M, Shackley F, Kerrin D, Sargur R, Condliffe A, Tipu HN, Kuehn HS, Rosenzweig SD, Turro E, Tavaré S, Thrasher AJ, Jodrell DI, Smith KGC, Boztug K, Milner JD, Thaventhiran JED. **Loss of the interleukin-6 receptor causes immunodeficiency, atopy, and abnormal inflammatory responses.** *J Exp Med.* 2019 Sep 2;216(9):1986-1998. doi: 10.1084/jem.20190344.

96. Staber PB, Herling M, Bellido M, Jacobsen ED, Davids MS, Kadia TM, Shustov A, Tournilhac O, Bachy E, Zaja F, Porkka K, Hoermann G, Simonitsch-Klupp I, Haferlach C, Kubicek S, Mayerhoefer ME, Hopfinger G, Jaeger U, Dearden C. **Consensus criteria for diagnosis, staging, and treatment response assessment of T-cell prolymphocytic leukemia.** *Blood.* 2019 Oct 3;134(14):1132-1143. doi: 10.1182/blood.2019000402.

97. Steinparzer I, Sedlyarov V, Rubin JD, Eislmayr K, Galbraith MD, Levandowski CB, Vcelkova T, Sneezum L, Wascher F, Amman F, Kleinova R, Bender H, Andrysik Z, Espinosa JM, Superti-Furga G, Dowell RD, Taatjes DJ, Kovarik P. **Transcriptional Responses to IFN-γ Require Mediator Kinase-Dependent Pause Release and Mechanistically Distinct CDK8 and CDK19 Functions.** *Mol Cell.* 2019 Nov 7;76(3):485-499.e8. doi: 10.1016/j.molcel.2019.07.034.

98. Tesch VK, Abolhassani H, Shadur B, Zobel J, Mareika Y, Sharapova S, Karakoc-Aydiner E, Rivière JG, Garcia-Prat M, Moes N, Haerynck F, Gonzales-Granado LI, Santos Pérez JL, Mukhina A, Shcherbina A, Aghamohammadi A, Hammarström L, Dogu F, Haskologlu S, İkincioğulları AI, Bal SK, Baris S, Kilic SS, Karaca NE, Kutukculer N, Girschick H, Kolios A, Keles S, Uygun V, Stepensky P, Worth A, van Montfrans JM, Peters AMJ, Meyts I, Adeli M, Marzollo A, Padem N, Khojah AM, Chavoshzadeh Z, Stefanija MA, Bakhtiar S, Florkin B, Meeths M, Gamez L, Grimbacher B, Seppänen MR, Lankester A, Gennery AR, Seidel MG; Inborn Errors, Clinical, and Registry Working Parties of the European Society for Blood and Marrow Transplantation (EBMT) and the European Society of Immunodeficiencies (ESID). **Long-term outcome of LRBA deficiency in 76 patients after various treatment modalities as evaluated by the immune deficiency and dysregulation activity (IDDA) score.** *J Allergy Clin Immunol.* 2019 Dec 27. pii: S0091-6749(19)32603-X. doi: 10.1016/j.jaci.2019.12.896.

99. Ulz P, Perakis S, Zhou Q, Moser T, Belic J, Lazzeri I, Wölfler A, Zebisch A, Gerger A, Pristauz G, Petru E, White B, Roberts CES, John JS, Schimek MG, Geigl JB, Bauernhofer T, Sill H, Bock C, Heitzer E, Speicher MR. **Inference of transcription factor binding from cell-free DNA enables tumor subtype prediction and early detection.** *Nat Commun.* 2019;10(1):4666. Published 2019 Oct 11. doi:10.1038/s41467-019-12714-4.

100. Unterhauser K, Pöltl L, Schneditz G, Kienesberger S, Glabonjat RA, Kitsera M, Pletz J, Josa-Prado F, Dornisch E, Lembacher-Fadum C, Roier S, Gorkiewicz G, Lucena D, Barasoain I, Kroutil W, Wiedner M, Loizou JI, Breinbauer R, Díaz JF, Schild S, Högenauer C, Zechner EL. **Klebsiella oxytoca enterotoxins tilimycin and tilivalline have distinct host DNA-damaging and microtubule-stabilizing activities.** *Proc Natl Acad Sci U S A.* 2019 Feb 26;116(9):3774-3783. doi: 10.1073/pnas.1819154116.

101. Unterleuthner D, Neuhold P, Schwarz K, Janker L, Neuditschko B, Nivarthi H, Crncec I, Kramer N, Unger C, Hengstschläger M, Eferl R, Moriggl R, Sommergruber W, Gerner C, Dolznig H. **Cancer-associated fibroblast-derived WNT2 increases tumor angiogenesis in colon cancer.** Angiogenesis. 2019 Oct 30. doi: 10.1007/s10456-019-09688-8.

102. Uras IZ, Maurer B, Nivarthi H, Jodl P, Kollmann K, Prchal-Murphy M, Milosevic Feenstra JD, Zojer M, Lagger S, Grausenburger R, Grabner B, Holly R, Kavirayani A, Bock C, Gisslinger H, Valent P, Kralovics R, Sexl V. **CDK6 coordinates JAK2V617F mutant MPN via NF-KB and apoptotic networks.** *Blood.* 2019;133(15):1677–1690. doi:10.1182/blood-2018-08-872648.

103. Valent P, Orazi A, Savona MR, Patnaik MM, Onida F, van de Loosdrecht AA, Haase D, Haferlach T, Elena C, Pleyer L, Kern W, Pemovska T, Vladimer GI, Schanz J, Keller A, Lübbert M, Lion T, Sotlar K, Reiter A, De Witte T, Pfeilstöcker M, Geissler K, Padron E, Deininger M, Orfao A, Horny HP, Greenberg PL, Arber DA, Malcovati L, Bennett JM. **Proposed diagnostic criteria for classical chronic myelomonocytic leukemia (CMML), CMML variants and pre-CMML conditions.** *Haematologica.* 2019 Oct;104(10):1935-1949. doi: 10.3324/haematol.2019.222059.

104. Yi G, Wierenga ATJ, Petraglia F, Narang P, Janssen-Megens EM, Mandoli A, Merkel A, Berentsen K, Kim B, Matarese F, Singh AA, Habibi E, Prange KHM, Mulder AB, Jansen JH, Clarke L, Heath S, van der Reijden BA, Flicek P, Yaspo ML, Gut I, Bock C, Schuringa JJ, Altucci L, Vellenga E, Stunnenberg HG, Martens JHA. **Chromatin-Based Classification of Genetically Heterogeneous AMLs into Two Distinct Subtypes with Diverse Stemness Phenotypes.** *Cell Rep.* 2019;26(4):1059–1069.e6. doi:10.1016/j.celrep.2018.12.098.

EU LIBRA Project Activities

The ultimate goal of the LIBRA project was to increase the representation and participation of women in leadership positions in the life sciences. In Europe, approximately half of all PhD students are women. However, the proportion of women researchers starts to decrease at the postdoctoral level and drops dramatically when it comes to leadership positions. These statistics point to a dramatic loss of talent and resources in research.

LIBRA was a 3.5 year EC Horizon 2020-funded project with the stated aim of unifying the innovative efforts by European research centers to achieve gender equality in academia. The project collectively involved one life sciences research institute each from ten different European countries. The institutes are all members of the EU-Life group alliance, already tasked with promoting excellence in the life sciences. CeMM, in collaboration with the Max Delbruck Center for Molecular Medicine, Berlin, coordinated LIBRA's centralized effort to promote recruitment without gender bias. The LIBRA project also covered topics such as career development and training, work-life balance, and the 'sex and gender' dimensions of research. The project concluded in 2019, at which time a final progress report was submitted. CeMM has been work package leader on the topic recruitment within the EC grant.

Final LIBRA meeting
The final LIBRA meeting was held at CeMM in March 2019. It included presentations on the many achievements of the project and an impact analysis. Discussions covered specific achievements in each of the ten individual institutes, as well as the degree to which the LIBRA project had improved general awareness of gender issues. The participating institutes also shared information about lessons learned and experiences of what proved effective.
A sustainability plan was finalized, as were plans for dissemination to the wider research community.

Annual LIBRA meeting
The annual LIBRA meeting was held in September at the Babraham Institute in Cambridge and attended by Binia Meixner, Head of HR at CeMM.

A workshop: How to design, implement and follow-up a Gender Equality Plan.
As part of the dissemination plan, LIBRA presented the second in a series of 2-day workshops, this one in Vienna in March 2019, entitled "How to design, implement and follow-up a Gender Equality Plan". The aim of the workshop was to share the experiences of the LIBRA project with a wider population of research organizations, and to support them in developing and implementing such a plan. In this instance, attendance was limited to 16 participants so as to ensure an interactive setting and encourage a collaborative atmosphere. The participants, from institutes in 10 different countries received information and guidance to enable them to support their own research organizations so as to reduce institutional barriers and promote gender equality.

Diversity lunches
In an informal setting, the diversity group at CeMM convenes weekly for lunch to discuss any recent topics or news relating to gender equality in science and to discuss any possible policies, procedures or practices that might be implemented.

Resources for staff
A subset of books relating to gender equality, unconscious bias and women in STEM is available at CeMM's library as recommended reading.

Final LIBRA meeting

Resources box for children
We have a resources box containing coloring materials, puzzles, and books available to help parents and carers to provide entertainment for their children should they need to bring them to work for a short period.

Christmas gifts for children
The children of CeMM staff are invited to attend the annual CeMM Christmas party, where each of them receives a small gift. In the spirit of the LIBRA project, it was decided to simplify these gifts by providing their parents with booklists containing suggestions for more gender-neutral literature as an option.

EU-Life Gender Equality Working Group
As part of the sustainability plan resulting from LIBRA, the EU-Life Gender Equality Working Group was formed and convened for its inaugural meeting in Milan in November 2019. The aim of this working group is to continue the work initiated by the LIBRA project and to coordinate the gender equality activities of the EU-Life institutes. The working group is composed of 17 members representing the 13 institutes of EU-Life, including institutes and members not involved in the original LIBRA project.
To advance further awareness and progress towards gender equality in science, the following priorities have been established:

+ develop a program against harassment and bullying;
+ develop common indicators to monitor gender equality at the institutional level; and
+ implement a second edition of the LIBRA Career Development Compass (continuing Postdoc career development training)

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 a network of 27 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. CeMM's research is strongly oriented towards medical needs and integrates research on fundamental biological processes with clinical expertise to gain new insights into human pathophysiology and to develop innovative diagnostic and therapeutic approaches. 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 14 renowned research centers (~540 research groups, 7,400 scientists). Partners include, for example, the Centre for Genomic Regulation (CRG) in Spain, the Flanders Institute for Biotechnology (VIB) in Belgium, the Netherlands Cancer Institute (NKI) and the Friedrich Miescher Institute (FMI) for Biomedical Research in Switzerland, all of whom 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 as part of the participatory, precise and personalized medicine of the future, 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.

Technology Transfer

CeMM's mandate is to do world-class research in biomedicine, to train researchers and medical doctors in molecular medicine and to accelerate the precise, personalized, participatory and preventative medicine of the future. 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 partners in this respect.

Project-specific research collaborations and technology transfer highlights

+ Pharmacoscopy is a method developed in CeMM Director Giulio Superti-Furga's group 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, the Robert Kralovics group at 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.
+ ChiPmentation, a new method developed in the group of CeMM PI Christoph Bock, introduced sequencing-compatible adaptors in a single-step reaction directly on bead-bound chromatin, which reduces time, cost and input requirements, thus providing a convenient and broadly useful alternative to existing ChIP-seq protocols.
+ In 2019, CeMM announced the start of a three-year research collaboration with Pfizer Inc. to explore a combination of technologies aimed at expanding the druggable proteome. CeMM Principal Investigators Georg Winter (project coordinator), Giulio Superti-Furga and Stefan Kubicek, in collaboration with researchers from Pfizer's Medicine Design organization based in Cambridge, USA, will aim to explore a discovery strategy that combines parallel, efficient ligand identification with focused degradation of individual targets.

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 in 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*

Community Services

Planning of Center for Technology Transfer on Medical Campus

In a large investment project, the Medical University of Vienna is going to build three centers on its Vienna General Hospital campus, specially designed for 21st century medicine: the Center for Precision Medicine, the Center for Translational Medicine and Therapies, and the Center for Technology Transfer. The Medical University of Vienna has started a fundraising campaign for the Center for Precision Medicine *(www.zpm.at)*, which also raises public awareness about precision medicine.

Heading the Steering Committee are MedUni Vienna Vice-Rector Michaela Fritz and Eva Czernohorszky Head of Technology Services at the Vienna Business Agency. CeMM Director Giulio Superti-Furga, who is also Professor for Medical Systems Biology at the Medical University of Vienna, has been asked by the Rectorate of the MedUni to coordinate a task force that is working on a concept for the new Center for Technology Transfer (CTT) in close cooperation with the Vienna Business Agency (VBA) and Life Science Austria (LISA).

Most of the Medical University of Vienna and CeMM start-up companies are currently located either in the 3rd district or at BOKU Vienna. Established companies are also looking for easier access to experts in both the pharmaceutical and medical technology sectors and closer proximity to the "place of action". The new Center for Technology Transfer aims to be a "marketplace" for encounters, ideas, financing collaborations and an incubator space for smaller and larger projects and companies. Catalyst projects and a dedicated building are needed to fuel the innovation value-added engine at the medical campus.

On 21 March 2019, the first brainstorming session of the new CCT task force took place at CeMM. We are grateful to all participants for a successful kick-off meeting and many interesting and fruitful follow-up discussions that further strengthened the planning and conception of the new Center for Technology Transfer.

End of of Giulio Superti-Furga's ERC Scientific Council membership

At the close of 2019, Giulio Superti-Furga, Scientific Director of CeMM and Professor for Medical Systems Biology of the Medical University of Vienna, ended his term as a member of the Scientific Council of the European Research Council, which began in January 2017. We thank Giulio Superti-Furga for this important scientific community service during difficult political times, for his strong advocacy of frontier research on new ideas as the best means to achieve innovation and economic welfare, and to sustain the foundations of democracy. Having been awarded two ERC Advanced Investigator Grants in the past and two ERC Proof-of-Concept Grants to explore the application potential of research ideas, Giulio Superti-Furga, who also acted as ERC panel member, will continue to be a strong supporter of the ERC, which celebrated its 10th anniversary in 2017 and is now preparing for Horizon Europe.

At the same time, renowned French mathematician Jean-Pierre Bourguignon came to the end of his term as ERC President, leaving behind a highly successful legacy of having further increased the prestige of the ERC and effectively safeguarded its budget. CeMM's-students, postdocs and faculty have a fond memory of his visit in Vienna in October 2017. As part of the scientific community, we thank Jean-Pierre Bourguignon for his inspiring leadership. From 2010 to 2013, Helga Nowotny, a Viennese Professor of Social Studies of Science, also held this prestigious position. We wish the new President success in leading the ERC in future years.

The European Research Council is the most important and prestigious funding institution for basic research conducted in any field within the European Union. Excellence is the sole criterion for selection, there are neither thematic priorities, nor geographical or other quotas for funding. With its different programs, it has created a very positive impact on the attractiveness of Europe as a research area.

Front row
from left to right
Markus Zeitlinger,
Sara Alkan,
Michaela Fritz,
Eva Czernohorszky,
Norbert Kraut,
Johannes Sarx,
Nikolaus Krall
Back row
from left to right
Brigitte Tempelmaier,
Thomas Berndt,
Michael Hoschitz,
Anita Ender,
Giulio Superti-Furga,
Peter Halwachs

Giulio Superti-Furga and Jean-Pierre Bourguignon at an ERC meeting in Brussels, December 2019

Making the Untouchable Tangible

A brand is a company's common denominator, a visible expression of its approach and culture. Why it is crucial for a research company like CeMM to become a brand and what we did to help build one.

Contribution by Kriso Leinfellner, who is together with Stefanie Lichtwitz principal of the communication design company *Lichtwitz Leinfellner visuelle Kultur KG*. The team is in charge of CeMM's visual matters since 2005. Aside from corporate design, web and editorial design projects, the interdisciplinary practice has a record in architecture related projects such as wayfinding systems or exhibition design.
www.lichtwitz-leinfellner.com

A brand creates a prejudice even before you come into direct contact with the thing it describes. A brand opens up associations and generates an impression by employing the right signals and codes. On the market, it provides orientation and allows differentiation from the competition. It should express continuity and reliability in order to gain public trust. But first and foremost, a brand should build an attraction force that creates and maintains ties.

In 2005, Giulio Superti-Furga clearly realised that a new-founded research center like CeMM, though it operates on limited public funds, must invest in becoming a brand in order to be successful. After all, it is competing with many others for excellent staff and partners, for funding and for companies that are supposed to one day monetize what has been achieved. And last but not least, it competes for attention both in science and in public.

Today, each of us comes into contact with around 300 brands every day (1), mostly on physical goods such as sneakers, cars or foods: visible and tangible things to which one can attach symbols like they used to brand cattle with (which is the origin of the word). But a brand for basic biomedical research? CeMM only produces knowledge, it trains people and contributes to future medicine, but there is no physical product. Some of the knowledge gained, however, may one day surface in the world of things in form of a pill. But it is more likely that the cure of the future will work on personalized scripts executed by genome or proteome editors – invisible and intangible to the patient.

(1) The first brand in modern terms was probably created by the Meissen Porcelain Factory in the year 1722. In fact, brands started to become important in the 18th century at the very moment products and services began being supplied to a greater geographical area where they were suddenly confronted with several competitors, and products were exposed to the market separately from their producers.

Building a brand

Because CeMM – especially before it got its own building – lacked something that could be seen or touched, we created something to embody the company's narratives, to represent the commitment to seek and speak the truth and to represent it unadulterated in its most immediate form. The Lab Journal, the central documentation tool in everyday lab work, was designed as a "blue book" that makes a frequent appearance in photos as a prop. With a premium linen binding in the company color and a gloss embossed logo, it became a symbol for CeMM's aspiration of being perceived as scientific and reliable.

CeMM, the Research Center for Molecular Medicine of the Austrian Academy of Sciences was given a well-chosen, memorable and phonetically valid name, which is a basic requirement for an effective brand. From this acronym we developed a simple but distinctive word mark presenting it as a fictitious molecule. In addition to the bonds between the atoms involved (with the element "Ce" having yet to be discovered), it offers an extra open bond for external partners to connect with. Using just a few graphical elements, this mark hints both at the topic of (bio-)chemistry and the notion of cooperation. Aside from the logo and the corporate color, a very characteristic and recognisable typeface complements the canon of visual vocabulary. But a brand is much more than a visual style: It is also about spaces, language, attitude, behavior and routines.

A brand as a "hyper-entity"

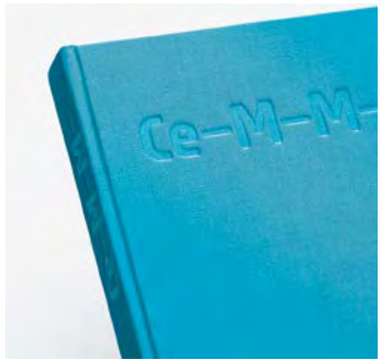
A visual identity should not be a straitjacket, nor a uniform or a fancy costume. Instead, it is a dress code that everyone involved is happy to agree on. A set of elements, rules and templates that make it easy to deal with everyday communication applications safely and with little effort.

A brand is a promise to the outside world that should be both coherent and authentic. Just as importantly, it also acts as a confirmation to a company's employees that they are part of a big, shared idea: An invisible "hyper-entity", a personality in its own right – with features and characteristics – that is always in the room, at whatever its protagonists are doing.

Having grown up for 15 years now, this brand personality is now entering a new phase of life. We hope she keeps her style!

15 Years of CeMM visual culture

You may have encountered some of CeMM's graphic design work in the form of research reports, websites, posters, signage, Christmas cards or coffee cups. We have collected some examples on this spread.



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: *www.cemm.at/artssociety/supporters*

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

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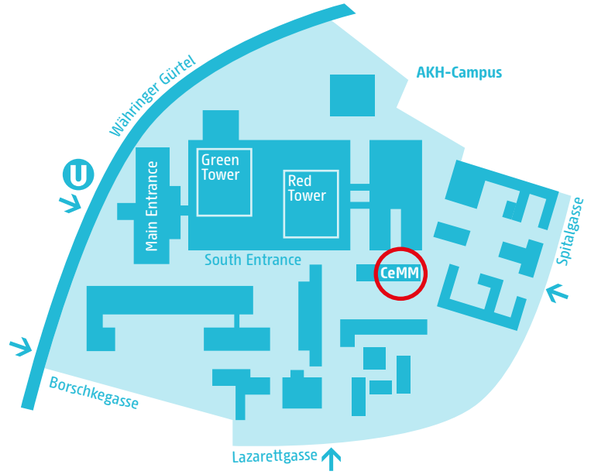

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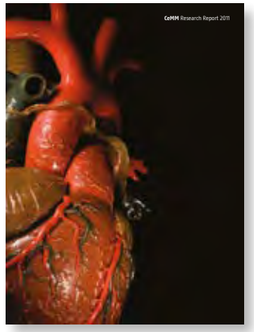

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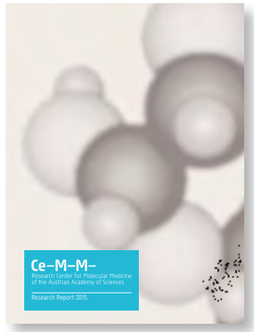

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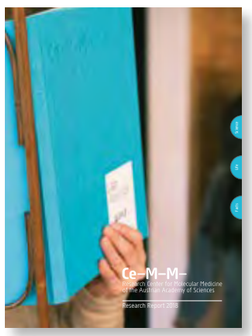

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