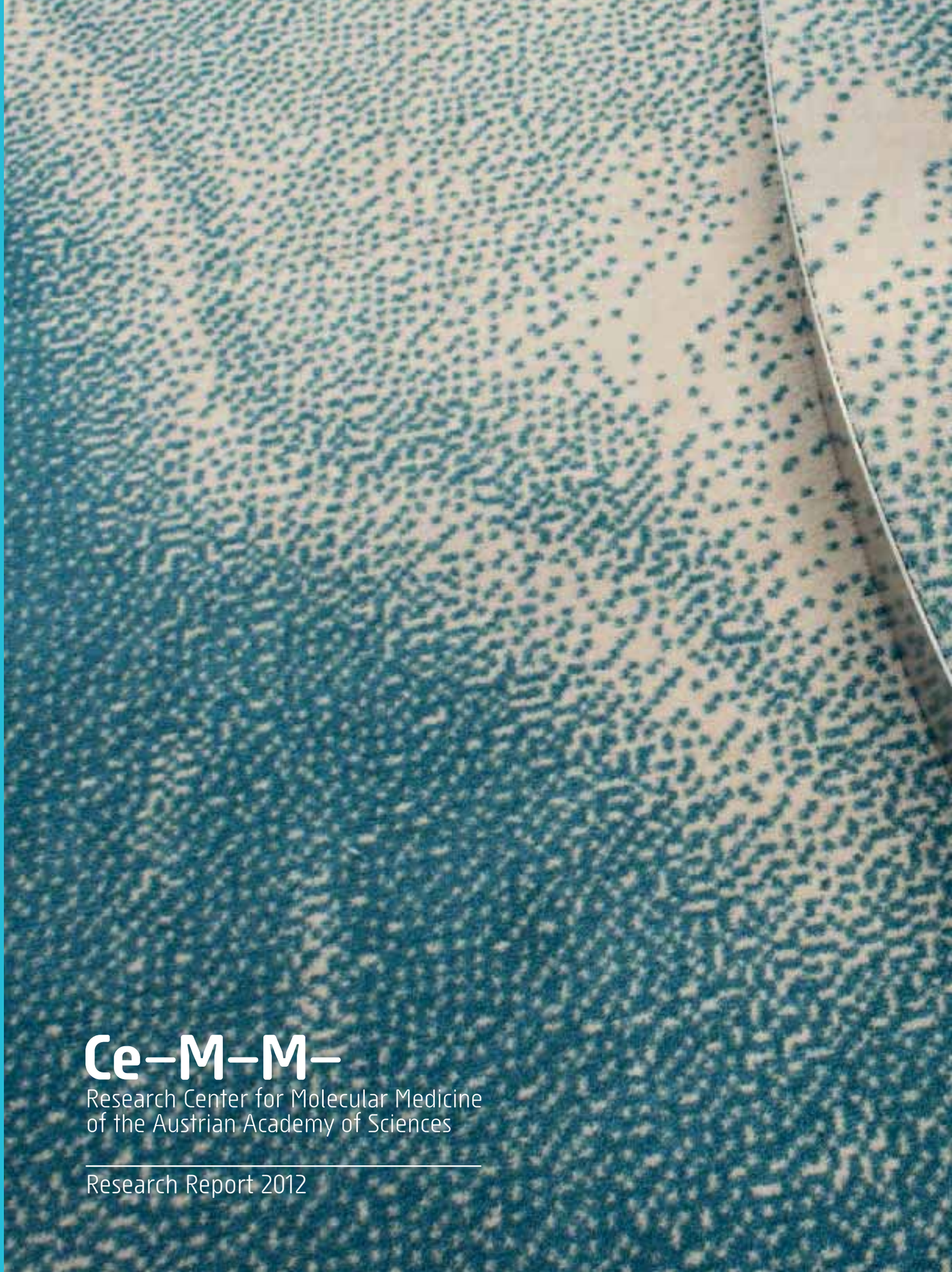

Ce–M–M–

Research Center for Molecular Medicine
of the Austrian Academy of Sciences

Research Report 2012

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CeMM Research Report 2012

Introduction by Giulio Superti-Furga

The designer duo Walking Chair, Fidel Peugeot and Karl Emilio Pircher with CeMM's Scientific Director Giulio Superti-Furga.

It is almost scary. After an "annus mirabilis" in 2011, the year 2012 has been just as full of events, advancements and achievements. The last few years have become one long adrenaline rush. Yet we are certainly still far from a peak of productivity, given the last Principal Investigator to join, Christoph Bock, started only in January 2012, and more than half of all researchers have been at CeMM for less than two years. The opportunity facing these rising stars is immense. The entire campus of the Medical University, our congenial partner, with its 2,000 medical doctors, is actively evaluating the merits of genome-informed medicine, and we are there to share the first ideas and provide fertile ground to support the growth of new initiatives. Christoph Bock, bearing a dual affiliation with the Medical University, has hit the ground running by establishing the CeMM/Medical University Biomedical Sequencing Facility, already very productive, and is building up a unique additional competence, namely computational epigenomics (the marks that tissues leave on genes), which is one of the next frontiers in biomedicine. Proteomics has also become more medically amenable, with its ability to characterize the expression of tens of thousands of proteins in a given tissue and make quantitative comparisons. Together with the informatics network-based evaluation of drug action, predictions on the most effective therapeutic strategies for treating individual patients is becoming more feasible. But make no mistake, this is still mostly at the experimental level, and it will be several years before we indeed can help patients. Yet we have been encouraged by the Scientific Advisory Board, who visited us in November, to accept the challenge for the next five years to pursue yet more translational projects without compromising on our mechanism-of-disease based research mode. I wish here to thank the entire scientific advisory board and particularly David Livingston, for open yet passionate suggestions.

There have been too many important scientific achievements to summarize them all here and I do not want to anticipate too much of the following report. Yet I would like to highlight the discovery of the mechanism by which a long non-coding RNA molecule, called *Airn*, negatively affects transcription of the IGFR2 gene from within the same genetic locus. The intellectual rigor and the uncompromising dedication with which Denise Barlow and her team have pursued the answer to this elusive problem counts as one of the very best scientific achievements in the field of epigenetic regulation in the last years, worldwide. As the rest of the best research we have done and we will do, the Barlow study relies on clever ideas. The little sparks of genius that sometimes strike us, I am afraid not often enough, like lightning. But where do they come from? And more importantly, can we induce them? Discussing this amongst ourselves (and also with artists and colleagues from the medical and the social sciences), it became apparent that the process of inspiration, of obtaining ideas, is something we do not usually dare to speak about. As if it is something a bit obscene or too intimate. Or something nobody would admit to lacking. It is as if we consider it a side product of our daily routine that happens perhaps under the shower, or, so the legend goes, in pubs after profuse alcohol intake. A dirty little secret. We found it paradoxical that the single most important step in the entire research process, the creative act, is precisely the one that is not acknowledged. It is also not budgeted, does not have a dedicated space in buildings, and isn't mentioned in the "methods" section of scientific papers. Yet what does the most sophisticated of scientific instrumentation and the hardest research work matter if the thought-out concept is not a good one? If the original idea is not truly good?

We decided to take action and have made a cultural statement: The Brain Lounge. More than a room: an art installation and open-end experiment dedicated to the power of thinking. Particularly in times of economic crisis and budgetary restrictions, the risk is to adopt a narrow, utilitarian view of the research process. We wanted to dispel the notion that research is just the "turning of a crank in a research engine". A mechanical, automatable process that can be reduced to the equation: x much money, over y much time, equals z much output. Breakthrough innovation in research is a much more complex process, strongly influenced by soft factors and cultural environment. The Brain Lounge is designed to symbolize the psychological and sociological importance of creativity in the cultural advancement process, not only in medicine, science, and technology, but also in the arts, economy, and politics. Seldom has society been so much in wanting of really new, good ideas. And again we were lucky. We found in the Vienna-based designer duo Walking Chair, Fidel Peugeot and Karl Emilio Pircher, two very congenial partners who made the Brain Lounge, against their own economic logic, a priority. Our joint ideas caught fire and captured a number of fantastic artists: Brigitte Kowanz, Esther Stocker, Martin Walde, Peter Kogler (who, of course was also the magical author of the CeMM facade), Eva Schlegel, Dorothee Golz, Thomas Feuerstein, Alois Mosbacher as well as the Berlin-based fashion designer Daniel Kroh. And yet more will join in its future. The result is a community project, a symbol, a totem, a living oracle, a vehicle for intellectual journeys and most importantly an ever-changing platform ideal for fostering interactions with the rest of society, beyond the boundaries of science and medicine and the campus of the General Hospital. I would like to thank the designers and artists along with the mainly private persons who so far have sponsored the project. We are recruiting more ideas and volunteers to test the Brain Lounge and would like to appeal to everybody who values the sheer beauty and importance of ideas to consider sponsoring the project (see page 122).

If CeMM has become in a relatively short time a research institute with impressive success, good international repute, and significant impact on the medical campus, it is due to its extraordinary research and teaching faculty. This is also proven for instance by two ERC and one FWF Starting Grant to Sebastian Nijman and Kaan Boztug and one ERC Starting Grant to Thijn Brummelkamp, our Adjunct Principal Investigator at the Netherlands Cancer Institute. Of all the privileges of the CeMM Scientific Director, the highest and most exhilarating is having this current team of clever, creative research group leaders as a fully accessible, fast-reacting and dedicated planning, sounding and execution board. I wish to thank the truly incredible amount of energy spent for the CeMM research cause. I dare hypothesize that we form one of the first modern groups of research "super-cooperators", in the diction of Martin Nowak, the Harvard-based Viennese biologist and game-theoretician. People who understand that the more efficient research paradigm is through modular and synergistic access to each other's brains and capabilities: The future is yours!

The scientific research process with all its unique requirements and idiosyncrasies is kept well functioning by a lean and efficient administration. Staying out of the limelight, they deserve a good share of the credit for CeMM's success. It has not been an easy year. While CeMM has grown in size, the budget hasn't, and extra work and creative solutions have been requested. On behalf of all scientists and collaborators I would like to thank the entire administration, particularly Gabriel Ó Ríordáin, Sigrid Strodl, Mischa Pilz, Eva Schweng and Stephan Boos-Waldeck, who lead their respective teams, and Anita Ender and Gerhard Schadler who have expertly orchestrated the entire process. Well done!

The Board and the management team of the Austrian Academy of Sciences are thanked for their support through time of great turmoil for their organization. We appreciated the enduring effort to do everything possible to help. And of course we thank the Ministry of Science and Research, CeMM's attentive patron.

The CeMM research report is structured around concepts that the art in the Brain Lounge inspired and that echo themes and properties of biological systems and their investigation: Influence, Reflection, Renewal, Accuracy, Association and Dynamics. Once again, the report has become much more than a list of people, projects and published papers. It has its own cultural identity and value as an integration of the CeMM research programs and medicine, arts, design, and photography. This is thanks to the merit of many people. First and foremost Eva Schweng, who project-leads with great love and attention. The text is crafted masterfully by Helen Pickersgill, a scientific writer of increasing elegance and effectiveness who now knows CeMM's research inside out and integrates text bites contributed by many people. This year we are privileged to enjoy the contributions of Gitti Huck, the renowned art historian and curator. Most of the pictures were taken by the wonderfully precise and truly illuminating photographer Iris Ranzinger. Finally, the graphic genius of the Lichtwitz and Leinfellner office for visual culture has so much permeated CeMM that it is now permanently part of its identity, as manifested in this report as well as in the soon-to-be web pages. Thanks to you all.

Finally I would like to thank all the CeMM scientists and all our colleagues and collaborators at the Medical University of Vienna and throughout the world. Your research is the reason CeMM exists and CeMM exists only to empower your research. We never forget this and are very grateful for your efforts in the past year.

To the reader I wish an entertaining journey through our sixth Research Report. Please continue to give us feedback and support; we always try to make the most out of it.

Giulio Superti-Furga
Scientific Director
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Discussion on the Origin of Ideas

A roundtable with Ulrike Felt, Brigitte Huck, Michael Freissmuth, Herbert Gottweis, Josef Smolen and Giulio Superti-Furga.

For more than 3.000 years, man has been searching for muses. Having good ideas is no push-button situation. Who or what inspires us?

One could think that research is an automatic process: You put in money, time and people, and you get an output. But the truth is that you can have a whole institute work on the wrong thing if the wrong ideas are on board. Historically, it is not about having the people, and the place, and the money. It is really about what you are doing, about the right idea. And there are of course parallels to this in art. To discuss the origin of ideas, Giulio Superti-Furga met five renowned specialists in their fields in the CeMM Brain Lounge: Gitti Huck, expert on modern art, Ulrike Felt, Professor of Social Studies of Science, Herbert Gottweis, Professor in the Department of Political Sciences, both of the University of Vienna, as well as Michael Freissmuth, pharmacologist, and Josef Smolen, rheumatologist, both department heads at the Medical University of Vienna.

Superti-Furga: We meet to discuss the origin of ideas, on when we had our last good idea. Did something happen just before we had that idea? Is it when we are sad, when we are happy? Is it when we are in love, or not in love, or when we are desperate? How much do the environment and cultural conditions affect and shape the quality or the substance of the idea we have. For 3,000 years man has been searching for muses. Having good ideas is no push-button-situation. Who inspires us?

Felt: What I find interesting is that the idea of time that we have in research has changed quite fundamentally over the last couple of decades. It is not that it gets faster but the time units become smaller so you feel like you don't have a lot of time, and you have to reason what you do and promise certain things. I get my best ideas when I have the feeling that I have a bunch of time when I can sufficiently wander for a while, and look at an issue from several sides, without having to come up with a result. There is very little time in academia for these kinds of enterprises. How would you argue that this is well-used time?

Huck: I think this is very similar to what is happening in art. When you are a very good artist and have produced a lot of good works, you are supposed to produce even more for exhibitions or for the market. The more renowned people are in the art world, the harder it is for them to stop being productive. There is no way to say: "I cannot go on working, because I don't have an idea at this moment!" The really great artists take their time to recover and have fresh ideas.

Freissmuth: This is true for fine art, but not for performing art. Science has both the performance aspect, which is the execution of the program, and the creativity, which is typically inspired by reading, and you need a lot of time to read. You need to have "Mußе, Negotium, Nichtstun" (time to move slowly and aimlessly).

Felt: It's not about doing nothing, it's about doing something without a particular aim or a timeline.

Smolen: Time off to recuperate and have new ideas wouldn't be the way I could live because I'm constantly refreshing, replenishing and doing. For me, creativity in science and art has multiple facets: inspiration; mentorship; time to think; shrinking time in order to be productive and not to lose ideas. Getting faster helps me capture ideas. When I speak of mentorship, I actually think that success is not necessarily down to the writer [mentee]. It is the publisher [mentor] who makes the writer. This is true for one of the most prolific times of art history – at least for me – which is the expressionistic time in 1910s–1920s, when there were publishers who started with nothing and ended up with people like Kafka or Benn, who hadn't even wanted to publish. These publishers were able to detect talents. You also need mentors in science who are able to inspire us, to help us, and to make us a little bit more creative and critical. We have to continue doing that with the younger people we work with.

Superti-Furga: Both you and Mischa Freissmuth speak of fortuitous interaction coming from reading a lot and meeting lots of people. Is this a male thing, to need the concentration and the speed?

Felt: There is a research cultural aspect also. It depends on how knowledge production works. What I said doesn't exclude that you continuously renew. But I think what is important is what this renewal actually means and how it redirects what you are doing. There are moments when it is important to stop and reflect, and think about what it means. I had once a very nice debate about how much scientific output is enough with students at ETH in Zurich. Is it reasonable for people to produce 100 top articles over three years? My comment was to think about what the notion "variation on a theme" means. When we push science into a kind of industrialized production of outputs, we also push similarity of things because you cannot be radically new.

Gitti Huck, Josef Smolen, Herbert Gottweis, Michael Freissmuth, Ulrike Felt and Giulio Superti-Furga in CeMM's Brain Lounge.

Smolen: But on the other hand if you have made a discovery it is fair to continue working on it. Artists like Kirchner and Miro have a style they continue for dozens of years - I don't think that you can call that machine production. I think that is putting down creativity. If you have a creative idea and have gotten to a point where you say, this is exactly what I want my art or science research question to be about, then you follow a superstructure and it is not illegitimate.

Felt: It is not a question of being legitimate or illegitimate. I just think that it is important to consider how change happens. The publication style has changed, because you need to publish faster and smaller portions, because that is strategically more important. And the question is where is there space for reflection?

Smolen: I agree in the sense that I hate slicing data. Some journals like the New England Journal of Medicine cut down manuscripts to 2,700 words, so you cannot publish everything. On the other hand, if you have a really good idea, and here are protagonists like Giulio, you are not going to publish it prematurely if you can eventually get a Nature paper. High quality work definitely cannot be published in a sliced way today. So I think in that aspect, science has matured a lot.

Superti-Furga: Connecting back to the Brain Lounge. The question is - if you take a Nature paper - where did the idea come from? Sometimes when I go to scientific meetings, and it doesn't matter whether they are good or bad, I have a Dadaistic storm and I connect some concepts or keywords. I wonder whether there is a random generator of combinations that can help scientists. When was the last time you had a really great thought, a great idea?

Gottweis: I want to pick up on space again. For me something really crucial for scientific creativity is how to create space, because we're living in a situation where space is becoming narrower in many different respects. You mentioned mentoring. I think mentoring can create space, but it can also do the opposite because some students need to be left alone to use space. We can always say that it's much better to direct, as in classical mentoring, but space seems to be something which is difficult to produce. How do you produce these spaces of creativity? I would say different strategies, in different contexts: a conference can be a perfect space, a workshop, meeting people from different walks of life, but they also might not be. I don't think there's a definitive answer for how you create this space, but I see that very often we don't have space. We are losing space. Things are getting narrower.

Smolen: It depends on which area you work on. We as physicians often have a clinical question. We see many patients with the same problem, and then we go into experimental work and form collaborations to encircle the problem, which creates space in a different way. Posing new ideas is how we get inspired. We get inspired by success and by failure. That is how we create our space. I recall that many years ago we thought that if we knock out a certain molecule it would reduce bone destruction. It turned out that knocking it out increased bone destruction, which became a very high profile paper that the other paper wouldn't have been. So sometimes it is serendipity. We live straight forward. You have to have space. Mentorship is also allowing side streams and orthogonal research activities. That is exactly what happens in laboratories, and what happens in arts as well.

Huck: In art, chance, "Zufall", is very important, hopefully more important than in science.

Freissmuth: There is the famous saying of Pasteur: Chance favors the prepared mind.

Felt: Young researchers in their Ph.D. or early Post doc phase would not agree. The risk strategy of seniors is totally different to juniors. Juniors' futures depend on their projects. So it also depends on your position.

Superti-Furga: I'm interested to hear from the sociologists who study the creative process in research: Are there patterns that you can observe, or creative environments? Can you detect behavioral patterns that are associated with high creativity or is it too complex?

Felt: That is difficult to answer. I actually think it's the kind of room for maneuver you have. One difference you can see between junior people is whether they thought there was a collective risk strategy or if risk was delegated to each individual. The boss has a risk strategy: he or she has conventional projects that will produce output to satisfy the watching institution, and then other projects that may be "the one". I think the bosses have this idea that they have room for maneuver because they have this strategy. Perhaps we are not sufficiently attentive to the junior people. In that sense, it's not a one-to-one mentoring, but maybe it's more about group mentoring, of creating the idea that there is a support and that it's not about individual short term failure or success. This creates an environment, a space, where things are done together. And in a world that has become so individualized and directly competitive, these spaces are shrinking.

Michael Freissmuth
Professor of Pharmacology, Medical University of Vienna

Gitti Huck
Expert on modern art

Josef Smolen
Professor of Rheumatology, Medical University of Vienna

Giulio Superti-Furga
Scientific Director, CeMM

Ulrike Felt
Professor of Social Studies of Science, University of Vienna

Herbert Gottweis
Professor in the Department of Political Sciences, University of Vienna

Smolen: I think mentoring is not about only telling people exactly what to do and putting handcuffs on flowers. Mentoring is providing an idea and trying to protect space, not to give space. I cannot give space to everyone because people have to work in the clinic and in the laboratory, but I can try to protect what they are doing. So from that perspective, mentoring is also about providing a safety net.

Superti-Furga: For young people, coming back to the artistis - could groups of artists solve the problem? So if one doesn't have a great idea, another one may have it.

Huck: It is a highly individual thing. There are few artists groups nowadays.

Freissmuth: When you are running a research group, you are actually not only interested in the product. You don't want the people to fail, and you don't want them to spoil their lives. You don't want them to end up like Rembrandt van Rijn. We can hardly separate from the sociology of science where each individual person wants to have credit.

Smolen: In science, there is primarily an institutional effort, whereas in art there is usually not. A group of individual artists can say: "Let's share a studio. Then all of a sudden, they influence each other and become famous or not." In research, it is not so easy. Individual young researchers outside a university probably cannot say: "Let's do science together …"

Superti-Furga: For example, the designer duo, Walking Chair, who made the Brain Lounge are a typical, beautiful, creative partnership. One can do something that the other one cannot do. If one doesn't have an idea, the other one has it. Do you think that art collectives work?

Freissmuth: The more you get into design and architecture, the more you have group efforts. Your question in the beginning was focused on the creative moment originally. When do we have a good idea, individually, what is the moment? And also, can you elicit it?

Superti-Furga: In advertizing, people know exactly what visual or oral cues you need to trigger certain reactions in your brain. Is something comparable for creative thinking? Can we elicit ideas with sparks of light, or with music?

Freissmuth: We could talk about a reward mechanism, an immediate somatic marker that tells you, oh - this was a brilliant idea. I think the environment you have to create is where this immediate reward of having an idea is somehow triggered.

Gottweis: Space is also a matter of spirit. Humans are specialists at reducing space. We are very good in organizing things. So let's organize a creative space. I think it's very important, but at the same time let's not forget about spirit space. That space is a matter of spirit, of an attitude.

Superti-Furga: I'm sure that the value of the Brain Lounge is not the room itself but the fact that one values the idea-giving process. It is a symbol. But the question is can we train people to be creative.

Smolen: Train your children to ask questions. I think that is something that is part of creativity. Make people aware that things are not how they look, and not to take things for granted.

Huck: You cannot train having good ideas.

Felt: But you can offer experiences.

Freissmuth: Coming back to the question: I get that spark just to think about the problem. But when does the moment happen that you propose one solution?

Smolen: Sometimes it happens by doing more and more experiments. Sometimes from listening to boring presentations. There has never been any meeting in my life that I found useless.

Superti-Furga: It's the best place to think about new questions. But the Brain Lounge was not a spark idea, it evolved.

Huck: It's not a good idea, especially in art, to think about fundamental questions, it's just too much. The good things come out of a little something. It can be something on the floor. Very often things happen for some reason. Things flow. There are situations where things can flow. And maybe there is a sort of spirit of space involved. And it's not something you can really anticipate. It is difficult to engineer. You cannot engineer spirit, but materialize it at some point.

Superti-Furga: The moment you want the muse, it will never come. You cannot say, "I want to have the inspiration." When we were discussing the Brain Lounge, we were saying that this could be the biggest single place where no ideas will ever happen because people come with the cause of getting ideas and the muse will just disappear. But there is something that has to do with inspiration, meditation, putting you in a state where you want without wanting.

Felt: … in a sense it is not the physically coming to the Brain lounge that matters, but the fact that there is a place like that within an institution.

Smolen: CeMM itself is a Brain Lounge.

Huck: We're always talking very abstractly about this - this is the place, this is the Brain Lounge, and this is where you have your ideas. It is good to have a place where you can have the ideas. But why are you never talking about this place as the place where the art is?

Superti-Furga: It is a place for the arts, you are totally right. But this is not where you come for personal meditation. This is a communication place.

Huck: But if this place is for the people who are working here, they might like the idea that there is a place in here for the arts.

Superti-Furga: I do believe that that is the essence of it. And I do believe that new and unprecedented thoughts are the best tribute to the art. Maybe that is the wrong connection, to say a nice piece of art triggers a poetic or creative type of thinking that then crosses with another. But you are right; one should calibrate one's expectation on this in a more passive way. "Come and enjoy the art," might be a better invitation, than, "come and have an idea".

Gottweis: Is it only to have an idea? For me, creativity has a lot to do with connecting with yourself. Usually most people are not connected with themselves, which is a problem when they think about what they should do, and what is or isn't interesting. To create a space where you can connect with yourself is not meditation in a narrow sense.

Superti-Furga: We assume that people here should venture outside their usual self and even adopt roles like in a theater. And in such a way create group dynamic discussions that otherwise would never occur because roles are prejudiced. I come in to this situation and dress differently, and a collaborator of mine dresses up. Then a role game starts. We also have a logbook that equals these games to journeys. The analogy is more a strange journey, an adventure that somehow puts you to a different way of thinking.

Smolen: So what is your idea about who should come here? Should work groups come here or should this be cross-fertilization, or just whoever wants to use it?

Superti-Furga: All of them. It's up for grabs, it's up for ideas. The only mantra we say is, don't use it in a routine sort of fashion. My analogy is with an oracle. Like the Delphi oracle: If you go every day to the Delphi oracle, you will get a stupid answer. But if you go there when you genuinely are open for an answer, it will work. So it should always be something special to come here. It should be associated with a pleasant and a playful type of atmosphere. I don't think the place profits from being abused by say a weekly meeting. We have so called teatime meetings where we are looking for the craziest idea that a particular person has and we discuss it, and it has to be remote from the daily operation. We are writing rules for use in a formal sense, but in an intellectual sense, we are looking for ways and ideas to enlarge the user group. If we are lucky, over the next ten years, in our logbook we will collect a lot of journeys of different people. It is an evolution, and it should be an evolution. An installation, an ongoing art project, an experiment.

Research at CeMM

The more advanced science gets, the closer it is to art.
The more advanced art gets, the closer it is to science.
Buckminster Fuller

American architect, engineer, designer, philosopher and writer Richard (Bucky) Buckminster Fuller was one of the most influential thinkers of the 20th century. A firm believer in the necessity of dialogue between art and science, he felt it offered incredible potential for discovering new ideas, developing visions, reaching the frontiers of knowledge and eventually surpassing them.

Watches: Adolf Roman, Ideas: Ernst Caramelle – an inscription above a shop entrance in Vienna's city center. This discrete text-based work has survived as "conceptual fall out" in the public space since 1988. Only insiders know about this secret attestation of Austrian conceptual art, through which Ernst Caramelle rethought contemporary time and space, turning it into an artistic act. Ideas, theoretical considerations and processes are at the center of his artwork. "My work always comes from the head," he says, "I never make anything from the gut."

CeMM's 8th floor has recently become home to the *Brain Lounge*. A cockpit of sorts for ideas, for creativity, an interface where medical research meets art and design. Karl Emilio Pircher and Fidel Peugeot, the internationally renowned designer duo known as *Walking Chair*, have interpreted the Brain Lounge as a nineteen-sixties style (space) capsule. Within this spacey environment, artists are now stirring up the disciplines.

In molecular research, as practiced at CeMM, there are terms used to describe the significance, effect and priority of individual areas of research. They are terms such as pattern, dynamics, communication, precision, association, influence, decision, renewal, reflection and insight. In the context of the community project Brain Lounge, they can serve to address issues that artists and designers also find themselves confronted within their work.

Influence

+ Joining Forces in Biology
+ The Influence of Protein Modifications
+ Influencing Biological Pathways
+ The Broad Influence of Drug Action
+ Influencing Gene Activity

Influence

Art and science were linked at the tenth edition of documenta in Kassel in 1997. In 2012, 15 years later, scientists and artists met on equal footing in the same context. For both disciplines, the subject of this exhibition, arguably the most important art exhibition in the world, was an investigation of the possibilities and definitions of reality.

The experimental apparatus contributed by Austrian quantum physicist Anton Zeilinger addressed the question of how light can be represented. Artist Brigitte Kowanz also works with light. She is interested in the relationship between technology and perception in the context of space and time, waging a pitched battle against the supposedly superficial, the phantasm of light, the poetry of optical phenomena. “My interest has shifted though,” says the artist, “toward the information content of light. In our society, light is a carrier for information. And thereby also a metaphor for knowing and recognizing.”

There is no biological entity, no protein or cell that works entirely alone. Each is influenced by many different factors such as the action of enzymes to chemically modify a protein and influence its activity, or environmental conditions that signal to the cell and influence its state.

Influences can be both positive and negative, either stimulating a biological process to continue or blocking its progress. This ensures tight control to avoid a malfunction that could potentially lead to disease.

Joining Forces in Biology

Traditionally scientists have studied components of biological systems in relative isolation. However the recent development of advanced tools and the evolution of biological thought has paved the way for a so-called systems view of science, where all the influential aspects of any biological process are, as much as possible, taken into consideration. This view is perhaps more relevant to how an actual molecule, cell or organism normally works, but it is also more complex, and often involves the production of large datasets that need to be interpreted to produce meaningful and novel biological insights.

Proteomics is the large-scale study of the structure and/or function of proteins and is often utilized in systems biology. It is a versatile and powerful technology used at CeMM to study a broad range of topics. Proteomics methods such as quantitative mass spectrometry have been established by Keiryn Bennett’s group at CeMM, and tailored for multiple applications from fundamental comparisons of protein expression in different biological samples to detection of protein interactions with different types of molecules. To process and analyze the large and diverse proteomics datasets produced by these methods, the bioinformatics group led by Jacques Colinge has been developing comprehensive statistical and computational platforms.

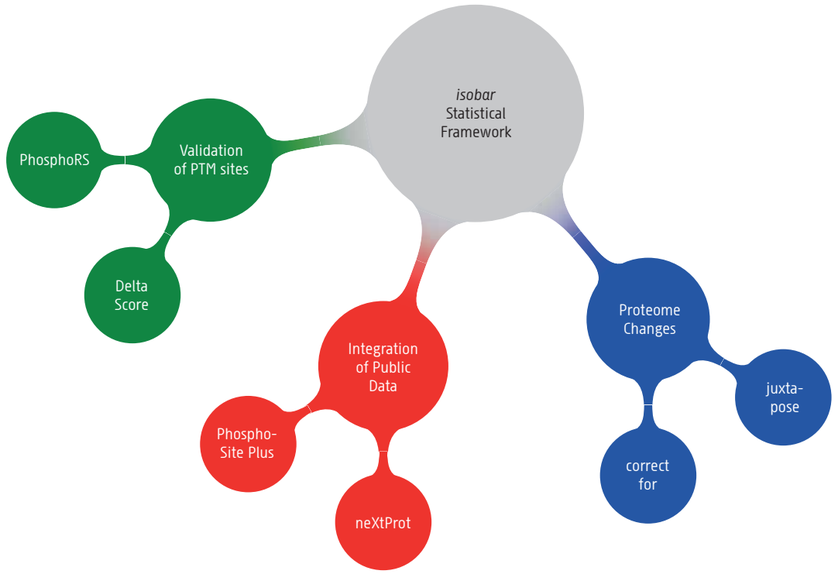


Fig. 1 The isobar framework (gray) provides essential statistical and data processing tools and capabilities for working with post translational modifications (PTMs). We added a PTM localization component (green) based on existing tools, a component to integrate known PTMs (red), as well as specific calculation, such as the correction of PTM regulation by general protein regulation (blue).

The Influence of Protein Modifications

In close collaboration with the Bennett group, the bioinformatics group introduced a new framework, known as isobar, to address the needs of quantitative proteomics in a comprehensive, intuitive, and mathematically rigorous way. Recently, they have established new statistical and computational tools to map the dynamics of posttranslational protein modifications in a variety of contexts, such as in patient samples, or to analyze the effects of drugs. Posttranslational modifications of proteins, e.g. phosphorylation, methylation, acetylation, or ubiquitination, are at the heart of a large number of CeMM projects, and are being studied in almost every laboratory. They regulate protein function and protein degradation, and are therefore highly influential, playing a pivotal role in many different cellular processes such as growth, DNA repair and cell death.

The isobar framework developed by the Colinge group now also provides statistical tools and analytical methods tailored to the study of modified proteins. It has also introduced a novel paradigm to report complex results to users as interlinked spreadsheets containing hyperlinks to Internet resources. This extended isobar framework also integrates several tools developed by other bioinformatics groups to validate the position of individual posttranslational modifications on proteins, as well as protein and modification databases. The framework is used in several projects at CeMM, with collaborators at the Medical University of Vienna (e.g. Peter Valent, Georg Stingl, and Ursula Schmidt-Erfurth) as well as abroad. It has been successfully utilized, for example, to study the synergies of protein kinase inhibitor drugs used to treat patients with leukemia, which was published in *Nature Chemical Biology* (Winter et al., 2012). The entire isobar framework has been developed open source and is distributed as part of the bioinformatics platform R Bioconductor.

Influencing Biological Pathways

Studying ubiquitination of key regulatory proteins can provide new angles for drug development.

To escape the normal control mechanisms that influence growth, cancer cells activate biological signaling pathways, which are composed of many different molecules, allowing them to grow uncontrollably. One such frequently deregulated pathway in cancer is known as the AKT/PI3K/mTOR signaling pathway. This pathway is also deregulated in other disease conditions including diabetes, and therefore many pharmaceutical companies are developing drugs to inhibit the activity of some of the protein components.

Many processes in the cell are influenced by the posttranslational modification ubiquitination, which is the covalent attachment of the small protein ubiquitin to a lysine in the target protein. This modification is reversible and a set of about 100 peptidases can cleave ubiquitin at the attachment site. In principle, the enzymes involved in ubiquitination and deubiquitination are drug targets as they can be used to influence protein activity. Therefore, studying ubiquitination of key regulatory proteins can provide new angles for drug development. A central control component of the AKT/PI3K/mTOR signaling pathway is a protein called PDK1. Although PDK1 is essential for the activation of AKT and various other kinases, fairly little is known about the molecular factors that influence the activity of PDK1 itself. The Nijman lab at CeMM has recently discovered that PDK1 is ubiquitinated and found one of the enzymes responsible (USP4), which was published in *PLoS ONE* (Uras et al., 2012). These results reveal new ways for pharmacological modulation of PDK1 activity and thereby the AKT/PI3K/mTOR pathway, which may prove useful for treating cancer and other diseases.

The Broad Influence of Drug Action

One of the major new trends in modern cancer treatment is targeted or personalised therapy. This is based on the idea of attenuating the activity of one protein that is known to play a key role in the disease. However, all drugs in clinical use inhibit more than one protein. This is known as polypharmacology and often causes severe side effects. Therefore, elucidating a drug's mechanism of action, i.e., how it influences cellular function, is important for improving the specificity particularly of anticancer therapeutics.

Chemical proteomics is a powerful technique for identifying many of the target proteins that interact with a specific drug. The combination of post-genomic drug affinity chromatography with high-end mass spectrometry and bioinformatic analyses can be used to assemble a target profile of a desired therapeutic molecule. Due to high demands on starting material, however, chemical proteomic studies have been mostly limited to cancer cell lines. As pioneered by the Superti-Furga Lab, the Bennett group at CeMM has developed a technique, in collaboration with Eric Haura and Soner Altiok from the Moffitt Cancer Center, to down-size these studies to enable the analysis of very low abundance samples such as those obtained from fine needle tumour biopsies. The methodology they developed is robust and generic, and holds many promises for the field of personalised health care.

Influencing Gene Activity

Sequencing of the human genome has shown that it takes about 23,000 genes to make a human being, but it gave no information on the mechanisms influencing the activity of genes and how these can go wrong and cause disease. Many factors can influence gene activity including epigenetic mechanisms, which are heritable changes in gene activity that are not encoded in the DNA. The Barlow group at CeMM has invested many years in understanding the epigenetic mechanism controlling genomic imprinting, a phenomenon in which parents leave their 'imprint' on one of the two parental copies of a gene inherited by their offspring, one of which is then switched off.

All mammals including human beings inherit a complete set of chromosomes from both their maternal and paternal parent, and consequently each cell has two copies of every gene. Normally, both parental gene copies are equally active in all cells, but for a minority of genes an epigenetic mechanism known as genomic imprinting silences one gene copy in a parental-specific manner. The study of imprinted genes has uncovered many unpredictable findings about what controls the on/off state of a gene that are likely also to be relevant for understanding how epigenetics affects other genes in our genome. In recent work, the Barlow lab has shown that it is specifically the transcription of a special class of long non-coding RNA (lncRNA) that is able to silence imprinted genes and not the lncRNA product itself. This result was published in *Science* (Latos et al., 2012), and the mechanism may also explain epigenetic gene control elsewhere in the human genome.

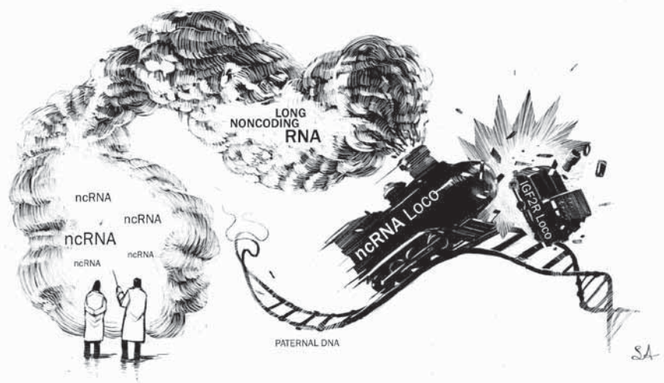


Fig. 2 A model for Airn lncRNA function: the Airn locomotive kicks the Igf2r locomotive off the DNA rails. The smoke (i.e., the Airn lncRNA product) is a by-product of the silencing mechanism, and blocked scientists from seeing the real function.

Reflection

+ Reflecting the Complexity of Cancer
+ Spotlight on the Immune Response

Reflection

The idea of the studiolo, that rarified, sophisticatedly furnished space in which scholars devote themselves to the study of the arts and contemplative reflection, has been with us since the Renaissance. The CeMM Brain Lounge could well serve as a modern-day counterpart with an enhanced intellectual practice.

By the mid-1960s, a new, definitive phenomenon had established itself in the international art world: Conceptual Art. Since that time, art has no longer concerned itself simply with physical objects, with form or material, but rather with communicating the work's underlying idea. Linguistic play and serial process play as important a role as does the participation of the audience. Under the new rules, the execution of the work by the artist is no longer necessary. For "Art as Idea as Idea" what matters are planning, context and meaning.

How can we best recognize the value of data and use it to make new discoveries? Indeed it's not always necessary to push through boundaries to learn something new. A careful look back, a reflection, on what we have already learned, can sometimes be just as informative.

Cellular function is managed and organized by networks of interacting molecules, the so-called biological pathways. Integrating existing knowledge of these pathways with the analysis of new datasets related to those pathways can help to better structure them and increase discovery power. The Colinge group at CeMM has successfully applied this philosophy to a variety of projects such as the analysis of virus-host interactions, and cancer genetics. For virus-host interactions, experimentally measured viral protein-human protein interactions covering 30 distinct viruses were generated by the Superti-Furga and Bennett groups at CeMM.

In this study, which was published in *Nature* (Pichlmair et al., 2012), they used known pathways and protein interaction networks to describe the general strategies used by viruses to take control of infected host cells. They showed that viral proteins preferably interact with human proteins that have multiple functions and are strongly connected with other human proteins. This allows the viruses to work efficiently to globally reprogram host cells, which is useful given that their genomes are limited in size and therefore their proteins must be optimally employed.

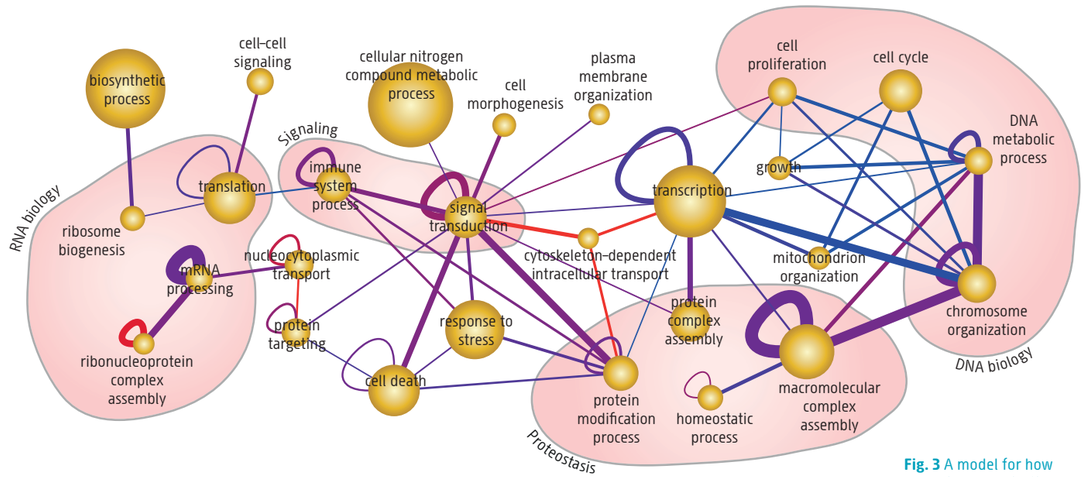


Fig. 3 A model for how normal communication between biological processes is perturbed by the action of viruses. A link between two processes indicates perturbation and the thickness is proportional to perturbation strength. Self links indicate that communication is perturbed between proteins within the same biological process. Adapted from *Nature* (Pichlmair et al., 2012).

Reflecting the Complexity of Cancer

Sebastian Nijman's group at CeMM has been focusing on cancer, perhaps the most heterogeneous human disease and one that will benefit from being perceived in different ways. Cancer genomics, abounding from the recent technological breakthroughs of next generation sequencing, is currently producing comprehensive lists of the many genetic aberrations found in different cancer subtypes at an astounding rate. This has led to the recognition that the genetic make-up of every patient and every tumor is different. Thus, one of the major new challenges for cancer therapy is matching the right therapy with the right patient.

The Nijman lab has been using knowledge of the genetic aberrations in cancer to engineer cell models to reflect the diversity observed in patients in a more simple and controlled way. This gives them a unique tool to analyze the activity of thousands of drugs on many of the different genotypes associated with cancer. The lab recently reported a mechanism of resistance to an emerging class of drugs in breast cancer. Using their engineered isogenic cell lines, they found that breast cancer cells with activated c-MYC/NOTCH signaling are resistant to PI3K inhibitors, showing that the approach can reveal overlooked and important new insights. The team is now continuing their search as well as expanding the approach to lung cancer. They have performed new screens with a panel of 100 cell lines and an equal number of drugs. The newly unearthed gene-drug interactions are the focus of intense studies and will keep the team busy for the coming year.

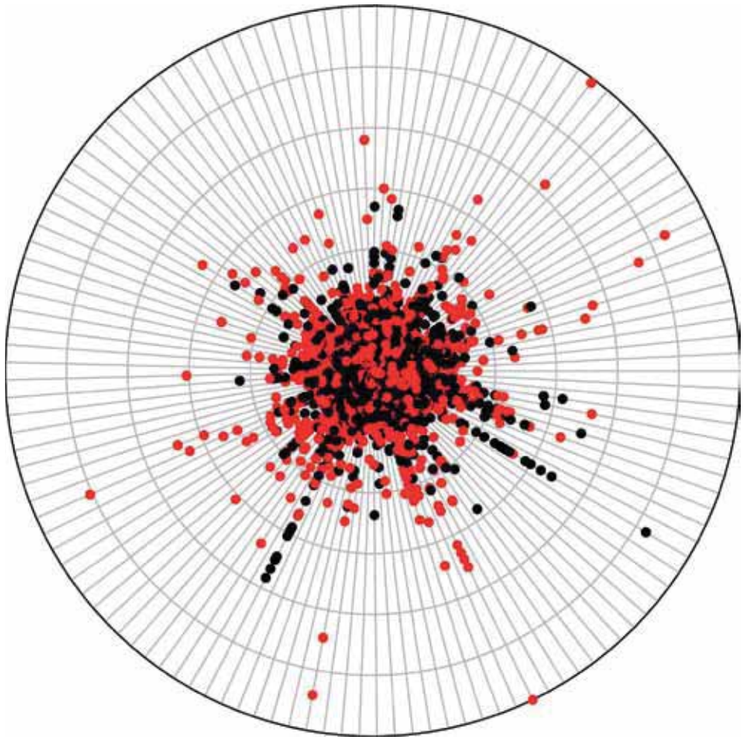


Fig. 4 Graphical illustration drug interaction screen in lung cancer cells. Each dot represents a gene-drug interaction measured in a panel of isogenic lung cancer cell lines treated with drugs. In total >10 thousand interactions were assessed. Each radial indicates a different drug treatment and the further away a dot is from the center the more significant the interaction scored in the screen. Red indicates more sensitive and black indicates more resistant to any drug. Identification of specific cancer vulnerabilities can help to bridge the gap between cancer genomics and effective treatments.

Spotlight on the Immune Response

Our immune systems use a highly sophisticated approach to search through the millions of diverse types of cells in our bodies to detect a very small number of invading pathogens. The ability to recognize pathogens as foreign is conferred by a multitude of dedicated molecules and cells, so pathogens must evolve elaborate ways of reflecting away their attention in order to be successful. Sylvia Knapp's group at CeMM has been studying how the bacteria *Staphylococcus aureus* and *Streptococcus pneumoniae* escape detection by shifting the focus of the immune system. Rather than inventing new ways to avoid the immune system, many pathogens use our own molecules to work against us. The Knapp group recently discovered that lipoteichoic acid (LTA) produced by *Staphylococcus aureus* binds to specific lipoproteins found in human serum, known as apolipoproteins (Apo) B100, ApoA1 and ApoA2. This enables the bacteria to severely inhibit the immune response and continue to propagate. This work was published in the *European Journal of Immunology* (Sigel et al., 2012). By investigating the precise function of these human proteins, they can identify novel mechanisms that can be targeted to help treat infections.

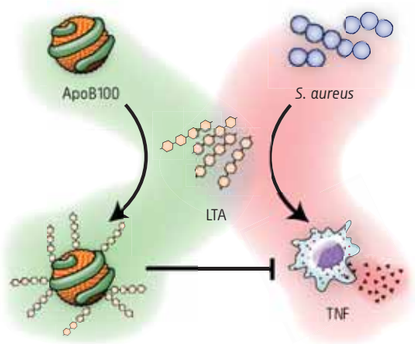


Fig. 5 Metabolism meets infection: The main lipoprotein in LDL, ApoB100, can bind bacterial molecules like lipoteichoic acid (LTA) from *Staphylococcus aureus* and thereby prevent the inflammatory response. This shows that serum lipid profiles can affect the antibacterial response. Adapted from *European Journal of Immunology*, 2012.

+ Repairing DNA Breaks
+ Protecting the Genome
+ Reversing Disease

Renewal

Renewal

Anyone entering the Brain Lounge may, if so inclined, slip into one of the jackets hanging from the ceiling. They are blue, have colorful patches and are intended to help the wearer step outside their daily routine. They were created by Daniel Kroh, a trained tailor and fashion designer, from recycled work clothes.

In recent decades, female artists in particular from Lygia Clark to Rosemarie Trockel and Cindy Sherman have explored the modalities of representation and examined the role that the present and absent body or the codes communicated through clothes play in the representation of identity. The various approaches include therapy and ritual, the erasing of boundaries between art and utilitarian objects, or taking pleasure in disguise and camouflage. Here the working methods of art and science find common ground on the level of the processive, of interaction and performance, of instructions for action and expanded art.

Renewal is a central theme in biology. To remain in a healthy state, cells and organisms must restore homeostasis in the face of many external and internal factors. Whilst renewal can be induced by medicine, there are many endogenous systems in the body that help to renew our molecules and cells in order to protect us against damage and disease.

For example, to mend the damage of DNA, which can occur by the action of carcinogens such as those found in tobacco, there are several dedicated 'renewal' systems known as DNA repair pathways. Maintaining the integrity of DNA is of utmost importance to every cell in our body as altering it can lead to cellular dysfunction or death, and to diseases such as cancer.

Repairing DNA Breaks

The controlled repair of DNA breaks is also critical for a process called somatic recombination, which occurs during the development of white blood cells known as lymphocytes. Somatic recombination enables the rearrangement of immunoglobulin genes and the subsequent generation of a diverse repertoire of antibodies that are required to mount an efficient immune response and eliminate pathogens from the body. Failure to efficiently repair these DNA breaks leads to immunodeficiency and can also cause the development of lymphoma. Joanna Loizou's group at CeMM is interested in understanding how key DNA repair proteins, such as the protein kinase ATM, fix programmed breaks in B and T lymphocytes.

The gene encoding for the ATM protein is mutated in a hereditary disease called Ataxia Telangiectasia, which is characterized by a deficient immune response and predisposition to cancer.

Indeed, ATM is a so-called tumor suppressor as its absence can lead to cancer. It is required to repair DNA breaks generated in immunoglobulin genes, but how ATM itself is regulated to carry out this function is unknown. Members of the Loizou lab are working on this by investigating the contribution of ATMs cofactors ATMIN (for ATM INteractor), and NBS (mutated in Nijmegen Breakage Syndrome) in B and T cell development. They have discovered that there is a partial requirement for ATMIN and NBS in the activation of ATM in lymphocytes. These roles in ATM activation are different during somatic recombination and immune system development, and unexpectedly ATMIN and NBS can also function independently of ATM. The group is now working on better characterizing what these ATM-dependent and -independent functions are.

Maintaining the integrity of DNA is of utmost importance to every cell in our body.

Protecting the Genome

Most cancer cells proliferate much faster than normal cells. When cells are exposed to such a growth pressure, known as replicative stress, specific regions within the genome known as 'fragile sites' can break. This leads to genomic instability and can ultimately promote the progression of cancer. To prevent this, DNA repair proteins coat fragile sites to shield them against erosion. As fragile sites are frequently mutated in cancer, the Loizou group has also been working on identifying the molecules and pathways that maintain their integrity under replicative stress.

By taking an unbiased, genome-wide approach, in collaboration with the Chemical Screening and PLACEBO lab at CeMM, headed by Stefan Kubicek, they have identified several proteins that are required for cells to respond to replicative stress and repair the associated DNA damage. ATMIN, the cofactor for ATM, is one of these proteins. In the absence of ATMIN, recruitment of DNA repair proteins as well as DNA damage signaling is affected. The outcome is that fragile sites are no longer protected, which may lead to increased DNA breaks within these regions of the genome. The group is now looking into which other proteins are involved in these genome maintenance functions, in collaboration with the Mass Spectrometry group at CeMM, and whether they may be useful therapeutic targets for treating cancer.

Reversing Disease

IL-13 administration could actually reverse pathological changes in the vascular wall after atherosclerotic lesions had developed.

Christoph Binder's group at CeMM works primarily on atherosclerosis, which is a disease of blood vessels that causes heart attack and stroke. A major risk factor for atherosclerosis is high blood cholesterol, which triggers the formation of inflammatory deposits (atherosclerotic lesions) in the artery wall. However, many patients who receive medication that effectively lowers cholesterol still develop progressive disease due to ongoing inflammation. Scientists in the Binder group have been studying the role of interleukin (IL)-13, which is a cytokine secreted by T helper type 2 cells, in murine atherosclerosis.

They found that IL-13 administration could actually reverse pathological changes in the vascular wall after atherosclerotic lesions had developed in hypercholesterolemic mice. This was caused by an increase in the collagen content and a decrease in the macrophage content of the preexisting atherosclerotic lesions. In contrast, IL-13 deficiency accelerated atherosclerosis development, which was found to be independent of cholesterol. This discovery, that IL-13 is a protective factor in atherosclerosis, was recently published in *EMBO Molecular Medicine* (Cardilo-Reis et al., 2012).

Recently, B cells of the immune system have also been identified as important mediators of atherosclerosis, even though they are not themselves found in atherosclerotic lesions. B cell depletion strategies are an emerging therapeutic approach for the treatment of several autoimmune diseases, such as systemic lupus erythematosus (SLE). Many of these diseases are also associated with increased cardiovascular risk, therefore these novel drugs represent potentially attractive tools to also treat atherosclerosis. Scientists in the Binder group have been dissecting the roles of B cells in the disease. Interestingly, the two major B cell subsets seem to have opposite effects. While B1 cells mediate protection via secretion of natural IgM antibodies, conventional B2 cells seem to promote atherogenesis. Thus, B cell depletion strategies should be developed to target one B cell subset selectively.

To further this line of research, in collaboration with Ziad Mallat from the University of Cambridge, the Binder group studied the role of the BAFF receptor (BAFF-R) in B cell regulation of atherosclerosis. They found that BAFF-R deficiency caused a selective depletion of B2 cells, and a reduction in atherosclerotic lesions. This work was published in *Arteriosclerosis, Thrombosis, and Vascular Biology* (Sage et al., 2012), and could potentially be exploited to develop a much needed therapeutic approach for atherosclerosis.

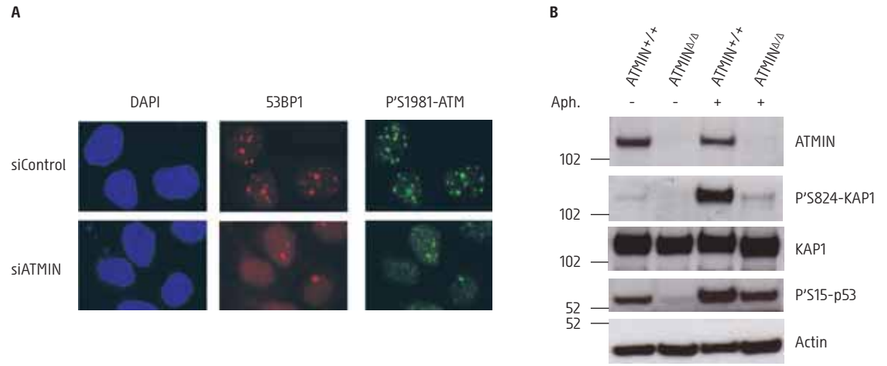


Fig. 6 ATMIN is required for signaling replicative stress. (A) Loss of ATMIN (siATMIN) reduces 53BP1 recruitment (red, middle panel) and ATM activation (green, right panel) within the nucleus of cells (DAPI, left panel) at sites of replicative stress induced DNA damage in HeLa cells. (B) Cells that lack ATMIN ($ATMIN^{\Delta/\Delta}$) fail to signal replicative stress appropriately, as marked by decreased phosphorylation of the proteins KAP1 (P'S824-KAP1) and p53 (P'S15-p53).

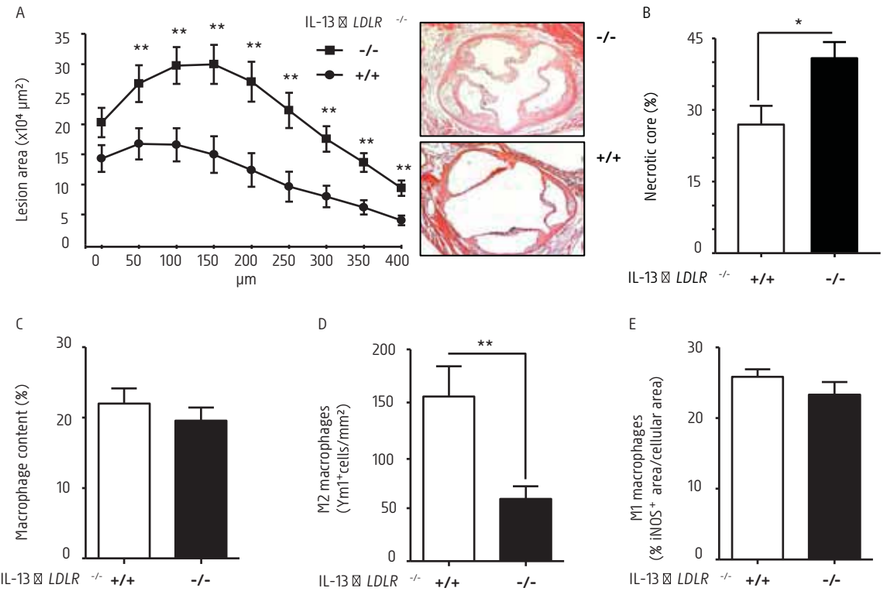


Fig. 7 IL-13 deficiency accelerates atherosclerotic lesion formation and alters macrophage activation in atherosclerotic plaques. *LDLR-/-* (LDL receptor knockout) mice were transplanted with bone marrow from either wild type (*IL-13+/+*) or *IL-13-/-* (knockout) mice and fed a high cholesterol diet to induce atherosclerotic lesions. IL-13-/- bone marrow increased atherosclerotic lesion size (A), and number with necrotic cores (B). The relative content of total macrophages (C) and M1 type macrophages (E) in lesions was equivalent, while *IL-13-/-* bone marrow treated mice had significantly less M2 type macrophages in lesions (D).

+ Precision Therapies
+ Targeting Chromatin
+ Precision in Technology
+ DNA Sequencing
+ Pinpointing the Cause of Disease

Accuracy

Accuracy

Sir Ernst Gombrich was a renowned Austrian-British art historian who rethought fundamental art historical questions and drew connections to other disciplines, from experimental psychology to humanistic research. In the book *The Sense of Order: A Study in the Psychology of Decorative Art*, he tried to empirically explain pattern and ornament on the basis of the Gestalt theory.

The basic motif of Esther Stocker's work is the grid. With the geometricized black and white of the North Wall, she references the traditions of Constructivist art and sets them in motion through shifts in perspective and overlay.

With her variations on reversible images, inversions and optical illusions, the artist negotiates not only the relativity of perception in general, but also casts a critical eye on rigid systems of order and the different levels of truth.

Many human diseases are highly complex. Successfully treating them requires both detailed knowledge of the underlying molecular processes, and drugs to modulate these processes in a rational and precise manner. The concept of personalized medicine is based on precision, or accuracy, and involves tailoring a treatment to the individual

Precision Therapies

HIV infection and cancer pose similar challenges for designing successful therapies. They are both driven by evolutionary processes and as such can evolve resistance to an initially successful drug. HIV therapy has become the poster child of personalized medicine. Although it is currently not possible to cure the disease, the use of antiviral combination therapies has had a tremendous clinical impact, converting HIV infection from a fatal disease into a chronic condition with relatively low mortality. Christoph Bock and his team want to build on these recent successes in personalized HIV therapy, and explore whether similar approaches may also contribute to improved treatment options for cancer. The rationale for their strategy was recently outlined in *Nature Reviews Cancer* (Bock and Lengauer, 2012).

Given the molecular complexity and patient-specific nature of drug resistance mechanisms, highly personalized therapies are needed that are selected based on a comprehensive molecular map of the resistance mechanisms in each patient. Towards this goal, the Bock group has been sequencing leukemia samples from patients that have been treated with chemotherapy in order to identify genetic and epigenetic mechanisms of resistance. They have also been establishing and validating cellular assays to measure resistance to epigenetic drugs *in vitro*, as well as developing bioinformatic algorithms that can predict personalized drug combinations for a given, genetically and epigenetically characterized, leukemia patient. By personalizing therapy in this way, they aim to help develop safer and more effective treatments for treating cancer patients.

Personalizing therapy can help develop safer and more effective treatments for treating cancer patients.

disease. This can also include, for example, using drug combinations to bypass the predicted development of resistance in individual patients. Christoph Bock's group at CeMM is working on developing patient-specific combination therapies for tackling drug resistance in cancer.

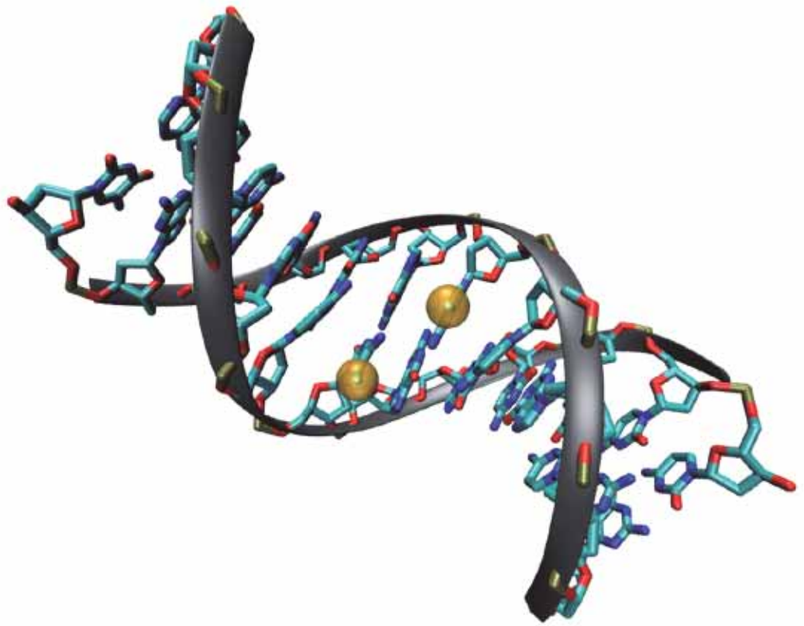


Fig. 8 Epigenetic alterations in DNA methylation are predictive of chemotherapy resistance in cancer.

Targeting Chromatin

The development of highly selective chromatin-targeting drugs may also be valuable for treating cancer.

A drug that can precisely inhibit a given target is another important aspect of personalized medicine. However, most small molecule drugs act on several different targets leading to severe side effects, which is particularly problematic when combinations of drugs are being considered. Stefan Kubicek's group at CeMM is identifying and also developing small molecules that can precisely modulate chromatin. Chromatin is composed of DNA and associated proteins such as histones, which regulate the structure and accessibility of the DNA and thereby control which genes are active in each cell type under specific conditions. The development of highly selective chromatin-targeting drugs may also be valuable for treating cancer by reverting the associated aberrant gene expression changes.

Epigenetics is the study of heritable changes in gene expression in the absence of alterations to the DNA sequence. One level of epigenetic control is exerted by histone modifications, which are small chemical groups attached to histone proteins. A wide variety of over 20 different histone modifications exist, and they are generated, recognized and removed by around 400 proteins. Small molecules are the perfect tools to study which histone modifications are in fact heritable and therefore truly "epigenetic". The challenge however is to generate highly potent and selective small molecules to target them. Indeed, the first molecules targeting histone-modifying enzymes are only now emerging. Although inhibitors of histone deacetylases and DNA methyltransferases are now approved drugs, for the vast majority of the 400 chromatin modifying proteins no targeting compounds exist. The Kubicek group has been developing inhibitors for the histone demethylating enzyme JMJD2C, which has been linked with the development of cancer.

Even for existing small molecules, it is unclear how specific their cellular effect is. This is because histones are found on all DNA sequences, and so the currently approved drugs change the activity of thousands of genes. Scientists in the Kubicek lab have been addressing whether chromatin-targeting compounds can be specific enough to turn on or off only a small set of genes. By studying the genome-wide transcriptional effects of 29 chromatin-targeting compounds in two cell types at three time points they discovered that inhibitors of the G9A/GLP methyltransferases only increase the expression of the cholesterol biosynthesis pathway. This finding shows that some chromatin modifications control very specific gene sets and gives hope that small molecules can be developed that enable turning single genes on and off at will, which would be the ultimate in precision targeting.

Precision in Technology

Technological breakthroughs often accompany great advances in knowledge. Two relatively recent technologies that have revolutionized many fields are mass spectrometry and next generation sequencing, which provide precise information about protein mass distributions and about DNA sequences, respectively. Since 2006, next generation sequencing has emerged as one of the fastest advancing technologies in the history of mankind, with an impressive 10,000-fold improvement in throughput and cost. These advances are already transforming biomedical research, and they provide huge opportunities for precise and patient-specific treatment decisions. The Biomedical Sequencing Facility at CeMM (http://biomedical-sequencing.at) was launched in 2012 in an effort to make the latest sequencing technology accessible to Austrian scientists and to foster its transformative role for biomedicine.

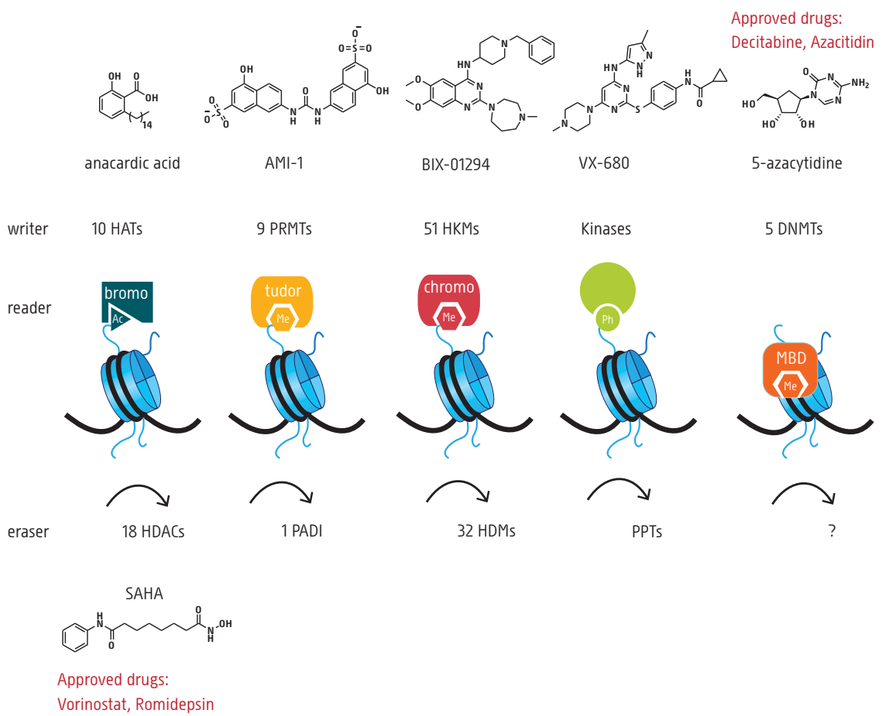


Fig. 9 Chromatin modifying enzymes can be categorized as writers, readers and erasers of posttranslational histone modifications. All of these classes are potentially druggable, yet currently high-quality probes exist only for selected subfamilies. Only for two classes of chromatin modifying enzymes, histone deacetylases and DNA methyltransferases, molecule inhibitors approved for clinical use.

DNA Sequencing

The Biomedical Sequencing Facility (BSF) is a joint initiative of CeMM and the Medical University of Vienna. Coordinated by CeMM Principal Investigator Christoph Bock, the BSF constitutes a broadly collaborative effort with major contributions from scientists at both institutions (including Martin Bilban, Berthold Streubel, Arndt von Haeseler, Martin Posch and Wolfgang Schreiner at the Medical University, as well as Kaan Boztug and Robert Kralovics at CeMM). Close collaboration and synergy also exist with the sequencing group of Andreas Sommer at the Vienna Biocenter and the Campus Service Support Facilities GmbH.

The BSF is equipped with the latest technology, including two Illumina HiSeq 2000 sequencers and cluster computing infrastructure, which provides sufficient throughput for large-scale genome analyses. Extensive expertise and hands-on practical support are available for biomedical sequencing protocols, including personal genome sequencing as the gold standard of genome-based diagnostics, exome sequencing for cost-efficient discovery and validation of disease genes, RNA-sequencing as a powerful technology for gene expression profiling and replacement of microarrays, as well as several epigenome mapping protocols that provide unprecedented insights into disease-associated alterations that occur outside of the genomic DNA sequence.

Importantly, the BSF also constitutes a technology hub and disseminates sequencing-related know-how widely throughout Austria's biomedical research community. To that end, the BSF organizes an annual symposium on next generation sequencing (together with Andreas Sommer) and contributes conceptual advice, hands-on help and formal support letters to projects and grant applications of scientists at CeMM, the Medical University of Vienna and beyond.

Pinpointing the Cause of Disease

Scientists in the Boztug group at CeMM are combining next generation sequencing and other state-of-the-art genomics approaches with a variety of functional approaches to pinpoint the molecular mechanisms underlying immune dysregulation and autoimmunity. Autoimmunity is caused by the failure of the immune system to properly distinguish host (self) from non-self, resulting in an immune attack on healthy cells in the body. Many human diseases are characterized by a multitude of autoimmune phenomena, however the underlying molecular mechanisms are often poorly understood.

The Boztug group is studying patients suffering from inherited defects of their immune systems, so-termed "primary immunodeficiency disorders". Many of these patients show features of (often severe) autoimmunity and immune dysregulation. This provides a unique opportunity to dissect some of the molecular mechanisms *in natura* rather than working with animal models that have less relevance for the human disease.

In a recent collaboration with Elisabeth Förster-Waldl, Medical University of Vienna, the St. Anna Kinderspital and Children's Cancer Research Institute, and the Klinik Wels-Grieskirchen, they were able to identify a novel inherited immunodeficiency disorder associated with severe systemic autoimmunity. The team has used Affymetrix-based genotyping of single nucleotides (SNPs) and exome sequencing and identified mutations in the gene encoding protein kinase C (PKC) delta as the underlying genetic cause of a hitherto unrecognized immunodeficiency disorder with severe Lupus erythematodes-like autoimmune phenomena. They could show that deficiency of PKC delta leads to hyperactive signaling via interleukin-6, which may be linked to the maintenance of autoreactive B lymphocytes. Taken together, their study identified a novel primary immunodeficiency syndrome associating an immunoglobulin class switch defect and severe systemic autoimmunity. Future studies will address whether the aberrant signaling cascades identified may represent attractive therapeutic targets in PKC delta-deficient patients or even other patients suffering from disorders of autoimmunity or immune dysregulation.

Many human diseases are characterized by a multitude of autoimmune phenomena.

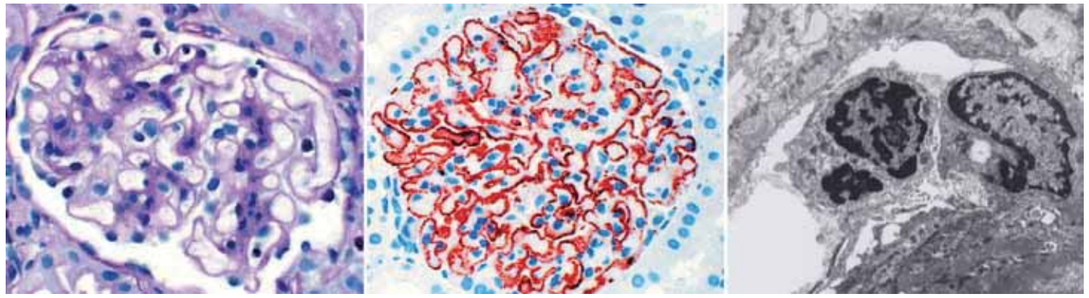


Fig. 10 Glomerulonephritis as one of the characteristic autoimmune features in a novel primary immunodeficiency caused by deficiency of Protein Kinase C delta (PRKCD). The pictures show segmental mesangial sclerosis and granular IgG deposits along the periphery of the capillary loops (images courtesy of Renate Kain, Dept of Pathology, Medical University of Vienna).

Association

+ Mechanisms of Drug Action
+ Pathogen-Host Interactions
+ Connected Proteins
+ Lethal Interactions for Cancer

Association

The backrests of the 14 armchairs assembled around the table feature artists' works formally rooted in the tradition of emblems, signs and symbols. Eva Schlegel and Thomas Feuerstein thematically address the subject of scientific research, while Alois Mosbacher and Martin Walde offer a sly wink, a watchdog, and puns.

Thomas Feuerstein in particular couples art and science in his work. His sculptures are equal parts experimental set-ups and dynamic transformation machines. Yet for Feuerstein, this sort of dialogue demands "that one discipline does not merely serve as a helpmate to the other, but that there are also moments of surprise." That it is never quite clear who is ultimately benefiting from whom: art from science, or rather science from art.

Scientists often talk about "mechanism of action", and deciphering it is an important goal in scientific research. It means gaining an understanding of how a biological process such as a viral infection or a drug treatment works in molecular detail.

Mechanisms involve complex associations between different factors such as genetic mutations, molecules and cells. Uncovering the biological mechanism of action is often challenging, but it can help lead to important new discoveries.

Mechanisms of Drug Action

The Superti-Furga laboratory at CeMM has been working on understanding the inner workings of leukemic cells. In particular, they have been investigating new strategies to inhibit an abnormal fusion protein known as BCR-ABL, which causes chronic myelogenous leukemia (CML). This protein contains a tyrosine kinase catalytic domain that is critical for its function. Specific anti-cancer drugs known as kinase inhibitors can bind to this catalytic domain and block its activity, and they have been used successfully to treat CML patients. However, leukemic cells can become resistant to the drugs through different mechanisms, including mutations in the drug's binding site.

The most frequent and one of the most harmful of such resistance mutations changes the amino acid threonine found at the so-called "gate-keeper" position 315 of the BCR-ABL protein to an isoleucine (known as the T315I mutation). This mutation blocks the binding of most of the tyrosine kinase inhibitor drugs. Scientists in the Superti-Furga group have investigated combinations of tyrosine kinase inhibitors that synergize only in CML cells harboring this specific BCR-ABL T315I mutation. Danusertib and bosutinib were the two drugs displaying the most significant and specific synergy.

To uncover the mechanism of action, the team applied a systems-level approach comprising phosphoproteomics, together with Forest White at MIT, transcriptomics, and chemical proteomics with the Bennett team at CeMM. Data integration, in collaboration with Jacques Colinge and his team, revealed that both compounds targeted the MAPK signal transduction pathway down-stream of BCR-ABL resulting in impaired activity of the protein c-Myc. Pharmacological validation revealed that the relative contribution of danusertib and bosutinib could be mimicked individually by MAPK inhibitors and collectively by downregulation of c-Myc. Thus integration of genome- and proteome-wide technologies enabled them to elucidate the mechanism by which a novel drug synergy targets BCR-ABL T315I CML cells. The work highlights the importance of so-called "systems pharmacology", and was published in *Nature Chemical Biology* (Winter et al., 2012). The approach itself can be applied to determine the molecular mechanism of action of single drugs, most of which are completely unknown.

Uncovering the biological mechanism of action can lead to important new discoveries.

Pathogen-Host Interactions

We lack a comprehensive understanding of the underlying molecular pathogenesis of persistent viral infection.

More than half a billion people suffer from persistent viral infections such as hepatitis B, hepatitis C or HIV. These diseases are associated with severe clinical symptoms and can be life threatening. However, we lack a comprehensive understanding of the underlying molecular pathogenesis, and as a consequence there are relatively few treatment options available. Andreas Bergthaler and his group at CeMM are studying the molecular mechanisms underlying persistent viral infections with the hope that the knowledge gained will lead to the development of urgently needed new treatments.

To address the vast complexity of pathogen-host interactions that are relevant for the human disease, the Bergthaler group uses an animal model based on a small mouse virus named lymphocytic choriomeningitis virus (LCMV). This virus has an impressive track record having contributed to fundamental scientific discoveries relevant for human health since the early 20th century. The group uses an integrative approach involving genetic perturbations in cell culture and animal models combined with molecular virology, immunology, pathology and systems biology, in order to identify and understand the molecular players and networks that shape the disease.

In particular, scientists in the Bergthaler laboratory have been investigating the mechanisms that the virus uses to evade the host's immune system and establish persistence. To bridge the gap between the experimental animal models and the patients they have initiated collaborations with clinical groups including Peter Ferenci and Michael Trauner, both at the Medical University of Vienna. Through their integrative and disease-centric approach they expect to gain an in-depth understanding of the general mechanisms underlying infectious pathogenesis.

Connected Proteins

The physical association between molecules can be a valuable way of identifying mechanism of action. For example, protein complexes form, dissociate and re-form in order to perform specific cellular functions such as transcribing a gene or degrading old molecules. However, these physical associations can be difficult to detect if they are particularly transient, or occur only under specific conditions. In addition, it can be challenging to identify all the proteins in a multi-component protein complex.

In collaboration with Klaus Kratochwill at the Medical University of Vienna and Matthias Gstaiger at the ETH in Switzerland, Keiryn Bennett's group at CeMM has been developing a method that can overcome this challenge. In their two-pronged protocol, non-covalent protein complexes are first isolated by affinity purification for subsequent identification of the components by liquid chromatography high-resolution mass spectrometry (LCMS). In the second prong of the approach, the affinity-purification strategy is layered with chemical crosslinking to "freeze" a series of concurrently formed, heterogeneous protein sub-complex species that are visualised by gel electrophoresis. This helps to reveal the dynamics of the individual components of protein complexes. The protocol is simple, robust and can be readily extended to the investigation of a range of protein complexes.

Lethal Interactions for Cancer

Synthetic lethality is an important concept that can be used to determine the mechanism underlying a specific biological process, and can also help find new approaches for treating cancer. It describes the association between two factors such as a genetic mutation and a small compound that individually causes no harm but together is lethal to a cell. Chromatin has recently emerged as an important drug target in cancer, and so-called epigenetic characteristics, which refer to heritable alterations in gene expression that do not alter the DNA sequence, are one of Hanahan and Weinberg's now infamous "Hallmarks of Cancer". Indeed, many chromatin proteins are misregulated in cancer or involved in synthetic lethal interactions with oncogenic signaling pathways. Scientists in the Kubicek group at CeMM are systematically identifying chromatin proteins involved in synthetic lethal interactions with breast cancer oncogenes, which could become the drug targets of the future.

Already today, four chromatin-targeting small molecules are approved for the treatment of cancer. The histone deacetylase inhibitors SAHA and Romidepsin are used in cutaneous T-cell lymphoma, and the DNA methyltransferase inhibitors 5-aza-cytidine and 5-aza-2'-deoxycytidine in myelodysplastic syndrome. However, for the majority of the 400 chromatin-modifying proteins no small molecules are available and it is unclear how to prioritize them for drug development. To systematically study the effects of chromatin factors on the proliferation of cancer cells, the Kubicek group has assembled a lentiviral shRNA knock-down library, in collaboration with the Broad Institute, to reduce the levels of each of the 400 chromatin proteins. This approach can identify synthetic lethal interactions between cancer-causing mutations and chromatin proteins, and also provide insight into their mechanisms of action. Their first results have identified cytostatic effects in cells with certain oncogenes specifically when the histone sumoylation pathway is lost. Further validation experiments are ongoing for other genes and compounds.

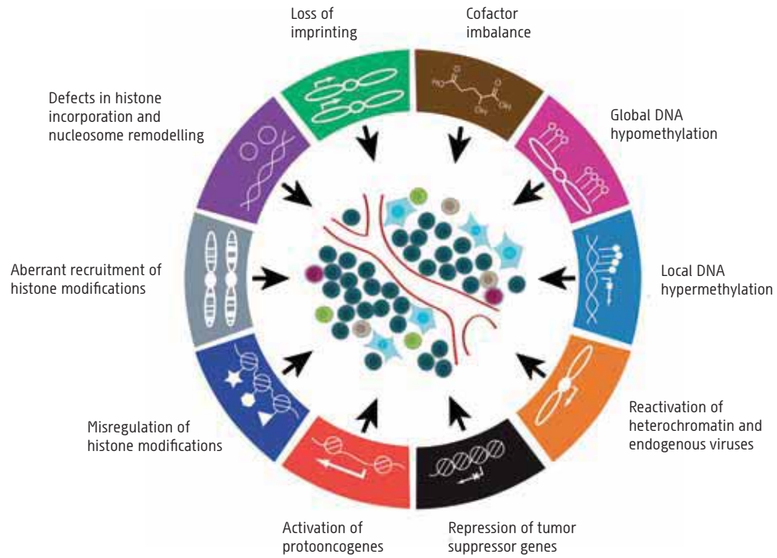


Fig. 11 Epigenetic hallmarks of cancer: Globally, DNA methylation is often lost in cancer (DNA hypomethylation), whereas it is aberrantly gained at promoters of tumor suppressor genes (DNA hypermethylation). Misregulation of DNA and histone modifications can result in the epigenetic activation of proto-oncogenes, repression of tumor suppressor genes, and reactivation of heterochromatin and endogenous viruses. Often, genetic mutations in chromatin modifiers are responsible for their aberrant activity in cancer, but also imbalance of their cofactors can be causal. Furthermore, loss of imprinting, and defects in histone incorporation and nucleosome remodeling have been observed in cancer. Inspired by D. Hanahan and R. Weinberg.

Dynamics

+ Varying Epigenetics in Cancer
+ Evolution of Leukemia
+ The Diversity of Cancer
+ RNA Dynamics in Cancer
+ The Changing Course of Infectious Disease
+ Controlling the Immune Response

Dynamics

The Brain Lounge is the place where the classic academic approach to work diffuses into another mode of knowledge production. Here a new genre is placed in the context of contemporary art: transdisciplinary conferences that largely dispense with scientific hierarchy and are responsive to social demands. The participants gather around a symbolic object to debate and exchange ideas: the round table. At the center of the rotating meeting element rests Peter Kogler's computer-generated image module Brain. The organ around which everything orbits, in the arts as in science.

Many of us get our first glimpses of biology in textbooks. Subsequent exposure comes from newspapers and scientific reports like this one. Scientists report their results in printed publications, and even the coveted "biological model", which combines the results from a series of experiments focused around a specific topic such as a pathogen infection, is mostly presented as a two-dimensional diagram.

All of these mediums fail to accurately portray arguably one of the most important characteristics of biology - its highly dynamic nature. Scientists at CeMM are studying several topics that illustrate this dynamism. For example, Christoph Bock's group is studying how epigenetic marks change during the development of leukemia.

Varying Epigenetics in Cancer

The genetic code of DNA provides a universal building plan for the cell's molecular machinery. But a second code is needed to organize 100 billion cells with identical genomes into 200 specialized cell types to make a healthy human being. This second so-called "epigenetic" code is altered in essentially every cancer patient. The changes include altered DNA methylation patterns and shifts in the genome-wide distribution of histone modifications and chromatin-associated proteins. The Medical Epigenomics program at CeMM is studying the dynamics of epigenome changes in patients that have been diagnosed with leukemia and in their response to successful and failed chemotherapy.

The emerging model of cancer as a disease that is also epigenetic in nature creates an exciting opportunity for new therapies. Rather than having to kill every single cancer cell through aggressive chemotherapy, it is becoming increasingly feasible to erase cancer-associated epigenetic aberrations through the use of epigenome-altering drugs.

However, before epigenetic therapies can be used with confidence for the treatment of a broad range of cancers, a more detailed understanding of the epigenome's functional role in cancer is required. To that end, Christoph Bock's laboratory is collaborating with Robert Kralovics's group at CeMM, and with Renate Panzer-Grümayer at the St. Anna Children's Cancer Research Institute to perform comprehensive epigenome characterization in leukemia patients that have been followed over time.

Their approach combines high-throughput assays, including genome-wide bisulfite sequencing for analyzing DNA methylation, with large-scale data integration and bioinformatic analysis. By applying these methods to the leukemia cohorts that have been analyzed over time, it will be feasible to pinpoint series of epigenetic events that contribute to disease progression. This work is highly complementary to the work of the International Human Epigenome Consortium and the European BLUEPRINT project, which CeMM joined as a project partner and work package leader in 2012.

The emerging model of cancer as a disease that is also epigenetic in nature creates an exciting opportunity for new therapies.

Evolution of Leukemia

Clearly, cancer is a highly dynamic disease. It originates from a single mutant cell that can outgrow other cells in the same tissue and evolve into a tumor. The "initiating" mutation in a single blood cell during the earliest phase of leukemia can have various forms such as a translocated chromosome, a chromosome with a missing or multiplied piece, or a point mutation in a single gene. Once the leukemic cell is formed, it sets out to multiply, and its progeny (the tumor mass) starts to compete for space and resources with healthy cells. The dynamic process of genetic evolution of leukemic cells is one of the main research topics in the laboratory of Robert Kralovics at CeMM.

During the division of each cancer cell, mutations accumulate and are passed to the next generation of cancer cells. Although the vast majority of these newly acquired genomic mutations do not provide any benefit to the cancer clone, some can be useful in the environment in which the cancer resides, thereby providing a selective advantage. Indeed, selection is the main driving force that shapes the cancer genome in a given environment. Different tissues have different selective forces. In leukemia, the leukemic clone of each patient takes on a unique evolutionary path. As a result, a mosaic of chromosomal changes accompanies the evolutionary trajectory of each leukemic clone.

Scientists in Robert Kralovics's group study the genomic architecture of leukemic cells in hundreds of patients diagnosed with different forms of leukemia. In each patient, the leukemic genome is evaluated using either DNA microchips that can read 1.8 million data points per genome, or whole genome (exome) sequencing. This enables them to "paint a genome mosaic" for each leukemic patient. When these analyses are done for hundreds of patients, it is possible to compare them and find similarities and differences. Using this approach they have discovered a number of frequent chromosomal defects that implicated a group of transcription factor genes in cancer progression.

The Diversity of Cancer

Each patient's leukemic cells evolve in a unique way not seen in any other patient.

Leukemia can originate de novo (i.e. without a previous history of a blood disease) or emerge after a chronic blood disorder such as myeloproliferative or myelodysplastic disorders (so called "secondary" leukemia). To study the evolution of leukemia, secondary leukemias are better disease models as they offer an insight into the genetic mechanisms preceding the leukemic transformation. In a recent study, the Kralovics group performed comparisons of the genetic patterns found in "de novo" and "secondary" leukemias. Using high-resolution genomic analysis, they found a huge number of genetic lesions, and only a handful of these were seen in specific diagnostic groups. This suggested that each patient's leukemic cells evolved in a unique way with a combination of genetic defects not seen in any other patient. These results were published in the *American Journal of Hematology* (Milosevic et al., 2012). If this pattern is confirmed, therapeutic strategies need to be found to tackle such genetic diversity. This challenge is also being addressed by some of CeMM's drug discovery projects.

RNA Dynamics in Cancer

The human genome contains vast numbers of so called long non-coding (lnc) RNAs that are predicted to control the activity of protein-coding genes during embryonic development and cell differentiation. LncRNAs are now also predicted to be involved in the abnormal activity or silencing of protein-coding genes in cancer. The Barlow group at CeMM has recently defined a novel class of lncRNAs known as macro lncRNAs whose lncRNA product appears to be dispensable for their function. They describe this class in a recent review published in the journal *RNA Biology* (Guenzl and Barlow, 2012). The Barlow group has two main research goals directed towards unraveling the function of lncRNAs and macro lncRNAs in human disease. First, they are investigating the molecular mechanism by which lncRNAs silence imprinted genes using a mouse embryonic stem (ES) that they developed in 2009. Second, they are using high-throughput RNA sequencing (one of CeMM's core technologies) in combination with a novel bioinformatics pipeline to identify lncRNAs.

The development of an RNA-Seq pipeline that can efficiently identify macro lncRNAs initially proved an experimental and bioinformatic challenge. Now the pipeline is operational and is being used to identify macro lncRNAs expressed in inbred mouse tissues where mouse mutants that lack a specific epigenetic gene can be used to determine how lncRNAs act to silence other genes. It is also being used to identify the dynamic expression of macro lncRNAs in normal human white bloods cells and in hematological malignancies. They aim to establish a database of robustly expressed lncRNAs (i.e. expressed in all volunteers at all time points) and non-robustly expressed lncRNAs (i.e. expression varies between different volunteers and at different time points), which can then be used to analyze changes that arise in hematological malignancies such as myeloproliferative neoplasms and leukemia. This project is being performed together with the CeMM groups of Robert Kralovics, an expert in hematological malignancies, Christoph Bock, an expert in high-throughput sequencing bioinformatics and Jacques Colinge, an expert in bioinformatic analysis.

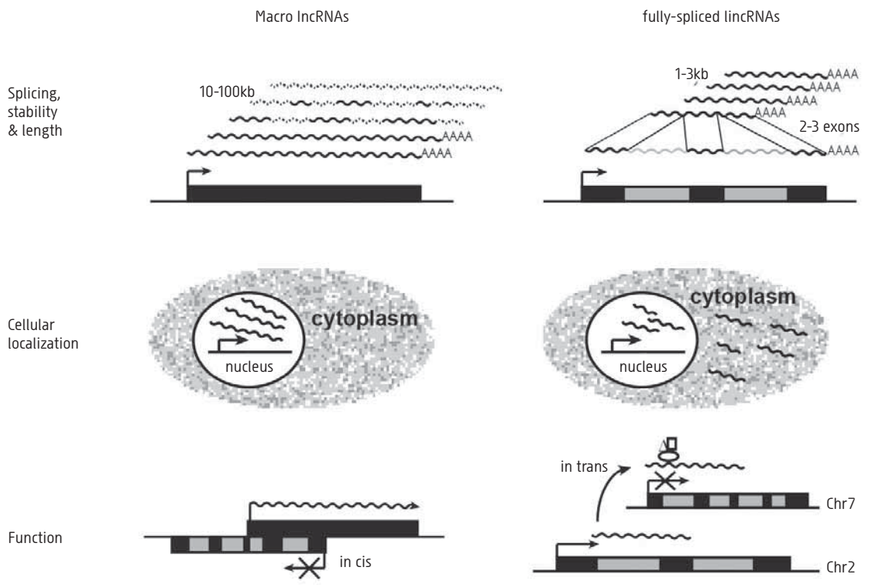


Fig. 12 Macro lncRNAs (left panel) are inefficiently spliced into long non-coding RNAs. They are ultra-long, lack sequence conservation and have a short half-life. Only spliced macro lncRNAs are exported to the cytoplasm. Macro lncRNAs repress gene transcription in two ways: through their lncRNA product or by transcriptional interference. LincRNAs (large intergenic or lincRNAs: right panel) are the prototype lncRNA and are defined only by a spliced product larger than 200nt. LncRNAs are considered to act in trans e.g., by binding and recruiting chromatin-modifying enzymes to regulate gene expression, they are fully-spliced, relatively stable and likely to be exported to the cytoplasm. Adapted from *RNA Biol.* (Guenzl and Barlow, 2012).

The Changing Course of Infectious Disease

In another example of dynamics in biology, Giulio Superti-Furga's group at CeMM is studying the dynamic course of the innate immune response to pathogen infection. During this process, one can roughly distinguish between a first alarm-call leading to the secretion of type I interferons and pro-inflammatory cytokines, and a second response and execution phase during which the pathogen is neutralized, presented to cells of the adaptive immune system, and the alarm is switched off. Scientists in the Superti-Furga laboratory, along with the laboratories of Keiryn Bennett and Jacques Colinge, have been launching a three-pronged affinity proteomics approach to reveal a comprehensive picture of these processes in molecular detail. This approach is largely covered by the Advanced ERC grant obtained by Giulio Superti-Furga in 2009.

The first approach utilizes proteins already known to be associated with innate immunity pathways. The second uses virus-associated molecular patterns to identify the host proteins that interact with them, and therefore are likely to be involved in either detecting them or destroying them. The third approach takes those proteins already implicated in immune-modulatory functions of the viruses to purify relevant host protein complexes. Using these approaches coupled to mass spectrometry, followed by bioinformatics and functional experiments, the CeMM-internal consortium has mapped in a step-wise fashion the cellular proteins that mediate the innate immune response to viral infection.

Controlling the Immune Response

Arguably the most important achievement of the Superti-Furga team in 2012 was the discovery of the strategies that viruses use to control the cellular immune response. Viruses infect humans, plants and other organisms causing a variety of acute and chronic diseases. In response, the host is equipped with an innate immune system that detects the invading pathogen by sensing so-called Pathogen Associated Molecular Patterns (PAMPs) that can specifically recognize foreign nucleic acids and proteins. Sensing of these danger signals by proteins such as the family of Toll-like receptors (TLRs) triggers a signaling cascade leading to the production of type-I interferons.

Viruses have evolved mechanisms to counteract the host immune response by modifying immune cell signaling. To systematically study the impact of these viral innate immune modulators, the team selected 70 of them from 30 different viruses designed to represent the many different types of viruses in existence. Using these proteins, they designed a molecular "hook" known as a tandem affinity tag to fish for interacting proteins in the cell, which could then be identified by mass spectrometry in the Bennett laboratory.

Their work resulted in the identification of some 600 different host proteins. Some of these were already known to be involved in the immune response to viral infections, validating their approach. Subsequent network analyses revealed general and specific mechanisms at work. In particular, they discovered that viral proteins preferentially target cellular factors that are highly connected to other proteins, and are involved in multiple signaling pathways. This appears to be a general strategy for controlling the host immune response. Using new bioinformatics methods they also showed that DNA viruses perturb processes associated with DNA biology such as "cell cycle and proliferation" and "chromosome biology" and RNA viruses perturb processes such as "RNA metabolism" and "RNA/Protein transport". The large dataset produced by this study, which was published in *Nature* (Pichlmair et al., 2012), should help guide the development of both specific and broad acting antiviral therapies.

This large dataset will help guide the development of both specific and broad acting antiviral therapies.

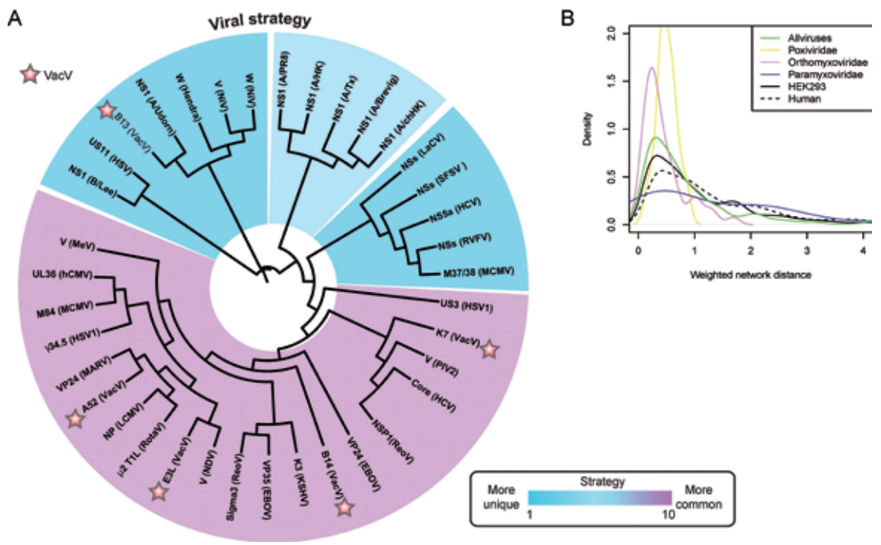
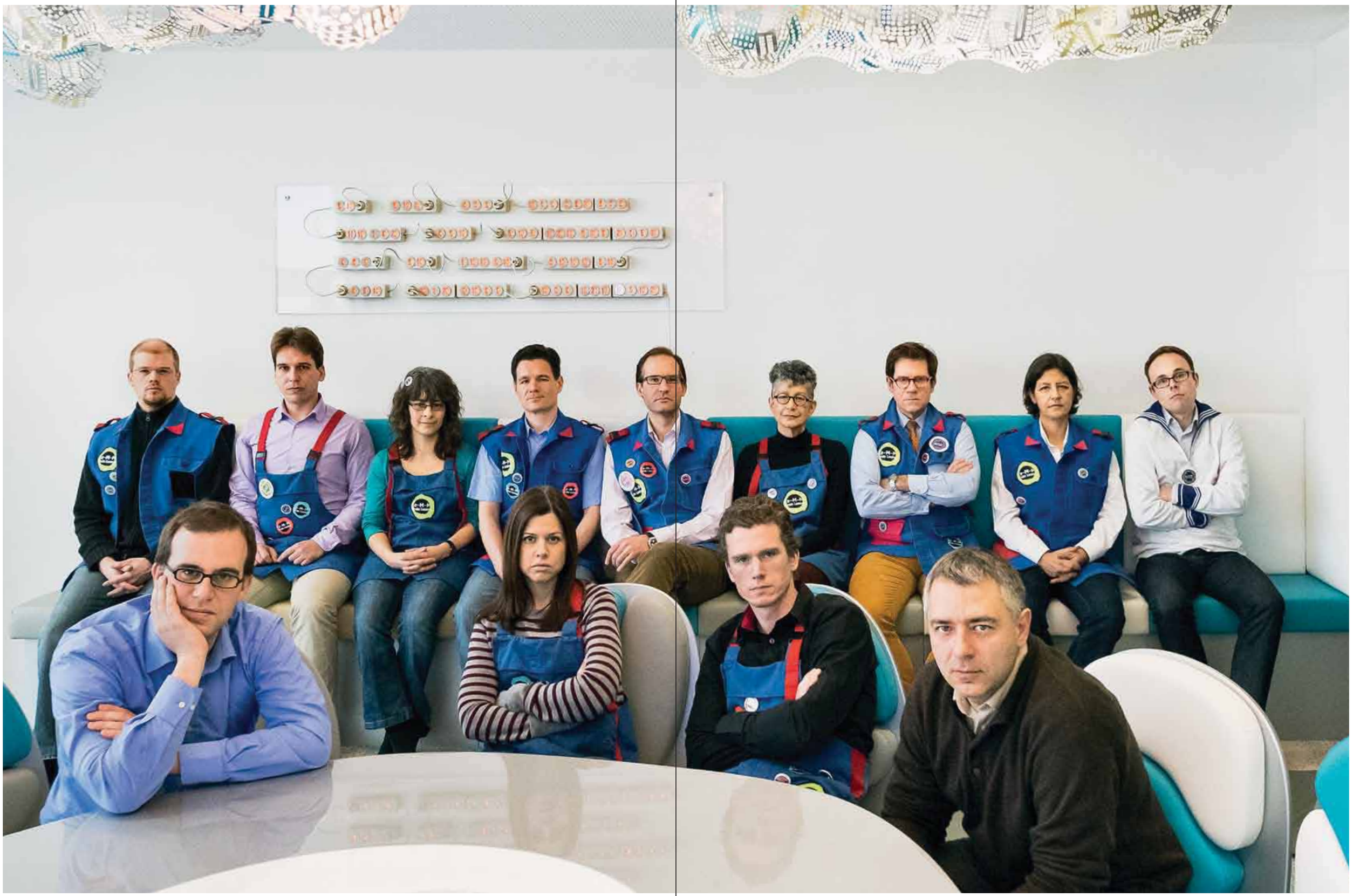


Fig. 13 (A) Viral proteins classified according to how they target the global network of human proteins and their pathways. In this dendrogram, the proteins from the same virus family tend to have closer distances (B). In part (A), we note that the 5 vaccinia virus (VacV) proteins indicated by stars are far from each other, thus indicating non redundant functions, which is a manifestation of the optimal use of a small viral genome. Adapted from *Nature* (Pichlmair et al., 2012).



Principal Investigators

Denise P. Barlow

Epigenetic Mechanisms in Development and Disease

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+ Joined CeMM in 2003
+ Group of 10 people

Main Research Interests
+ Molecular basis and function of genomic imprinting in mice and humans
+ Identification and characterization of macro long non-coding (lnc) RNAs in the mouse and human genomes
+ The potential of macro lncRNAs as tumor biomarkers in human cancer

Denise Barlow is a British national who joined CeMM in 2003 and is an Honorary Professor at the University of Vienna. Denise initially trained as a State Registered Nurse in the UK and afterwards completed her undergraduate studies at Reading University (UK) and a Ph.D. on the interferon system in early mouse development at Warwick University (UK). Post-doctoral work studying mouse embryonic development followed at ICRF (London, UK) with Dr. Brigid Hogan, and on genome biology at EMBL (Heidelberg, D) with Dr. Hans Lehrach. Denise has also held group leader positions at the IMP (Vienna, A) and the NKI (Amsterdam, NL). On returning to Austria in 2000, Denise was appointed Head of the Dept. of Developmental Genetics at the Austrian Academy IMB Institute (Salzburg, A), and then returned to Vienna in 2003 as a Principal Investigator with CeMM.
One of the Barlow lab's major achievements was the discovery in 1991 of the first imprinted gene in mammals to show parental-specific gene expression. Their subsequent identification that epigenetic silencing of this imprinted gene is induced by expression of an unusual long non-coding (lnc) RNA, has led them to investigate how lncRNAs act throughout the mouse and human genome as regulators of gene expression in development and disease. The lab continues to use the model of genomic imprinting to dissect how lncRNAs epigenetically silence genes, and uses this as a platform together with high throughput sequencing technology to extend these results into human diseases such as cancer.

Relevant/Important Publications

Airn transcriptional overlap, but not its lncRNA product, induces imprinted Igf2r silencing.
Latos PA, Pauler FM, Koerner MV, Şenergin HB, Hudson QJ, Stocsits RR, Allhoff W, Stricker SH, Klement RM, Warczok KE, Aumayr K, Pasierbek P, Barlow DP. *Science.*
2012 Dec 14;338(6113):1469-72.

A downstream CpG island controls transcript initiation and elongation and the methylation state of the imprinted Airn macro ncRNA promoter.
Koerner MV, Pauler FM, Hudson QJ, Santoro F, Sawicka A, Guenzl PM, Stricker SH, Schichl YM, Latos PA, Klement RM, Warczok KE, Wojciechowski J, Seiser C, Kralovics R, Barlow DP.
PLoS Genet. 2012;8(3):e1002540.
a collaboration with the CeMM Kralovics group and MedUni Vienna Seiser group.

Mechanisms of long-range silencing by imprinted macro non-coding RNAs. Pauler FM, Barlow DP, Hudson QJ. *Curr Opin Genet Dev.*
2012 Jun;22(3):283-9. Review.

Keiryn L. Bennett

Mass Spectrometry and Proteomics

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+ Joined CeMM in October 2004
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Main Research Interests
+ Proteomics of innate immunity/ immunology
+ Proteomics of protein-protein interactions including chemical crosslinking; and protein-drug interactions
+ Phospho-, acetyl- and quantitative proteomics
+ Integration of mass spectrometry with biology and bioinformatics

Keiryn Bennett, Ph.D., obtained her Bachelor of Science with First Class Honours from the University of Tasmania; and her Ph.D. in protein mass spectrometry from the University of Wollongong, Australia. KB spent 2½ years as a post-doctoral fellow in the laboratory of one of the fore-fathers of modern-day protein mass spectrometry, Professor Peter Roepstorff, (Odense, Denmark). This was followed by 4 years under the supervision of Matthias Mann at MDS Proteomics (Odense, Denmark). KB is respected worldwide in the field of protein mass spectrometry and proteomics, with more than 16 years of experience including 4 years managing a high-throughput industrial proteomic laboratory. KB joined the laboratory of Giulio Superti-Furga in 2004 and established the mass spectrometry/proteomic research group at CeMM. Since 2009, KB has had an independent group leader position and currently the laboratory consists of a total of 5 people. The mass spectrometry research group is involved in a number of interdisciplinary fields such as understanding the role of Hdac1 and Hdac2 in T-cell differentiation; and investigating infiltrating CD20+ B-cells in the progression of human melanoma. These research areas involve the study of protein-protein interactions; and drug-protein interactions by mass spectrometry and are supplemented by technological advancements in chemical crosslinking, quantitative-, acetyl- and phosphoproteomics.

Relevant/Important Publications:

A method to resolve the composition of heterogeneous affinity-purified protein complexes derived from a common protein by chemical crosslinking, gel electrophoresis and mass spectrometry. Rudashevskya EL, Sacco R, Kratochwill K, Huber ML, Gstaiger M, Superti-Furga G, Bennett KL. *Nat. Protoc.* 2013;8, 75-97

An efficient tandem affinity purification procedure for the characterisation of protein complexes in mammalian cells. Bürckstümmer T, Bennett KL, Preradovic A, Hantschel O, Superti-Furga G, Bauch A. *Nat. Methods.* 2006;3, 1013-1019.

Systematic identification of protein complexes in *Saccharomyces cerevisiae* by mass spectrometry. Ho Y, Gruhler A, Heilbut A, Bader GD, Moore L, Adams S-L, Millar A, Taylor P, Bennett K, Boutilier K, Yang L, Wolting C, Donaldson I, Schandorff S, Shewnarane J, Vo M, Taggart J, Goudreault M, Muskat B, Alfarano C, Dewar D, Lin Z, Michalickova K, Willems AR, Sassi H, Nielsen PA, Rasmussen KJ, Andersen JR, Johansen LE, Hansen LH, Jespersen H, Podtelejnikov A, Nielsen E, Crawford J, Poulsen V, Sørensen BD, Matthiesen J, Hendrickson RC, Gleeson F, Pawson T, Moran MF, Durocher D, Mann M, Hogue CWV, Figeys D, Tyers M. *Nature.* 2002;415, 180-183.

Andreas Bergthaler

Viral Immunobiology

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+ Joined CeMM in July 2011
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Main Research Interests
+ Viral pathogenesis (e.g. virus persistence, immunosuppression, hepatitis)
+ Antiviral immune responses (CD8 T cell, innate immunity, B cells)
+ Mouse infection models
+ Systems biology

Andreas Bergthaler, born 1977, studied veterinary medicine at the University of Veterinary Medicine in Vienna and spent clinical and research stays at the Royal (Dick) School of Veterinary Studies, Edinburgh, the University of Tokyo, the University of Zurich and the Danish Veterinary Institute, Copenhagen. For his graduate studies he joined the Institute of Experimental Immunology at the University / ETH Zurich (Profs. Hans Hengartner and Nobel Laureate Rolf Zinkernagel). After postdoctoral work in Zurich and in the laboratory of Prof. Daniel Pinschewer at the University of Geneva he joined Prof. Alan Aderem's group at the Institute for Systems Biology in Seattle, WA. In 2011 he co-founded a vaccine start-up company. Andreas Bergthaler's research is focused on the molecular mechanisms which govern virus-host interactions. To this end the Bergthaler laboratory studies viral infections in mouse models through an interdisciplinary approach of pathology, molecular biology, virology, immunology and systems biology. The employed experimental models are well-defined and bear great patho-physiological relevance to human disease. This enables his group to dissect novel molecular determinants and interaction networks that impact viral pathogenesis and the antiviral immune system. Eventually, this may pave the way for the development of much-sought clinical treatments against viral diseases in man.

Relevant/Important Publications:

A FOXO3-IRF7 gene regulatory circuit limits inflammatory sequelae of antiviral responses. Litvak V, Ratushny AV, Lampano AE, Schmitz F, Huang AC, Raman A, Rust AG, Bergthaler A, Aitchison JD, Aderem A. *Nature.* 2012 Oct 18;490(7420):421-5. doi: 10.1038/nature11428. Epub 2012 Sep 16.

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Interferons direct Th2 cell reprogramming to generate a stable GATA-3(+)T-bet(+) cell subset with combined Th2 and Th1 cell functions. Hegazy AN, Peine M, Helmstetter C, Panse I, Fröhlich A, Bergthaler A, Flatz L, Pinschewer DD, Radbruch A, Löhning M. *Immunity.* 2010 Jan 29;32(1):116-28. Epub 2010 Jan 14.

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Christoph Binder

Atherosclerosis and Immunity

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+ Joined CeMM in April 2006
+ Group of 9 people

Main Research Interests
+ Role of innate immunity in inflammation and oxidative stress
+ Elucidate the protective capacities of natural IgM antibodies in atherosclerosis
+ Discover ways to modulate natural immunity as therapy for cardio-vascular diseases

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Christoph Binder was born in 1973 in Vienna, Austria. Following his studies of medicine at the Medical Faculty of Vienna University, where he obtained his M.D. degree in 1997, he entered a Ph.D. program at the University of California in San Diego. Working with world-famous atherosclerosis researcher Joseph Witztum, he obtained his Ph.D. 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. C. Binder 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 of the natural IgM T15/E06 (Binder et al., 2003). His research group discovered that certain oxidation-specific epitopes are major targets of natural antibodies (Chou et al., 2009) and of complement factor H (Weismann et al., 2011). He also first identified the atheroprotective roles and mechanisms of the cytokines IL-5 (Binder et al., 2004) and IL-13 (Cardilo-Reis et al., 2012). Christoph Binder has won numerous prestigious fellowships and awards and has authored 60 publications in important journals, including Nature Medicine and Nature.

Relevant/Important Publications

Interleukin-13 protects from atherosclerosis and modulates plaque composition by skewing the macrophage phenotype. Cardilo-Reis L, Gruber S, Schreier SM, Drechsler M, Papac-Milicevic N, Weber C, Wagner O, Stangl H, Soehnlein O, Binder CJ. *EMBO Mol Med.* 2012 Oct;4(10):1072-86

Complement factor H binds malondialdehyde epitopes and protects from oxidative stress. Weismann D, Hartvigsen K, Lauer N, Bennett KL, Scholl HP, Charbel Issa P, Cano M, Brandstätter H, Tsimikas S, Skerka C, Superti-Furga G, Handa JT, Zipfel PF, Witztum JL, Binder CJ. *Nature.* 2011 Oct 5;478(7367):76-81.

Oxidation-specific epitopes are dominant targets of innate natural antibodies in mice and humans. Chou MY, Fogelstrand L, Hartvigsen K, Hansen LF, Woelkers D, Shaw PX, Choi J, Perkmann T, Bäckhed F, Miller YI, Hörkkö S, Corr M, Witztum JL, Binder CJ. *J Clin Invest.* 2009 May;119(5):1335-49.

Pneumococcal vaccination decreases atherosclerotic lesion formation: molecular mimicry between Streptococcus pneumoniae and oxidized LDL. Binder CJ, Hörkkö S, Dewan A, Chang MK, Kieu EP, Goodyear CS, Shaw PX, Palinski W, Witztum JL, Silverman GJ. *Nat Med.* 2003 Jun;9(6):736-43.

Innate and acquired immunity in atherogenesis. Binder CJ, Chang MK, Shaw PX, Miller YI, Hartvigsen K, Dewan A, Witztum JL. *Nat Med.* 2002 Nov;8(11):1218-26.

Christoph Bock

Medical Epigenomics and
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+ Group of 5 people

Main Research Interests
+ Epigenomic basis of hematopoietic diseases
+ Bioinformatic dissection of cellular identity
+ Diagnostics using next generation sequencing

Christoph Bock is a Principal Investigator at the Research Center for Molecular Medicine of the Austrian Academy of Sciences, a guest professor at the Medical University of Vienna's department for laboratory medicine and an adjunct group leader at the Max Planck Institute for Informatics. His research focuses on medical epigenomics, studying the role of DNA methylation in cancer and developing methods for rational design of epigenetic cancer therapies. Christoph graduated from the Max Planck Institute for Informatics and Saarland University in 2008, where he was involved in the EU-FP7 CANCERDIP project. During his postdoc at the Broad Institute of MIT and Harvard, he contributed to the work of the Roadmap Epigenome Mapping Consortium, and since 2011 he has been as work package leader within the EU-FP7 BLUEPRINT project. In 2009, Christoph was awarded an Otto Hahn Medal by the Max Planck Society for pioneering work in computational epigenetics.

Relevant/Important Publications

Analysing and interpreting DNA methylation data. Bock C. *Nat Rev Genet.* 2012; 13, 705-719.

Managing drug resistance in cancer: lessons from HIV therapy. Bock C, Lengauer T. *Nat Rev Cancer.* 2012; 12, 494-501.

DNA methylation dynamics during in vivo differentiation of blood and skin stem cells. Bock C, Beerman I, Lien WH, Smith ZD, Gu H, Boyle P, Gnirke A, Fuchs E, Rossi DJ, Meissner A. *Mol Cell* 2012; 47, 633-647.

Reference Maps of human ES and iPS cell variation enable high-throughput characterization of pluripotent cell lines. Bock C, Kiskinis E, Verstappen G, Gu H, Boulting G, Smith ZD, Ziller M, Croft GF, Amoroso MW, Oakley DH, Gnirke A, Eggan K, Meissner A. *Cell.* 2011; 144, 439-452.

Quantitative comparison of genome-wide DNA methylation mapping technologies. Bock C, Tomazou EM, Brinkman AB, Müller F, Simmer F, Gu H, Jäger N, Gnirke A, Stunnenberg HG, Meissner A. *Nat Biotechnol.* 2010; 28, 1106-1114.

Kaan Boztug

Malignant Hematological Disorders of Childhood

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+ German
+ Joined CeMM in January 2011
+ Group of 7 people

Main Research Interests
+ Molecular genetics of primary immunodeficiencies and congenital bone marrow failure syndromes
+ Molecular genetics of malignant hematological disorders of childhood

Kaan Boztug, born in 1977, was appointed as a Principal Investigator at CeMM in January 2011. He studied Medicine at the Universities of Düsseldorf, Freiburg and London. For his MD thesis, he spent a year of research in the laboratory of Iain L. Campbell at the Scripps Research Institute, La Jolla, CA, USA, where his work was focused on neuroimmunology.

From 2005 until 2010, Kaan Boztug worked at Hannover Medical School in the Department of Pediatric Hematology/Oncology headed by Christoph Klein with a dual affiliation combining clinical training and postgraduate laboratory work. He developed a strong interest in the molecular genetics of primary immundeficiency disorders and was able to elucidate a novel primary immunodeficiency which combines congenital neutropenia and complex organ malformations, caused by deficiency in the glucose-6-phosphatase catalytic subunit 3 (G6PC3). In another sentinel work, he was one of the lead authors in the identification of the first monogenic causes of childhood inflammatory bowel disease (IBD), caused by mutations in the genes encoding the interleukin-10 receptor.

At CeMM, Kaan Boztug works on the genetics of primary immundeficiencies and congenital bone marrow failure syndromes but has also broadened his interest to genetics of malignant disorders of childhood. He holds a dual appointment with the Children's Hospital of the Medical University of Vienna. In 2012, he received the START Prize of the Austrian Science Fund (FWF) and a Starting Grant of the European Research Council (ERC StG).

Relevant/Important Publications

A syndrome with congenital neutropenia and mutations in *G6PC3*. Boztug K, Appaswamy G, Ashikov A, Schäffer AA, Salzer U, Diestelhorst J, Germeshausen M, Brandes G, Lee-Gossler J, Noyan F, Gatzke AK, Minkov M, Greil J, Kratz C, Petropoulou T, Pellier I, Bellanné-Chantelot C, Rezaei N, Mönkemöller K, Irani-Hakimeh N, Bakker H, Gerardy-Schahn R, Zeidler C, Grimbacher B, Welte K, Klein C. *N Engl J Med.* 2009; 360: 32-43.

Early-onset inflammatory bowel disease caused by loss-of-function mutations in the *IL10-receptor* genes. Glocker E-O*, Kotlarz D*, Boztug K*, Gertz EM, Schäffer AA, Noyan F, Perro M, Diestelhorst J, Allroth A, Murugan D, Hätscher N, Pfeifer D, Sykora KW, Sauer M, Kreipe M, Lacher M, Nustede R, Woellner C, Baumann U, Salzer U, Koletzko S, Shah N, Segal AW, Sauerbrey A, Buderus S, Snapper SB, Grimbacher B, Klein C. *N Eng J Med.* 2009; 361: 2033-45.

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Thijn Brummelkamp

Genetics of Cancer and Infectious Diseases

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Main Research Interests
+ Cancer research
+ Infectious disease
+ Drug action

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Thijn Brummelkamp uses genetic approaches to identify genes that play a role in human disease. His primary interests are cancer research, infectious disease and drug action. Brummelkamp has developed technologies to accelerate genetic analysis of cultured mammalian cells. A 'stable RNA interference' process, which he and his colleagues first described, is now widely used to manipulate and study gene function in mammalian cells. Brummelkamp has used stable RNA interference to inhibit thousands of human genes, in order to find specific genes that play a role in human disease. 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. 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 Rene Bernards and received his Ph.D. cum laude from Utrecht University in 2003. In 2004 he was appointed as a Whitehead Fellow to initiate his independent research program at the Whitehead Institute for Biomedical Research in Cambridge, USA. In 2011 his laboratory moved to the Netherlands Cancer Institute and he became an Adjunct PI 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 the Kimmel Scholar Award (2006).

Relevant/Important Publications

Ebola virus entry requires the cholesterol transporter Niemann-Pick C1. Carette JE, Raaben M, Wong AC, Herbert AS, Obernosterer G, Mulherkar N, Kuehne AI, Kranzusch PJ, Griffin AM, Ruthel G, Dal Cin P, Dye JM, Whelan SP, Chandran K, Brummelkamp TR. *Nature.* 2011 Aug 24; 477(7364):340-3

Haploid genetic screens in human cells identify host factors used by pathogens. Carette JE, Guimaraes CP, Varadarajan M, Park AS, Wuethrich I, Godarova A, Kotecki M, Cochran BH, Spooner E, Ploegh HL, Brummelkamp TR. *Science.* 2009 Nov 27;326(5957):1231-5.

YAP1 increases organ size and expands undifferentiated progenitor cells. Camargo FD, Gokhale S, Johnnidis JB, Fu D, Bell GW, Jaenisch R, Brummelkamp TR. *Curr Biol.* 2007 Dec 4;17(23):2054-60. Epub 2007 Nov 1. *Erratum in: Curr Biol.* 2007 Dec 4;17(23):2094.

A system for stable expression of short interfering RNAs in mammalian cells. Brummelkamp TR, Bernards R, Agami R. *Science.* 2002 Apr 19; 296(5567):550-3.

Jacques Colinge

Bioinformatics

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+ Group of 6 people

Main Research Interests
+ Computational proteomics
+ Protein interaction network analysis
+ Systems biology and OMICS data integration
+ Drug mechanism of action and side-effects modeling
+ Protein complex predictions from mass spectrometry data
+ Application of computational statistics and mathematics

Jacques Colinge was born in Switzerland and heads bioinformatics at CeMM since 2006. He obtained a Ph.D. in mathematics from the University of Geneva, Switzerland, in collaboration with the Swiss Institute of Technology. After completing his PhD, Jacques joined the Serono Pharmaceutical Research Institute as a bioinformatician to work mainly on differential gene expression data analysis. In 2000 he moved to GeneProt Inc. to head a group in charge of mass spectrometry-related bioinformatics and parallel computing. In 2005, he joined the Upper Austrian University of Applied Sciences at Hagenberg to serve as a Professor of Bioinformatics before moving to CeMM in September 2006.
In 2009, Jacques obtained a Habilitation in bio-informatics from TU Graz. The bioinformatics lab does research to develop data analysis methods aimed at understanding the biological function of networks of interacting proteins. The group also develops and maintains data processing pipelines and databases to analyze and manage mass spec-trometry data, and to support protein interaction network analyses.

Relevant/Important Publications
Systems biology analysis of protein-drug interactions. Colinge J*, Rix U, Bennett KL, Superti-Furga G. *Proteomics Clin Appl.* 2011 Dec 27.

General statistical modeling of data from protein relative expression isobaric tags. Breitwieser FP, Müller A, Dayon L, Köcher T, Hainard A, Pichler P, Schmidt-Erfurth U, Superti-Furga G, Sanchez JC, Mechtler K, Bennett KL, Colinge J. *J Proteome Res.* 2011 Jun 3;10(6):2758-66.

Initial characterization of the human central proteome. Burkard TR, Planyavsky M, Kaupe I, Breitwieser FP, Bürckstümmer T, Bennett KL, Superti-Furga G, Colinge J. *BMC Syst Biol.* 2011 Jan 26;5:17.

Using iTRAQ combined with tandem affinity purification to enhance low-abundance proteins associated with somatically mutated EGFR core complexes in lung cancer. Haura EB, Müller A, Breitwieser FP, Li J, Grebien F, Colinge J, Bennett KL. *J Proteome Res.* 2011 Jan 7;10(1):182-90.

A computational approach to analyze the mecha-nism of action of the kinase inhibitor bafetinib. Burkard TR, Rix U, Breitwieser FP, Superti-Furga G, Colinge J. *PLoS Comput Biol.* 2010 Nov 18;6(11):e1001001.

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Sylvia Knapp

Innate Immunity and Bacterial Infections

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+ Group of 11 people

Main Research Interests
+ Exploit molecular mechanisms of host-pathogen interactions
+ Receptor cross-regulation in innate immunity

Sylvia Knapp's Group is located at the
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Sylvia Knapp was born in Austria and studied Medicine at the Free University in Berlin and the University of Vienna. She obtained her MD degree in 1993 and started her residency in Internal Medicine at the University Hospital Vienna.
In 2000 she received her License in Internal Medicine and in 2004 she obtained a "Habilitation" in Intenal Medicine at the Medical University of Vienna. After several residencies, mostly in areas like Infectious Diseases, AIDS and Intensive Care Units, she became a Ph.D. student in Tom van der Poll's laboratory at the University of Amsterdam and studied the inflammatory response to severe bacterial infections. Sylvia's most important achievements include the identification of the anti-inflammatory role of alveolar (lung) macrophages as well as the biological function of several pattern recognition receptors during Streptococcus pneumoniae pneumonia. Sylvia joined CeMM in 2006 and continues her work on the innate immune response to bacterial infections, focusing on the molecules involved in the initiation and resolution of the innate immuneresponse to clinically relevant pathogens and on the role of bacterial virulence factors and their interactions with host structures and pathways. Sylvia main-tains her responsibilities at the Intensive Care Unit at the Medical University Vienna and was appointed Professor of Infection Biology in 2012.

Relevant/Important Publications
TLR2 and CD14 mediate innate immunity and inflammation to Staphylococcal Panton Valentine leucocidin in vivo. Zivkovic A, Sharif O, Stich K, Doninger B, Biaggio M, Colinge J, Bilban M, Mesteri I, Hazemi P, Lemmens-Gruber R, Knapp S. *J. Immunol* (2011) 186,1608-1617

TREM-1 activation alters the dynamics of pulmonary IRAK-M expression in vivo and improves host defense during pneumococcal pneumonia. Lagler H, Sharif O, Haslinger I, Matt U, Stich K, Furtner T, Doninger B, Schmid K, Gattringer R, de Vos AF, Knapp S. *J Immunol* (2009) 183, 2027-2036

Baumann CL*, Aspalter IM*, Sharif O*, Pichlmair A, Blüml S, Grebien F, Bruckner M, Pasierbek P, Aumayr K, Planyavsky M, Bennett KL, Colinge J, Knapp S#, Superti-Furga G#. CD14 is a coreceptor of Toll-like receptors 7 and 9. *J Exp Med* (2010) 207: 2689-2701.

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Genetics of Hematological Disorders

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+ Czech
+ Joined CeMM in June 2006
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Main Research Objectives and Questions
+ Identify mutations in early steps of disease development in hematological malignancies
+ How mutant stem cells evolve genetically, how they respond to therapy?
+ What gene mutations cause familial predisposition to hematological malignancies?
+ How does genetic variability contribute to disease?
+ How to diagnose the diseases in early stages of development?

Robert Kralovics, born 1970, is Czech and joined CeMM in June 2006. He obtained his first degree in Molecular Biology and Genetics at the Comenius University in Bratislava and later his Ph.D. in Biophysics at the Academy of Sciences of the Czech Republic in Brno. He did his post-doctoral work on the genetics of myeloproliferative disorders working with Josef Prchal at the University of Alabama in Birmingham, USA. He followed Prchal as an Assistant Professor at the Baylor College of Medicine in Houston. From mid 2001, Robert was a project leader with Radek Skoda in Basel. Robert's research interests are primarily in myeloproliferative disorders (MPDs) and in myeloid malignancies in general. One of his major achievements so far has been the identification of a gain-of-function mutation in the JAK2 kinase gene (V617F), which plays an important role in MPD pathogenesis. Robert continues this work at CeMM to identify new mutations causing familial predisposition to hematological malignancies using advanced genomics approaches, and is working towards understanding how genetic variability contributes to the disease.

Relevant/Important Publications

Genome integrity of myeloproliferative neoplasms in chronic phase and during disease progression. Klampfl T, Harutyunyan A, Berg T, Gisslinger B, Schalling M, Bagienski K, Olcaydu D, Passamonti F, Rumi E, Pietra D, Jäger R, Pieri L, Guglielmelli P, Iacobucci I, Martinelli G, Cazzola M, Vannucchi AM, Gisslinger H, Kralovics R. *Blood.* 2011 Jul 7;118(1):167-76

p53 lesions in leukemic transformation. Harutyunyan A, Klampfl T, Cazzola M, Kralovics R. *N Engl J Med.* 2011 Feb 3;364(5):488-90

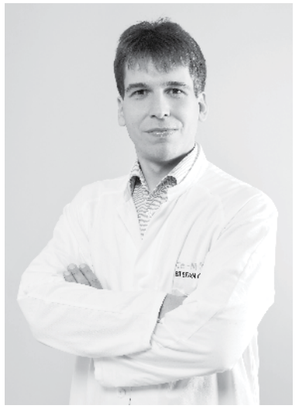
A common JAK2 haplotype confers susceptibility to myeloproliferative neoplasms. Olcaydu D, Harutyunyan A, Jäger R, Berg T, Gisslinger B, Pabinger I, Gisslinger H, Kralovics R. *Nat Genet.* 2009 Apr;41(4):450-454

A common JAK2 haplotype confers susceptibility to myeloproliferative neoplasms. Olcaydu D, Harutyunyan A, Jäger R, Berg T, Gisslinger B, Pabinger I, Gisslinger H, Kralovics R. *Nature Genetics.* 2009. 41(4):450-4

A gain-of-function mutation of JAK2 in myeloproliferative disorders. Kralovics R, Passamonti F, Buser AS, Teo SS, Tiedt R et al. *N Engl J Med.* 2005. 28;352(17): 1779-90

Stefan Kubicek

Chemical Biology and Epigenetics



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Main Research Interests
+ Chemical Epigenetics
+ Identification and development of small molecule probes for biological processes and host factors in infectious disease
+ Contribution of histone lysine methylation to cancer development and progression
+ Role of chromatin in the specification of pancreatic cell types

Stefan Kubicek, born 1978, is Austrian and joined CeMM in August, 2010 . He obtained an MSc in synthetic organic chemistry from Vienna University of Technology following a diploma thesis at ETH Zürich. For his Ph.D. in Thomas Jenuwein's lab at the IMP in Vienna, he changed fields to Molecular Biology. He then performed post-doctoral research working on Chemical Biology with Stuart Schreiber at the Broad Institute of Harvard and MIT.
Stefan Kubicek heads the chemical screening platform and PLACEBO (Platform Austria for Chemical Biology), a task he is well equipped for based on previous screening experiences with Boehringer Ingelheim and at the Broad Institute. These activities have resulted in the identification of the first selective histone methyltransferase inhibitor, BIX-01294, and a small molecule inducer of insulin expression in pancreatic alpha cells, BRD7389. The Kubicek lab is working on the role of chromatin in the definition of cell types and cell states. Projects focus on defining the contribution of histone methylation to cancer development and progression, the development of new assays and compounds to quantify and modulate chromatin modifications, and their potential for transdifferentiation of celltypes.

Relevant/Important Publications

Compounds targeting chromatin modifying enzyme induce specific cell-type independent transcription signatures in the endocrine pancreas. Kubicek S, Gilbert J, Fomina-Yadlin D, Gitlin A, Yuan Y, Wagner F, Holson E, Luo T, Lewis T, Taylor B, Gupta S, Shamji AF, Wagner BK, Clemons PA, Schreiber SL. *Proc Natl Acad Sci U S A.* 2012; 109; 5364-5369.

A selective inhibitor and probe of the cellular functions of Jumonji C domain-containing histone demethylases. Luo X, Liu Y, Kubicek S, Myllyharju J, Tumber A, Ng S, Che KH, Podoll J, Heightman TD, Oppermann U, Schreiber SL, Wang X. *J Am Chem Soc.* 2011 Jun 22;133(24):9451-6.

Small-molecule inducers of insulin expression in pancreatic alpha-cells. Fomina-Yadlin D*, Kubicek S*, Walpita D, Dancik V, Hecksher-Sørensen J, Bittker JA, Sharifnia T, Shamji A, Clemons PA, Wagner BK, Schreiber SL. *Proc Natl Acad Sci U S A.* 2010;107(34):15099-104.

Reversal of H3K9me2 by a small-molecule inhibitor for the G9a histone methyltransferase. Kubicek S, O'Sullivan RJ, August EM, Hickey ER, Zhang Q, Teodoro ML, Rea S, Mechtler K, Kowalski JA, Homon CA, Kelly TA, Jenuwein T. *Mol Cell.* 2007 Feb 9; 25(3):473-81.

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DNA Repair and Genomic Stability

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+ Group of 5 people

Main Research Interests
+ Signaling and repairing DNA damage
+ Repair of physiological DNA breaks generated in immune T and B cells during somatic recombination
+ Maintenance of genome integrity to suppress leukemia and lymphoma

Joanna completed her undergraduate studies in the UK, having moved there from Cyprus. Subsequently, she commenced Ph.D. work at the University of Manchester (and University of Sussex) investigating mechanisms of DNA repair. During this time Joanna identified for the first time a requirement for the kinase CK2 in the DNA damage response. Postdoctoral work followed at the International Agency for Research on Cancer (IARC), World Health Organization (WHO), France where Joanna investigated the role of epigenetic modifications, mainly histone acetylation, in DNA repair. Joanna showed that cells use shared molecules in transcription and DNA repair. It was also during this time she chose to work on the immune system and showed that histone acetylation is important in maintaining haematopoietic stem cells. Joanna wanted to build on this experience and focus on the role of genomic instability leading to cancers of the blood, hence she joined the London Research Institute (LRI) at Cancer Research UK (CR-UK), where she continued to work on DNA repair and its importance in the development of the immune system and in suppressing leukemia and lymphoma. At CeMM Joanna's group investigates the mechanisms by which cells respond to, and repair, DNA damage in order to maintain genomic stability and suppress tumorigenesis. Joanna focuses on physiological DNA damage generated by replicative stress or during the process of somatic recombination that occurs in immune B and T cells. Joanna is interested in understanding the pathways responsible for the repair of such breaks that allow for the maintenance of genome integrity but also for the maturation of immune cells.

Relevant/Important Publications

ATMIN is required for maintenance of genomic stability and suppression of B cell lymphoma. Loizou JI, Sancho R, Kanu N, Bolland DJ, Yang F, Rada C, Corcoran AE, and Behrens A. *Cancer Cell.* 2011; 19, 587-600.

Histone acetyltransferase cofactor Trap is essential for maintaining the hematopoietic stem/progenitor cell pool. Loizou JI, Oser G, Shukla V, Sawan C, Murr R, Wang ZQ, Trumpp A, and Herceg Z. *J Immunol.* 2009;*183*, 6422-6431.

Histone acetylation by Trrap-Tip60 modulates loading of repair proteins and repair of DNA double-strand breaks. Murr R*, Loizou JI*, Yang YG, Cuenin C, Li H, Wang ZQ, and Herceg Z. *Nat Cell Biol.* 2006; *8*, 91-99.

The protein kinase CK2 facilitates repair of chromosomal DNA single-strand breaks. Loizou JI, El-Khamisy SF, Zlatanou A, Moore DJ, Chan DW, Qin J, Sarno S, Meggio F, Pinna LA, and Caldecott KW. *Cell.* 2004;*117*, 17-28.

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Sebastian Nijman

Functional Cancer Genomics

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Main Research Interests
+ Chemical genetics of cancer
+ Identify novel strategies to treat cancer (cancer vulnerabilities)
+ Functional genetic screens to identify cancer-related genes

Sebastian Nijman was born in the Netherlands (1975). He studied medical biology at Utrecht University and specialized in Molecular Biology and Biochemistry in the labs of Hans Bos and Rene Medema. Sebastian also holds a Masters of Arts degree from the University of Maastricht (Science, Society and Technology Studies) and was involved in clinical research at a Contract Research Organization. In the lab of Rene Bernards at the Netherlands Cancer Institute, he performed his Ph.D. work, focusing on functional genetic screens in cancer-relevant pathways. He performed the first RNAi screen in mammalian cells that led to the identification of the cylindromatosis tumor suppressor as a regulator of NF-kappaB signaling. This work has led to a rational therapeutic approach for treating cylindromatosis and is one of his major achievements so far. In 2006 he joined the lab of Todd Golub at The Broad Institute of Harvard and MIT, USA. There he developed novel genomic approaches to discover the functions of genes and identify new angles for cancer treatment. Since joining CeMM, Sebastian's research is mostly focused on the identification and understanding of cancer vulnerabilities using chemical genetic screens.

Relevant/Important Publications

A chemical-genetic screen reveals a mechanism of resistance to PI3K inhibitors in cancer. Muellner MK, Uras IZ, Gapp BV, Kerzendorfer C, Smida M, Lechtermann H, Craig-Mueller N, Colinge J, Duernberger G, Nijman SM. *Nat Chem Biol.* 2011 Sep 25;7(11):787-93.

Synthetic lethality: general principles, utility and detection using genetic screens in human cells. Nijman SM. *FEBS Lett.* 2011 Jan 3;585(1):1-6.

A genomic and functional inventory of deubiquitinating enzymes. Nijman SM, Luna-Vargas MP, Velds A, Brummelkamp TR, Dirac AM, Sixma TK, Bernards R. *Cell.* 2005 Dec 2;123(5):773-86.

The deubiquitinating enzyme USP1 regulates the Fanconi anemia pathway. Nijman SM*, Huang TT*, Dirac AM, Brummelkamp TR, Kerkhoven RM, D'Andrea AD, Bernards R. *Mol Cell.* 2005 Feb 4; 17(3):331-9.

Loss of the cylindromatosis tumour suppressor inhibits apoptosis by activating NF-kappaB. Brummelkamp TR*, Nijman SM*, Dirac AM*, Bernards R. *Nature.* 2003 Aug 14;424(6950):797-801.

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Pathological Networks in Leukemia and Immunity

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+ Joined CeMM in January 2005
+ Group of 22 people

Main Research Interests
+ Mechanism of action of drugs
+ Molecular networks affecting leukemias
+ Molecular basis of innate immunity

Giulio Superti-Furga is an Italian national and he joined CeMM as Director in January 2005. He performed his undergraduate and graduate studies in molecular biology at the University of Zurich, Switzerland, at Genentech Inc., South San Francisco, USA, and at the Institute for Molecular Pathology in Vienna (I.M.P.), Austria. He was a post-doctoral fellow and Team Leader at the European Molecular Biology Laboratory (EMBL) until 2004. For several years he served as Professor of Biotechnology at the University of Bologna. In 2000, he co-founded the biotech company Cellzome, where he was Scientific Director. Some of Giulio's major achievements to date are the elucidation of basic regulatory mechanisms of tyrosine kinases in human cancers and the discovery of fundamental organization principles of the proteome of higher organisms. Giulio's work on the organization of the eukaryotic proteome is the most highly cited in the field. He is a full member of the Austrian Academy of Sciences, the German Academy of Sciences Leopoldina, the European Molecular Biology Organization and the European Academy of Cancer Sciences. He is chair of the EMBL Alumni Association. He uses and develops high-throughput "omics" approaches to study several areas including the mechanism of action of proteins and drugs, the identification of molecular networks underlying leukemia and the molecular basis of innate immunity. In 2009 he received the prestigious Advanced Investigator Grant awarded by the European Research Council (ERC), and he was awarded the Knight Officer Order of Merit of the Republic of Italy for his contributions to science. In 2011 he received the Prize of the City of Vienna for Natural Sciences, and was honored as Austria's Scientist of the Year.

Relevant/Important Publications

Viral immune modulators perturb the human molecular network by common and unique strategies. Pichlmair A, et al., *Nature.* 2012 Jul 26;487(7408):486-90.

Targeting the SH2-kinase interface in Bcr-Abl inhibits leukemogenesis. Grebien F, et al., *Cell* 2011 Oct 14;147(2):306-19.

A network solution. Henney A, Superti-Furga G. *Nature.* 2008 Oct 9; 455(7214):730-1.

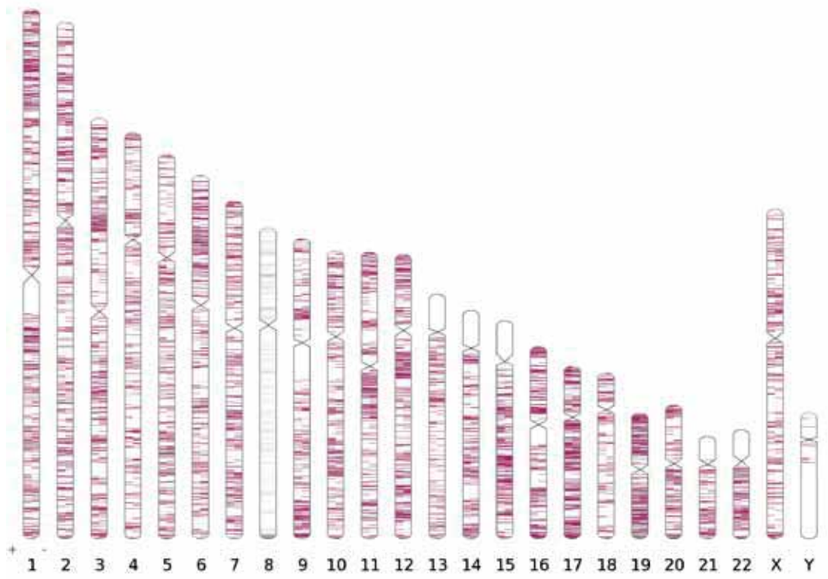
Functional organization of the yeast proteome by systematic analysis of protein complexes. Gavin AC, et al., Superti-Furga G. *Nature.* 2002. 415(6868): 141-7.

A Collection of Human Knockout Cells as a Toolkit for Biomedical Discovery

By "knocking out" a gene and studying the biological consequences one can learn about its functions. Therefore, collections of individual gene knockouts in model organisms such as yeast are cherished research tools. However, a comparable collection for human cell lines is not yet available. The main reason for this is that until recently the tools to generate such a library of mutants were not available. This problem has now been overcome by employing "haploid genetics".

A major obstacle for knocking out genes in human cells (and indeed most higher organisms) is that all genes are present in two copies. One is inherited from the mother and the other from the father, together making up a diploid human genome. However, this diploidy means that inactivating single gene copies typically does not result in a detectable phenotype as the second remaining allele compensates for the loss. CeMM adjunct PI Thijn Brummelkamp circumvented this obstacle by knocking out genes in a rare human cell line that only carries one copy for >95% of its genes. This "haploid" cell line has proven to be an extremely powerful tool for performing genetic screens to link genes with phenotypes. In such a screen all genes are essentially knocked out one-by-one using a gene-trap virus yielding a large pool of as many as 100 million "knockout" cells. Indeed, this technology is now being employed by several groups at CeMM to study host-pathogen interactions and mechanisms of drug action.

Importantly, the same technology can be used to isolate single mutants to compile a collection of human knock out cells. Such a collection would be as valuable for the scientific community working on human cells as the yeast collection has been for the yeast community. About two years ago scientists from CeMM and the spin-out Haplogen teamed up in a public-private partnership to make such a collection a reality. The team, headed by Tilmann Buerckstuemmer, has already isolated tens of thousands of clones and many of the scientists at CeMM are using these knockouts for their experiments. Furthermore, this collection will provide researchers with new tools to address a whole range of questions from infection biology to cancer.



Schematic overview of the human chromosomes and all the "genetrap" insertions that have been mapped by the Haplogen-CeMM team. Each genetrap insertion can inactivate the expression of a gene thus generating a "knockout". All these knockouts cell lines are isolated and will be available for detailed characterization or genetic screens to identify for instance new drug targets.

Next Generation Sequencing – a Transformative Technology Well-Supported at CeMM

Biomedical Sequencing Facility (BSF). The BSF is Austria's first technology platform dedicated to next generation sequencing in biomedicine. It was launched in spring 2012 as a consolidation of earlier efforts at CeMM and at the Medical University of Vienna. The BSF is coordinated by CeMM Principal Investigator Christoph Bock and run as a collaborative effort with major contributions from several research groups at CeMM and Medical University. The facility is currently equipped with two HiSeq 2000 sequencers and staffed with one expert technician and one Ph.D.-level bioinformatician. A comprehensive robotics solution for sample preparation will be added in the first quarter of 2013, thus providing a substantial increase in throughput compared to the already remarkable number of 1,000 samples that were sequenced at CeMM in 2012. The BSF supports all of biomedicine's most relevant sequencing protocols, including: whole-genome sequencing, exome sequencing and high-throughput sequencing of candidate loci; gene expression profiling using various subtypes of RNA-seq; and epigenome mapping using genome-scale bisulfite sequencing as well as ChIP-seq. It is complemented by a powerful IT infrastructure that is being upgraded with 50-100 terabytes of storage every year to keep up with the massive growth of data produced by the next generation sequencing machines at CeMM. In summary, the BSF provides essential infrastructure and expertise for catalyzing the development of genomic medicine in Vienna and Austria.

Additional information is available on the website of the BSF: http://biomedical-sequencing.at

ERC Starting Grants for Kaan Boztug and Sebastian Nijman

The European Research Council awarded the prestigious ERC Starting Grants to two CeMM Principal Investigators: Kaan Boztug and Sebastian Nijman. ERC Starting Grants support promising young scientific leaders with proven potential for success in creating new research teams to perform world-class independent research in Europe. Kaan Boztug, Group Leader at CeMM and Visiting Professor at the Department of Pediatrics and Adolescent Medicine of the Medical University of Vienna was chosen for his research project "Integrated Genetics of Congenital Defects of Innate Immunity", which will focus on the elucidation of Mendelian disorders of the human immune system. Sebastian Nijman was awarded the starting grant for his proposal "Discovering Gene-Drug Interactions in Breast Cancer With a Systematic and Genetically Tractable Model". Each grant amounts to approximately 1.5 Million Euro for a period of up to 60 months.

Funded Project: Sebastian Nijman
Discovering Gene-Drug Interactions in Breast Cancer With a Systematic and Genetically Tractable Model

Biomedical research has been very successful in finding the genes that are deregulated in cancer. However, it has proven much more challenging to translate this knowledge into effective treatments. One complication is that cancer cells typically carry many mutations and every tumor displays a unique pattern. This patient-to-patient heterogeneity complicates treatment as it often interferes with patient response. Thus, unraveling the complex interplay between cancer genes and drugs is of great importance for effective patient-stratified cancer therapy. Besides playing a role in drug resistance, molecular changes also result in cancer cells becoming uniquely dependent on certain gene products or pathways. These cancer "vulnerabilities" offer opportunities for targeted therapies. The aim is to identify cancer vulnerabilities and drug resistance mechanisms with a specific focus on breast cancer. By building models systems of breast cancer cells that capture the variability and heterogeneity of the disease, they can develop more effective therapies. Together, this project aims to improve therapies in breast cancer by identifying patient cohorts that are most likely to benefit from a given drug and revealing novel cancer Achilles' heels.

Funded Project: Kaan Boztug
Integrated Genetics of Congenital Defects of Innate Immunity

Primary immunodeficiency disorders involving innate immunity are characterized by recurrent and life-threatening infections. However, the molecular etiology of these disorders is often unknown. The aim is to identify novel genetic defects in innate immunity and decipher their molecular pathophysiology using a discovery engine consisting of an exclusive combination of genomic technologies, including single nucleotide polymorphism (SNP) chip arrays and high throughput DNA sequencing technology ("next generation sequencing"), together with functional proteomic technologies. The engine will be complemented by biochemical, immunological and imaging technologies to systematically assess the consequences of the genetic deficiency, and to map the respective protein products onto molecular pathways. The proposed investigations are expected to contribute significantly to the understanding of the molecular processes that structure the human innate immune system. This will not only enable a more comprehensive molecular classification system of primary immunodeficiency disorders, but also improve patient care by aiding molecular diagnosis and prognosis in individual patients suffering from these disorders. The investigations will serve as the basis for future development of targeted therapies such as gene therapy or pharmacological interventions targeting affected signaling pathways.

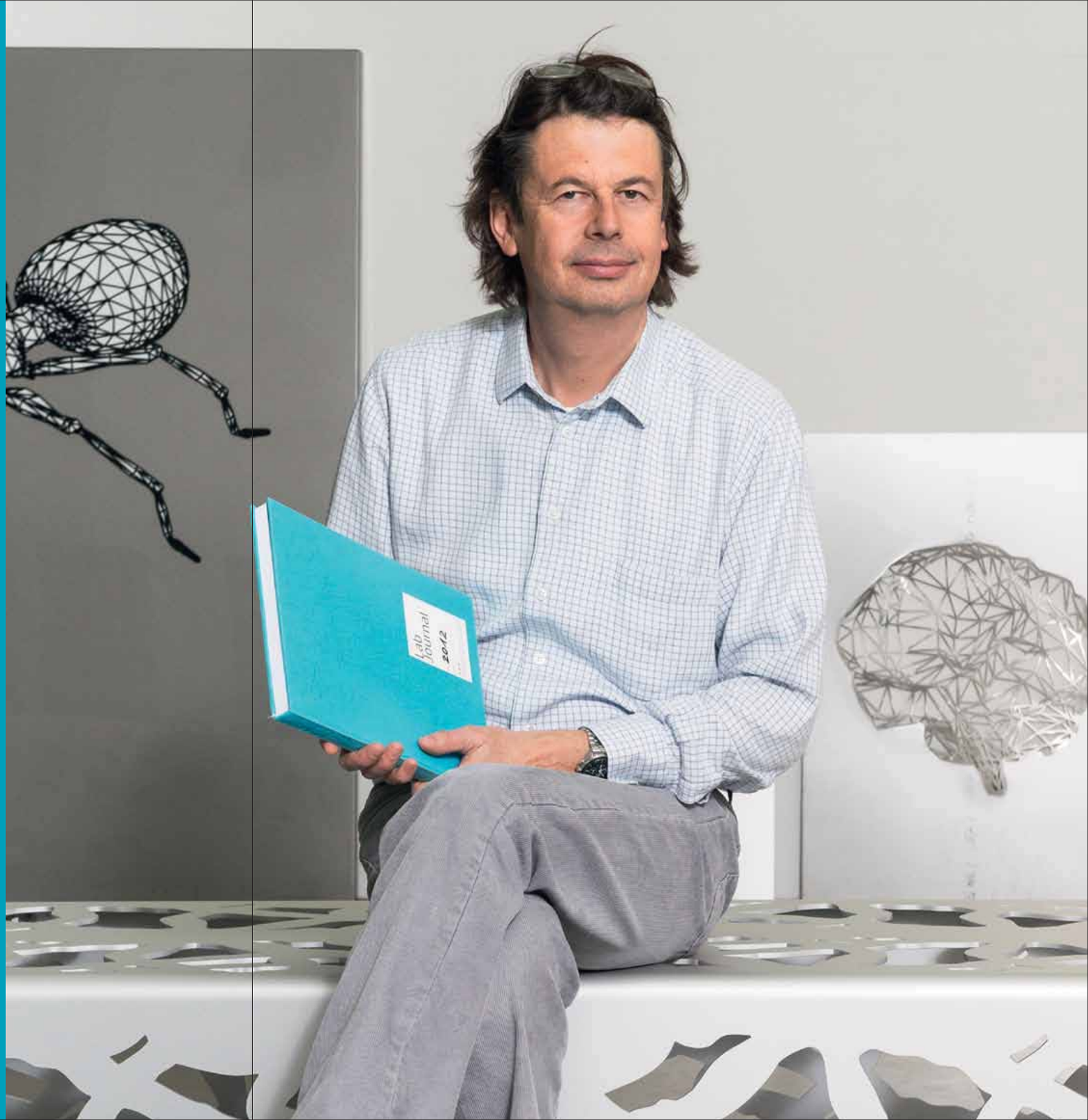
Austria's START Prize Awarded to Kaan Boztug

START Prize awardee Kaan Boztug and his group at the FWF summer party 2012.

Kaan Boztug is one of seven young scientists out of 54 applicants who has been accepted into the 2012 START Program of the Austrian government. The START Program is Austria's most renowned funding scheme for excellent young scientists and is open to all disciplines. This year's awardees were announced on June 12, 2012 by Austria's Federal Minister for Science and Research Karlheinz Töchterle and FWF President Christoph Kratky. Kaan Boztug was chosen for his research project entitled "Integrated Genetics of Congenital Defects of Innate Immunity", which will focus on characterizing Mendelian disorders of the human immune system.

“CeMM is a place where science and art come together in a most stimulating way.”

Peter Kogler (*1959, Innsbruck, Tyrol)
Peter Kogler studied stage design at the Academy of Fine Arts, Vienna. His work juxtaposes the perfectionism of new technologies with physical and organic motifs. Kogler regularly participates in numerous exhibitions, including participation in the documenta IX and X in 1992 and 1997, as well as in the Biennale Venice Biennial in 1995. He creates illusionistic spaces, as can be seen on the 400m2 art façade of the CeMM research building. For the CeMM Brain Lounge, Kogler contributed a brain as a centerpiece for the table.



"The artistic exploration of the present, its foundations, ideas, materials and technologies is a prerequisite for the framing of questions that can also continue to gain significance in the future."

Brigitte Kowanz (*1957, Vienna)
Brigitte Kowanz studied at the Academy of Applied Art, Vienna (1975-1980) and has worked as Professor for Transmedia Art at the University of Applied Arts, Vienna since 1997. In 2009 she was awarded the Austrian State Prize for Fine Arts (Großer Österreichischer Staatspreis). The main theme of Brigitte Kowanz's works is the different visual forms which light can take. To the CeMM Brain Lounge she contributed a light installation as a loan.

Lecture Series

CeMM's organized seminars and lecture series held throughout the year provide an important source of information and inspiration not only to the scientists at CeMM, but also to scientists and medical professionals at other local institutes and universities, and sometimes to the interested general public.

Overview CeMMinar/Impromptu Series

30.01.2012
CeMMinar
Meinrad Busslinger
The Research Institute of Molecular Pathology (IMP), Vienna
"Lineage commitment and plasticity of B lymphocytes"
Host: Giulio Superti-Furga

31.01.2012
Joint MedUni Vienna - CeMM Impromptu
Nima Rezaei
Tehran University of Medical Sciences, Children's Medical Center, Iran
"Primary immunodeficiencies in Iran"
Hosts: Rudolf Valenta (MedUni Vienna) & Kaan Boztug (CeMM)

02.02.2012
Impromptu
Ann-Sofie Jemth
Dept. of Genetics, Microbiology and Toxicology, Stockholm University Arrhenius Laboratory
"Turning cancer defects into cure: Targeting DNA repair"
Host: Kilian Huber

06.02.2012
CeMMinar
Kristian Helin
Biotech Research & Innovation Centre (BRIC), University of Copenhagen
"Functional Roles of TET proteins and Hydroxymethylation in Stem Cells and Cancer"
Host: Stefan Kubicek

13.02.2012
CeMMinar
Bodo Grimbacher
Research group "Experimental Immuno-deficiency", Centre of Chronic Immuno-deficiency, Freiburg
"A novel monogenetic defect causing autoimmunity and hypogammaglobulinemia"
Host: Kaan Boztug

20.02.2012
CeMMinar
Magnus Nordborg
Gregor Mendel Institute of Molecular Plant Biology (GMI), Vienna
"Investigating the genotype-phenotype map using Arabidopsis"
Host: Giulio Superti-Furga

27.02.2012
CeMMinar
Axel Behrens
CR-UK London Research Institute
"Stress and DNA damage signalling in stem cells and cancer"
Host: Joanna Loizou

28.02.2012
Impromptu
Stefan Stricker
UCL Cancer Institute, University College London, UK
"Reprogramming human brain cancer cells to test the relevance of epigenetic anomalies"
Host: Denise Barlow

05.03.2012
CeMMinar
Kai Johnsson
Institute of Chemical Sciences & Engineering, École Polytechnique Fédérale de Lausanne
"Spying on drugs and metabolites in living cells"
Host: Giulio Superti-Furga

12.03.2012
CeMMinar
Laurence Calzone & Emmanuel Barillot
Computational Systems Biology of Cancer, Institute Curie, Paris
"A Systems Biology Approach for modeling signalling network involved in Cancer"
Host: Jacques Colinge

14.03.2012
Impromptu
Clemens Grabher
Karlsruhe Institute of Technology (KIT), Institute of Toxicology and Genetics (ITG)
"Facilitating drug discovery: An automated high-content inflammation assay in zebrafish"
Host: Kilian Huber

20.03.2012
Impromptu
Amanda M. Jamieson
Max F. Perutz Laboratories (MFPL), University of Vienna & Medical University of Vienna
"Host Response to Influenza Virus/ Bacterial Coinfections: Trade-offs and vulnerabilities"
Host: Andreas Bergthaler

26.03.2012
CeMMinar
Jean-Laurent Casanova
St. Giles Laboratory of Human Genetics of Infectious Diseases, The Rockefeller University
"Toward a genetic theory of infectious diseases"
Host: Giulio Superti-Furga

27.03.2012
Impromptu
James Bradner
Department of Medicine, Harvard Medical School & Hematologic Neoplasia/Malignancies, Dana-Farber Cancer Institute
"Chemical Inhibition of Human Bromodomains"
Hosts: Stefan Kubicek and Sebastian Nijman

02.04.2012
CeMMinar
Julie Magarian Blander
Immunology Institute, Mount Sinai Medical Center, NY
"Vita-PAMPs: Signatures of Microbial Viability"
Host: Sylvia Knapp

16.04.2012
CeMMinar
Forest White
Department of Biological Engineering, Massachusetts Institute of Technology (MIT) and Koch Institute for Integrative Cancer Research, USA
"Using Quantitative Proteomics to Connect Genotype to Phenotype"
Host: Keiryn Bennett

23.04.2012
CeMMinar
Philippe Sansonetti
INSERM U786 "Unité de Pathogénie Microbienne Moléculaire", Institut Pasteur, Paris
"Commensal and pathogens at mucosal surface: the Yin and the Yang of innate immunity"
Host: Giulio Superti-Furga

07.05.2012
CeMMinar
Claus Nerlov
MRC Centre for Regenerative Medicine SCRM Building, The University of Edinburgh
"Identification of novel pathways & mechanisms of hematopoitic lineage specification"
Host: Giulio Superti-Furga

10.05.2012
Impromptu
Maurizio Scaltriti
Department of Medicine, Mass General Hospital Cancer Center, Boston, MA
"Overcoming targeted therapy resistance: hypothesis-based drug combinations"
Host: Sebastian Nijman

14.05.2012
CeMMinar
Michael J. Eck
Department of Cancer Biology, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA
"TKinase Targets in Lung Cancer: Structure, mechanism and inhibition of EGFR and TBK1"
Host: Giulio Superti-Furga

21.05.2012
CeMMinar
Amos Bairoch
Director of Structural Biology and Bioinformatics Department, Swiss Institute of Bioinformatics, University of Geneva
"The CALIPHO group: neXtProt, a new knowledge platform on human proteins and on-going work toward the characterization of some human proteins"
Host: Jacques Colinge

04.06.2012
CeMMinar
Maria Sibilia
Institute for Cancer Research, Dept. of Medicine I, Comprehensive Cancer Center, Medical University of Vienna
"Defining the functions of EGFR in Cancer and beyond"
Host: Denise Barlow

18.06.2012
CeMMinar
Garret A. FitzGerald
Department of Pharmacology, Institute for Translational Medicine & Therapeutics (ITMAT), Perelman School of Medicine, University of Pennsylvania
"Peri-pheral Clocks in Cardiometabolic Function"
Host: Christoph Binder

25.06.2012
CeMMinar
Michael Hemann
Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)
"Using mouse models to identify new cancer drug targets"
Host: Sebastian Nijman

23.07.2012
CeMMinar
Andrew McKenzie
MRC Laboratory of Molecular Biology, Cambridge, UK
"Type-2 innate lymphoid cells in protective immunity and asthma "
Host: Sylvia Knapp

21.08.2012
Impromptu
Liliana Krasinska
Institute of Molecular Genetics of Montpellier (IGMM), National Center for Scientific Research (CNRS), Montpellier, France
"A novel chemical biology approach to understanding the CDK network"
Host: Sebastian Nijman

30.08.2012
Impromptu
Matteo Iannacone
Division of Immunology, Transplantation and Infectious Diseases, San Raffaele Scientific Institute
"In vivo imaging of anti-viral immune responses in lymph nodes and in the liver"
Host: Andreas Bergthaler

04.09.2012
Impromptu
Patrick Collombat
Genetics of normal and pathological development, Centre de Biochimie, INSERM, Nice
"Alpha-cell-mediated beta-cell regeneration in the context of type 1 diabetes"
Host: Stefan Kubicek

01.10.2012
CeMMinar
Matthias Mann
Department of Proteomics and Signal Transduction, Max Planck Institute of Biochemistry
"Comprehensive proteome analysis and some of its applications"
Host: Keiryn Bennett

03.10.2012
Impromptu
Anne-Claude Gavin
Molecular Biology Laboratory, EMBL, Heidelberg
"Systematic screens for protein–lipid interactions in Saccharomyces cerevisiae"
Host: Giulio Superti-Furga

03.10.2012
Special Seminar
Inder Verma
Irwin and Joan Jacobs Chair in Exemplary Life Science, American Cancer Society Professor of Mol.Biology, The Salk Institute, Laboratory of Genetics, CA
"Glioblastomas: reprograming & transdifferentiation"
Host: Giulio Superti-Furga

08.10.2012
CeMMinar
Paul Flicek
EMBL Outstation – Hinxton, European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge
"Comparative regulatory genomics provides insight into the evolution of transcriptional regulation"
Host: Christoph Bock

15.10.2012
CeMMinar
Christoph Plass
Department of Epi-genomics and Cancer Risk Factors, German Cancer Research Center in the Helmholtz Association
"Global epigenetic alterations in chronic lymphocytic leukemia"
Host: Christoph Bock

24.10.2012
Impromptu
Hendrik Luesch
Department of Medicinal Chemistry, University of Florida
"Discovery, Mechanistic Characterization & Development of Anticancer Agents from Marine Cyanobacteria"
Host: Kilian Huber & Giulio Superti-Furga

29.10.2012
CeMMinar
Michael White
University of Texas, UT Southwestern Medical Center
"Oncogenome - selective vulnerabilities in lung adenocarcinoma"
Host: Sebastian Nijman

06.11.2012
Impromptu
(PostDoc Interview)
Adrian Schwarzer
Institute of Experimental Hematology OE6960, Hannover Medical School
"Receptor tyrosine kinases, Notch mutations and PTEN loss converge on mTOR in T-ALL and cause addiction to cap-dependent translation"
Host: Sebastian Nijman

29.11.2012
Joint MedUni Vienna CeMM Special Seminar
Hiroshi Takayanagi
Dept. of Immunology, Graduate School of Medicine & Faculty of Medicine, The University of Tokyo
"Osteoimmunology - shared mechanisms and crosstalk between the immune and bone systems"
Host: Shinya Sakaguchi (MedUni Vienna) & Andreas Bergthaler (CeMM)

03.12.2012
CeMMinar
Anne Corcoran
Nuclear Dynamics Programme Babraham Institute, Cambridge, UK
"Non-coding RNA transcription and nuclear organisation play key roles in immunoglobulin Recombination"
Host: Joanna Loizou

17.12.2012
Special Seminar
Wolfgang Weninger
Raymond E. Purves Professor and Chair, Discipline of Dermatology, Sydney Medical School
"Real-time imaging of cutaneous innate immune responses during inflammation and infection"
Host: Georg Stingl (MedUni Vienna/ Austrian Academy of Sciences) and Giulio Superti-Furga (CeMM)

18.12.2012
Special Seminar
Rolf M. Zinkernagel
(Nobel Laureate 1996)
Institute for Experimental Immunology, University of Zurich
"Immunology taught by viruses"
Host: Andreas Bergthaler

1st CeMM SMART Lecture

* SMART – Science, Medicine, Art, Research & Technology

Inauguration of the CeMM SMART series of Lectures by Dr. Norbert Bischofberger
The first CeMM SMART* Lecture was inaugurated on Monday 19 March 2011 by Dr. Norbert Bischofberger, Executive Vice President of Research and Development and Chief Scientific Officer of Gilead Sciences, Inc. This new series of lectures address contemporary challenges of science at the interface of science and society, and science and art, and in an interdisciplinary manner. In the first SMART lecture, entitled "Antiviral Drug Discovery and Development: Combating the Global Threat of HIV and HCV", Dr. Bischofberger talked about the evolution of HIV and Hepatitis C (HCV), both in terms of the diseases they cause, and how the medical community has worked to develop more effective treatments. It was an intriguing tale of two diseases and a company.

Towards SMARTer Drugs
In 1996, when the first HIV treatments became available, patients were required to take a complex mixture of over 30 drugs, some with fluids some without. Unsurprisingly, these complicated regimes had a profoundly negative impact on the patients' quality of life. Norbert explained the rationale and the scientific breakthroughs that enabled the transition, around 10 years later, to fewer, more effective and better-tolerated anti-HIV drugs with the subsequent dramatic improvement in quality of life. Gilead has also launched an access program involving 132 low-income countries with the aim to provide these drugs at no profit. The lecture was followed by a panel discussion and questions from the audience. One topic that was aired was the possibility of developing an effective HIV vaccine, which has thus far remained elusive. Norbert stated that despite his overall optimism concerning therapeutics for HIV, he does not consider it likely that a vaccine will be developed in the near future. Rather, he felt that modern technologies will enable more efficient, targeted, and better tolerated compounds that, when combined with policy changes, can contribute to the more global availability of drugs.

Around 150 guests joined the first smart lecture of Norbert Bischofberger.

6th CeMM Karl Landsteiner Lecture

Ruslan M. Medzhitov listens to Jussuv Karajev's impromptu violin playing after concert and lecture.

The Karl Landsteiner Lecture is held annually at CeMM in honor of the achievements of the Austrian biologist and physician noted for his discovery of human blood groups in 1900. This discovery revolutionized medicine by enabling the safe performance of blood transfusions. In recognition of this, the lectureship is awarded to a pioneer in molecular medicine who is carefully selected by the faculty at CeMM. This year marked the sixth Karl Landsteiner Lecture, which was presented by Prof. Ruslan M. Medzhitov, the David W. Wallace Professor of Immunobiology, and Howard Hughes Medical Institute Investigator at Yale University School of Medicine in the U.S. Ruslan is a pioneer in the field of innate immunity. He has been working on the intricacies of the molecular mechanisms of innate immune recognition and the control of adaptive immune responses for more than 20 years. "How does an organism distinguish self from non-self?" was the central question of his lecture, delivered on May 3rd 2012 to more than 300 guests in the magnificent Festive Hall of the Austrian Academy of Sciences.

Dealing with Foreign Invaders
Being able to distinguish between the body's own cells and foreign pathogens such as bacteria and viruses is critical for the immune system to function effectively. In his talk, Ruslan Medzhitov outlined the three strategies that humans and other organisms deploy in order to deal with foreign invaders: avoidance, to reduce exposure to a pathogen; resistance, to reduce the pathogen burden; and tolerance, to reduce a pathogen's negative effects. The main focus of the talk was to convey to the audience that understanding tolerance to a pathogen is a crucial parameter in immunology. Analyzing virulence from an evolutionary point of view, reciting examples such as the Spanish flu of 1918, as well as describing novel experimental approaches, Ruslan created an intense public engagement that continued in the reception that followed. The lecture was exceptionally well attended and the historic Festive Hall was filled to capacity, with many prominent researchers among the guests. We would like to thank Jussuv Karajev (violin) and Marija Köhler (piano) for the wonderful music that framed the event and managed to transport us to the majestic world of the Silk Road with folk dances from central Asia.

“The scientist, like the artist, presses forward into previously unexplored or unnamed areas. It is no coincidence then that with the CeMM Brain Lounge a place has been created where art and science come together. As an artist, I am driven by a certain joy in exploration. My work and installations are always experimental arrangements addressing specific questions. They are questions regarding “humanness,” or what it is that makes up this world that we perceive subjectively. I formulate notions and make assertions, try to make possibilities tangible. Unlike the scientist, I fortunately do not have to provide logically verifiable evidence. I am aided instead by the power of poesy. One thing is certain: inspiration is the key that opens unexplored worlds. This is as true for the scientist as it is for the artist. Insight generally grows from notions; notions make both scientific and artistic work possible.”

Dorothee Golz (*1960, Muehlheim, Germany)
Dorothee Golz studied art in Strasbourg and in parallel art history and anthropology at the University of Freiburg. She has lived and worked in Vienna since 1988. Following her participation in documenta X (1997) her works have achieved an international reputation. For the CeMM Brain Lounge she created a chair backrest artwork.

“CeMM – we share the excitement and are drawn into it – we passionately pursue, hold our breath and wish the best of luck.”

Martin Walde (*1957, Innsbruck, Tyrol)
Martin Walde studied at the Academy of Fine Art, Vienna. Among other things, he was awarded the Otto Mauer Prize in 1991 and the City of Vienna’s Prize for Fine Art (Preis der Stadt Wien für Bildende Kunst) in 2012. Martin Walde is an internationally acclaimed artist, participant in many important international exhibitions including the Venice Biennial in 1986 and 2001 and documenta X in 1997 . His contribution to the CeMM Brain Lounge is the textile artwork ANACONDA, 2012, which is part of the series Hallucigenia products, 2003, as well as a chair backrest artwork.

Workshops and Conferences

Conferences are an essential part of scientific research. They enable direct communication of results between scientists of different disciplines and with diverse backgrounds. They also promote dicussions, and provide a breeding ground for new ideas and research directions. CeMM sponsors several national and international conferences each year. In 2012, four conferences at the cutting-edge of biological sciences were organized by CeMM scientists and held at the institute. The organizers would like to thank all the speakers and participants that contributed to the success of these meetings.

iBiolMath Workshop

Approximately 120 scientists attended the first iBiolMath Workshop on February 16, 2012, at CeMM. Initiated by Heinz Engl, Rector of the University of Vienna and Director of the Johann Radon Institute for Computational and Applied Mathematics (RICAM), Giulio Superti-Furga, CeMM Director, and Magnus Nordborg, Gregor Mendel Institute (GMI) Director, the workshop was designed to integrate molecular biology and biomedical sciences with computational biology and applied mathematics, which are becoming increasingly interlinked. The one day workshop, organized by Jacques Colinge (CeMM) and Philipp Kügler (RICAM), stimulated interdisciplinary research activities among Viennese scientists working in the areas of mathematics linked to biology or medicine. Thirteen presentations, an inspiring keynote lecture by Peter Schuster, as well as a poster session formed the basis for lively discussions and networking among the large number of participants.

Austrodrugs 2

Beginning in 2011, the Austrodrugs Initative aimed to bring together the Austrian community of academic chemical biologists and industrial drug discoverers. To strengthen and expand this community and shape future European public-private initiatives, Giulio Superti-Furga and Stefan Kubicek organized the second Austrodrugs meeting on March 19, 2012, at CeMM. Together with CeMM Principal Investigators (PIs) Sebastian Nijman and Christoph Bock, they highlighted the development of high-impact chemical biology publications and the Platform Austria for Chemical Biology (PLACEBO). In 10-minute "speed-dating" presentations, new members of the community had the chance to present their expertise and resources. Steffen Hering introduced the doctoral program "Molecular Drug Targets" to educate the next generation of Austrian chemical biologists. Renate Schnitzer, Head of Screening at Boehriger Ingelheim Vienna, and arguably the industrial high-throughput biology expert in Austria, gave an excellent presentation on research and technological focus of the company, and Georg Casari, CEO of the start-up Haplogen presented its focus on haploid cells for experimental human genetics in a test tube. The meeting was followed by a workshop co-organized by Ylva Huber from the Austrian research promotion agency (FFG), and Hemma Bauer from the Austrian Ministry for Science and Research (bmwf), where opportunities and challenges of the initiative, and possibilities for future interaction and collaborations were discussed in a networking session.

Together with Giulio Superti-Furga Stefan Kubicek organized the second Austrodrugs meeting.

VIIRUS Symposium

Thanks to new molecular medical facilities at CeMM, the Medical University of Vienna, the Vienna Biocenter, and the Institute of Science and Technology (IST) Austria, the Vienna region has emerged as an internationally recognized scientific research hotspot for immunology and infection. The first Vienna Infection Immunology Researchers - United Symposium (VIIRUS) held at CeMM on May 24, 2012, was designed to provide an overview of the cumulative know how and combined resources of this growing bio-research cluster. Organized by CeMM PIs, Sylvia Knapp and Andreas Bergthaler, it brought together more than 30 research groups actively involved in this topic. Around 100 scientists from various disciplines, including medicine, molecular biology, biochemistry, veterinary medicine and systems biology set the stage for collaborations, common grants and future local symposia.

The Viirus meeting brought together more than 30 research groups involved in immunology and infection.

ECBS Meeting 2012 Small Molecules for Big Biology

More than 130 researchers from all over the world joined the ECBS Conference in the Austrian Academy of Sciences, organized by CeMM. Notice that many participants have a fan in their hands.

Small molecules can have a profound impact on biological systems. To discuss topics such as "finding the small molecules", "big questions on the cell cycle", "big roles - big tasks", "one drug - one system approach", the third European Chemical Biology Symposium / second CeMM Vienna Drug Action Conference took place at CeMM and in the Festive Hall of the Austrian Academy of Sciences. The 3 day conference, from the 1st to the 3rd of July, 2012, was literally the hottest conference to be held at CeMM, with temperatures of 40 degrees Celsius due to a local heatwave. The meeting was attended by more than 130 researchers from all over the world, sharing an interest in the interdisciplinary field of Chemical Biology. It opened with a key-note lecture by Stuart Schreiber, Director of the Chemical Biology Program of the Broad Institute of Harvard and MIT, and comprised 20 talks by invited speakers as well as short talks from participants and extended poster presentations. The sessions encompassed a broad spectrum of modern chemical biology research from drug screening and drug discovery to cell differentiation and therapeutic innovation in the systems biology era.

CeMM and Society

Scientific research produces many social and economic benefits, and is an integral part of any society. It is therefore critical for institutes and universities where research is performed to embrace the societies in which they reside in order to actively integrate the diverse views and cultures into their own values and operations. This involves promoting communication between society members and scientists. In 2012, CeMM was honored with several important visitors, including Prof. Karlheinz Töchterle, Federal Minister of Science and Research and; the Presidium of the Austrian Academy of Sciences; Dr. Michael Häupl, Mayor of Vienna; and EU-Commissioner Dr. Johannes Hahn.

Visitors to CeMM

March 12, 2012 CeMM was honored with a visit from Prof. Karlheinz Töchterle, Federal Minister of Science and Research and the Presidium of the Austrian Academy of Sciences. “The importance of basic research for the long-term improvement of medical care is evident”, Karlheinz Töchterle summarized, emphasizing the advantages of CeMM’s focus on bridging the laboratory bench and the clinic, and it’s location adjacent to the Vienna General Hospital and the Medical University. “CeMM is a role model for successful collaboration between a flagship institute of the Austrian Academy of Sciences and the Medical University of Vienna.”

April 24, 2012 Federal Minister Karlheinz Töchterle accepted another invitation to join the presentation of CeMM’s 2011 annual report, which was held in the historic reading room of the Josephinum. The choice of location reflected the central theme of the report: to build a bridge from the exceptional anatomical wax models displayed in the Josephinum to the molecular medical research performed at CeMM. Among the guests: Liechtenstein Ambassador to Austria, Her Excellency Maria-Pia Kothbauer; the Rectors of the Medical University, Wolfgang Schütz, Christiane Druml, Karin Gutiérrez-Lobos, and Franz Wurm; the President of the Austrian Academy of Sciences, Sigrid Jalkotzy-Deger; and the Brain Lounge designer duo of “Walking Chair”, Karl Emilio Pircher and Fidel Peugeot.

July 19, 2012 Dr. Michael Häupl, Mayor of Vienna and one of the fathers of the institute visited CeMM for the first time. In-depth discussions with the trained biologist made the visit a memorable event. Mayor Häupl highlighted the importance of CeMM, and its close collaboration with the General Hospital and the Medical University of Vienna, for medical-oriented research.

August 31, 2012 EU-Commissioner Johannes Hahn paused on a trip through Europe to visit CeMM. The former Minister of Science and Research was one of CeMM’s supporters in the early stages. It was his first visit to the new building, where he received an update on the progress and spirit of optimism of the young and dedicated team.

October 31, 2012 U.S. Ambassador to Austria William C. Eacho and Mrs. Eacho also visited the institute to learn about the developments of modern molecular medical research going on at CeMM. They were particularly interested in the PLACEBO Lab, Mass Spectrometry and the Next Generation Sequencing Unit.

“Science is the surrogate of art.”

Bela Julesz (1995)
Dialogues on Perception,
THE MIT Press, Boston, Mass.

Esther Stocker (*1974, Silandro, Italy)
Esther Stocker studied at the Academy of Fine Arts, Vienna (1994-1999), at the Accademia die Belle Arti di Bera, Milano (1996) and the Art Center College of Design, Pasadena, CA (USA, 1999). In 2001 she received a state scholarship in Visual Arts. Esther Stocker has been honored with many important awards, including the Visual Art Award of the City of Vienna (Preis der Stadt Wien, 2009), the South Tyrolean Award for Site-Specific Art (Südtiroler Preis für Kunst am Bau, 2002) and the Otto Mauer Preis (2004). She lives and works in Vienna. For the CeMM Brain Lounge she created the north wall (film on wood).

“Art and science address common issues, yet approach them in different ways. They complement each other through the respective differences in their methods, which only too rarely intersect in places to germinate new questions. One such place is CeMM.”

Thomas Feuerstein (*1968, Innsbruck, Tyrol)
Feuerstein’s work encompasses installations, objects, drawings and paintings as well as sculptures, photographs and videos. Substantial aspects of his art are modes of connection and analogies between art and science, sociology and biology that regulate the interdependence between organisms and environment. For the CeMM Brain Lounge he created a chair backrest artwork.

Brain Lounge Opening

Let's go for a little fresh thinking!
On November 19, 2012 the opening of the CeMM Brain Lounge, a special think room and "Gesamtkunstwerk" took place as part of Vienna Art Week, which is an art event with international resonance. The scientific community and many art lovers were invited to interact with the designers and artists that developed the Brain Lounge, which is situated on the eighth floor of the CeMM building, overlooking Vienna's skyline. The opening began with a surprise performance by the experimental theatre group Toxic Dreams, which was projected live into the CeMM seminar room, before the guests were invited to become part of the think fest themselves.

Merry Go Round
A Turning Set of Active Tableaus

Fidel Peugeot, Karl E. Pircher and Giulio Superti-Furga at the opening ceremony.

Spin around, think around, reload your brain …
The central piece of the Brain Lounge is a carousel with 14 leather chairs. Their reverse side is detachable and meant to be designed by artists, currently they present work by Eva Schlegel, Thomas Feuerstein, Martin Walde, Alois Moosbacher and Dorothee Golz. The walls display artworks of Esther Stocker and Brigitte Kowanz, and the ceiling is full of "sister blister" lamps by Walking Chair, which look like clouds. The fashion designer Daniel Kroh, working in Berlin, is responsible for the design of the special Brain Lounge costumes. With the designers Karl Emilio Pircher and Fidel Peugeot leading the way, they joined CeMM in creating a space that serves as a knowledge-generating environment. Most of the artists were present at the inauguration. While the actors of Toxic Dreams celebrated the "birth of thoughts" in three acts in the Brain Lounge the guests could follow the performance via video from the CeMM lecture hall and prepare themselves for a ride in the Brain Lounge's thinking carousel. Christiane Druml, Vice Rector of the Medical University of Vienna, Ulrike Felt, Professor of Social Studies of Science, Vienna University and journalists and communications experts Conny Bischofberger and Michael Fleischhacker were designated captains of the first journeys and the lucky passengers were selected by a card game. Every Brain Lounge journey begins with a ritual meant to abandon the daily routine and professional habitus and encourage the participant to assume a new identity. Then, by being exposed to an environment of changing art and a science fictional ambience, riders of the Brain Lounge can be induced into a different, playful state of mind. The slow turning of the sitting carousel provides a constant change of views and evokes a sense of communality amongst fellow travelers. A logbook is available to record the intellectual journeys. With its synergy of art, science, medicine and design, the Brain Lounge should act as a breeding ground for new ideas. The first travels were enthusiastically navigated and the entries in the logbook report strong intellectual breezes and even some storming thoughts!

We thank all artists, donors and sponsors who have helped us to realize the project this far.

Tableau 1 - The life of thinking monkeys.
The table turns counter clockwise. The performers wear monkey masks. While turning, they perform gestures of thinking monkeys (e.g. scratching the head, shaking arms violently, dismissing each others mode of thinking). Music: cartoon Looney Tunes and a dramatic score taken from the Japanese version of King Kong. (2 to 3 min)

Tableau 2 - Sweet life.
The table turns clockwise, slow speed. The performers dress as if on a Hawaiian vacation (flower garlands etc.). They perform a slow dance, alternating between seating and standing. Music: Hawaiian. (2 to 3 min)

Tableau 3 - Brain feeder.
The table turns clockwise at the fastest speed. The performers wear underwear. They touch, stroke their bellies in different speeds alternating between sitting and standing. They eat candy-bars while moving. Music: Junk is no good baby, Brion Gysin (2:05)

A performance by:
Toxic Dreams
Written and directed by:
Yosi Wanunu
Produced by:
Kornelia Kilga










Ph.D.-Program and Social Life at CeMM

According to a recent survey conducted by The Scientist published on 1 August 2012, CeMM is the best academic place to work in Europe. Internationally, CeMM was in fourth place. The survey ranks academic and personal satisfaction in the work place and has been conducted by the journal for the last 10 years.

CeMM is a lively, international place. The young institute for molecular medicine runs a very popular and successful Ph.D. program. In 2012, about 550 young scientists applied for 8 positions. In total, there are currently 45 Ph.D. students at various stages of their studies enrolled in the Ph.D. program at CeMM. Of course, the level of scientific skill and knowledge are placed high on the list of important requirements in the selection process. On top of these is something else. CeMM looks for outstanding personalities and is willing to support talent and offer room for creativity and interaction. For example, the sport/activity program at CeMM includes a wide range of different goings-on. Ranging from a sophisticated bridge circle to a venturesome climbing group, a yoga troupe, several serious and ‘run-for-fun’ athletes and, of course, a soccer team. Specific events have become established, annual traditions.
An outing in autumn, the Halloween Ball and Christmas party are regular events in the intensive social life at CeMM.

Ph.D. Program

October 2012 marked the start of the fifth CeMM Ph.D. program for 8 new Ph.D. students, who were selected from almost 550 applicants. The first phase of the program involved an intensive schedule of lectures, soft skill courses and workshops presented by PIs from CeMM and the neighbouring Medical University of Vienna. In order to gain insight into the different projects and technologies, to get to know the people in other groups and foster potential future collaborations, students spend a few weeks in two different laboratories at CeMM throughout November and December. There were also excursions to two historically important institutions: the Austrian Academy of Sciences, the statues in which provided inspiration for the 2009 Research Report; and the Josephinum, which houses an extensive collection of medical wax models; some of which were presented in the 2011 Research Report. There were also trips to several local prestigious research institutes, specifically IMBA and IMP, both located in the third district of Vienna, and IST Austria, near to Klosterneuberg.

CeMM as Intellectual Hub

One of the new Ph.D. students, Bernd Boidol, describes his experience of the selection process and his first few months at CeMM, including laboratory rotations, exciting guest speakers, and the odd party.

Bernd Boidol

"After a challenging, two-day selection round with various panel interviews, a presentation of my previous research projects, and numerous conversations with other applicants and CeMM scientists, I was excited to finally receive an offer to join the CeMM Ph.D. program. The first month consisted of a densely-packed schedule of introductory lectures and workshops on project planning, scientific writing, and presentation skills. Moreover, we got to know every principal investigator's area of research and received valuable advice on how to make the best of the forthcoming 3 years as Ph.D. students. Additionally, we were in charge of organizing the annual Halloween Ball, which was a great opportunity to work together as a team and introduce ourselves to the CeMM community. The subsequent lab. rotations in two different groups allowed me to gain deeper insight into methods and techniques that I am now frequently using for my own projects. I greatly benefited from my supervisors' dedication during that time and the outstanding support from the host groups. Furthermore, these two months enabled me to build a network of peers with whom I can discuss my research on a regular basis, even outside of the weekly project meetings. CeMM not only urges groundbreaking research, it also supports its employees with a collaborative and community-like framework to achieve this goal. Annual excursions and extracurricular activities are part of the life at CeMM and help to make new friends, get to know people's research, and have a fun time outside of work. The multitude of invited speakers from top universities and research centers all over the world, a steady exchange of ideas with scientists from the adjacent General Hospital and the Medical University of Vienna, as well as national and international collaborations, make this place one of the intellectual hubs in Europe and the world. For me, it is extremely exciting to be part of this venture and I am glad to have the opportunity to earn my Ph.D. degree at CeMM."

CeMM PhD students visiting the Josephinum with Professor Dontscho Kerjaschki.

Some of the other Ph.D. students that started in 2012 have also shared their thoughts on CeMM.

Katrin Hoermann

"I can't think of any other cutting-edge research institute offering a Ph.D. program where curiosity and passion for science blends in so perfectly with practicing yoga or performing a legendary Harlem Shake."

Cecilia Domínguez Conde

"The high standards of research at CeMM and in particular the strong focus on immunological aspects of disease were crucial for my decision to join the CeMM Ph.D. program."

Johanna Klughammer

"Getting a new (PhD) project started is hard work, but with CeMM's amazing culture of collaboration, interaction and communication you can be sure to find people who will readily share their experience and knowledge."

Anna Skucha

"What I can say is that I'm amazed that we – as CeMMies – are such a great team. Even though everybody has some friends outside of CeMM we spend lots of time together, doing sports, having fun etc."

Social Activities

Sport
The year of 2012 saw the introduction of yoga classes at CeMM. As busy scientists, we spend too much time confined to physically sedentary lifestyles and abominable periods sitting hunched over a computer thereby causing undue muscle tension to the detriment of good posture. What better way to meld scientific minds with relaxation and stress release and ease of access to exercise on site. Michelle Froehlich was recruited to teach the style of yoga-flow. Also, 2012 was a successful year for the soccer team. With fancy footwork and a high team spirit spurred on by exceptional cheerleading talent, the team earned a fabulous second place in the soccer tournament for scientists - SURF 2012.

Long Night of Science
Team spirit was also an important factor for success during the participation of CeMM at "Die Lange Nacht der Forschung" in the Hall of Sciences in the first disctrict of Vienna. Together with other institutes of the Austrian Academy of Sciences, CeMM took the chance to present our research to the public in order to raise awareness for research and development in Austria. Presentations, small experiments and especially an entertaining pipetting contest and a quiz attracted many visitors; particularly children and adolescents.

Outing
The institutionalized autumn event (fortunately always on a very sunny day) is designed to greet the new semester with enthusiasm and to take the chance of meeting old and new colleagues in a relaxed atmosphere. The outing for 2012 was a cultural trip through the history of Austria from the Romans to the Baroque period, from the Archeological Park Carnuntum to the Imperial Palace Hof. During the stay at the hunting lodge for Prince Eugene of Savoy, the new Ph.D. students took the chance to introduce themselves and involve their colleagues in an amusing quiz.








Parties






Halloween
The organization of the Halloween Ball is an integral part of the first few months of the Ph.D. program. The exercise is designed as a team building event and a training exercise to develop organizational skills. On top of this, it is a show of exceptional creativity in preparing fancy costumes, acting and dancing.

Christmas Party
Each year it is becoming increasingly difficult to organize the Christmas party for the expanding CeMM team. This is challenging as several requirements need to be fulfilled: the location has to have a cosy and comfortable dining room, excellent food, a well-equipped theatre for organized and impromptu input from our creative CeMM people, a perfect dance floor and concert hall. Additionally, it is important to maintain harmony such that no neighbours are disturbed in the wee hours of the morning. A stone's throw away from CeMM, the perfect location was the Projektraum at WUK.

“Penthouse office goes Brain Lounge. We wish you a happy, inspiring voyage! Let us sing:

Anything can happen so
let it go, let it go, let it go
Many things will be happening
when you know, know, know

I know that you know,
so you make me know
Now you know that I know
and I let you go

Many things will be clear
when you go around
Anything can be highlighted
when you roll around and around

Now you know what I know
and you say oh, oh, oh,
Then I know what you say
means we go, we go, let’s go”

Walking Chair – Karl E. Pircher and Fidel Peugeot
After working as a mechanical engineer and teacher, Karl E. Pircher (*1963), a native of South Tyrol, studied with Ron Arad at the University of Applied Arts, Vienna and received several international design-awards. Fidel Peugeot (*1969), a Swiss national, has had a successful career as a graphic designer and font designer, also touring as a musician in a number of bands. The two met in projects for the Lomographic Society and immediately perceived each other to be the essential completion. Together they established the Walking Chair Design Studio in 2003. Karl and Fidel are responsible for the CeMM Brain Lounge design.

“The virus of art is permanently present at the CeMM brain lounge!”

Eva Schlegel (*1960, Hall, Tyrol)
Eva Schlegel studied with Oswald Oberhuber at the University of Applied Arts, Vienna (1979-1985) and served as Professor for Photography at the Academy of Fine Arts, Vienna (1997-2006). After participating in the Venice Biennial in 1995, she was commissioner of the Austrian Pavilion in 2011. For the CeMM Brain Lounge she created a chair backrest artwork.

Scientific Advisory Board

The fourth evaluation of the Scientific Advisory Board (SAB) took place from November 11-13, 2012. Eight members were able to participate. They were Richard Flavell/Yale University, James D. Griffin/Dana Farber Institute Boston, Carl-Henrik Heldin/Ludwig Institute Uppsala, Denis Hochstrasser/ Geneva University Hospital, David Livingston (CHAIR)/Dana-Farber & Harvard Cancer Center Boston, William E. Paul/NIAID Bethesda, Hidde Ploegh/Whitehead Institute Cambridge and Nadia Rosenthal/ Australian Regenerative Medicine Institute. On the next page the general part of their report is presented.

Excerpt from the Report of the CeMM Scientific Advisory Board

"Scientific performance of CeMM as reflected by the presentations of its trainees:
One day of our visit was fully occupied by concise scientific presentations by 25 research trainees (a mixture of students and post docs) who represent all of the Center's research laboratories. We also received presentations from Jacques Colinge, Head of Bioinformatics, and Keiryn Bennett, Head of Mass Spectrometry.

The overarching impression of these talks was that: a) the science at CeMM is world class. All laboratories are doing superb work. The collective publication record of CeMM in the past two years is enviable, with multiple papers in the highest profile journals, b) The science at CeMM has advanced significantly in breadth and depth during the past year; c) The trainees it has attracted and is attracting now are as fine a group as exists in any superb European research center and in many top American ones, as well; and d) The two largest and most advanced core functions at CeMM Bioinformatics and Proteomics are also of excellent quality.

The overarching message of these presentations is that, despite its small size, cancer science and research on human immunological disease, atherosclerosis, infection and epigenetics at CeMM are outstanding. This is an enviable accomplishment, and the fact that this level of accomplishment has been achieved in a short period of time is remarkable.

Giulio Superti-Furga as CeMM leader:
In our view Dr Superti-Furga is an outstanding, vigorous, and strong leader of CeMM and a superb scientist. He is a role model for his faculty colleagues. We urge his reappointment most enthusiastically. A better leader would be hard to imagine, much less to be found for CeMM, Few – if any – would have led a new and very small Institute with an ambitious agenda to the levels of success now on record in only 6–7 years.

We also urge most strongly that he be appointed as a tenured Professor at MUV without major teaching or administrative obligations. His dedication to and uniquely effective leadership of CeMM are, we believe, a formula that will also benefit MUV. It will do so in ways that are especially beneficial to MUV as a neighbor, a natural research partner of CeMM, and a center of clinical research that can be significantly enriched through translational and basic scientific collaboration with CeMM.

We are also aware of the growing responsibilities for mentoring young faculty and overseeing the daily science of CeMM, now that it has expanded to its physical limits. Dr Barlow has done well in this regard, and her efforts are greatly appreciated by the CeMM faculty. As she approaches retirement, we are concerned lest the post of deputy director not be created and filled.
Dr. Superti-Furga has too many responsibilities to be able to handle his own portfolio and that of a deputy director charged in part with mentoring and daily scientific operations oversight, not to speak of her/his own research program. We therefore urge the Academy to allocate funds to recruit a senior faculty member who is both a distinguished and highly successful scientist as well as a proven leader with respected administrative ability."

Contributing Members: Richard Flavell, James Griffin, Carl-Henrik Heldin, Denis Hochstrasser, David Livingston, William Paul, Hidde Ploegh, Nadia Rosenthal

For issues of confidentiality, including comments on individual scientists and intellectual property, it was decided to publish here only the general summary of the report.

Members of the CeMM Scientific Advisory Board

In strategic and scientific questions CeMM is advised by a board of international top-scientists:

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

Prof. Dr. James D. Griffin
Chair, Department of Medical Oncology,
Dana Farber Cancer Institute, Boston, USA

Prof. Dr. Carl-Henrik Heldin
Director, Ludwig Institute for Cancer Research,
Uppsala University, SE

Prof. Dr. Denis Hochstrasser
Head, Central Clinical Chemistry Laboratory,
Geneva University Hospital, CH

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

Prof. Dr. William E. Paul
Chief, Laboratory of Immunology,
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Member, Whitehead Institute for
Biomedical Research, Cambridge, USA

Prof. Dr. Nadia Rosenthal
Australian Regenerative Medicine Institute,
Melbourne, AU

Prof. Dr. Louis M. Staudt
Head, Molecular Biology of Lymphoid
Malignancies Section, National Institutes of Health,
National Cancer Institute, Bethesda, USA

The Austrian Academy of Sciences

The Austrian Academy of Sciences, founded in 1847, is the leading organisation promoting non-university academic research institutions in Austria. It developed from being a mere learned society into an organisation promoting modern scientific research institutions. In the awareness of its social, cultural and economic responsibility, the Academy conducts basic research which is open for practical applications, and its members support this function by making their broad range of expertise available to the public and advising decision makers in politics and business. The Academy is currently promoting 28 research institutions with more than 1100 employees, which are located in several federal states of Austria, with the headquarters in the Old University in the center of Vienna. In the stunning 18th century frescoed festive hall of the Austrian Academy of Sciences (where Haydn and Beethoven conducted premieres of their work) CeMM holds its yearly Landsteiner Lecture.

The Academy gave new impetus by taking up forward-looking research areas. Scientific quality, innovation potential and sustainability are the main criteria for its research profile. The connection between basic research and clinical research has been established by setting up CeMM, one of several Academy institutes that stand the test of international competition.

The main building of the Austrian Academy of Sciences in the 1st district of Vienna.

Sponsor Us!

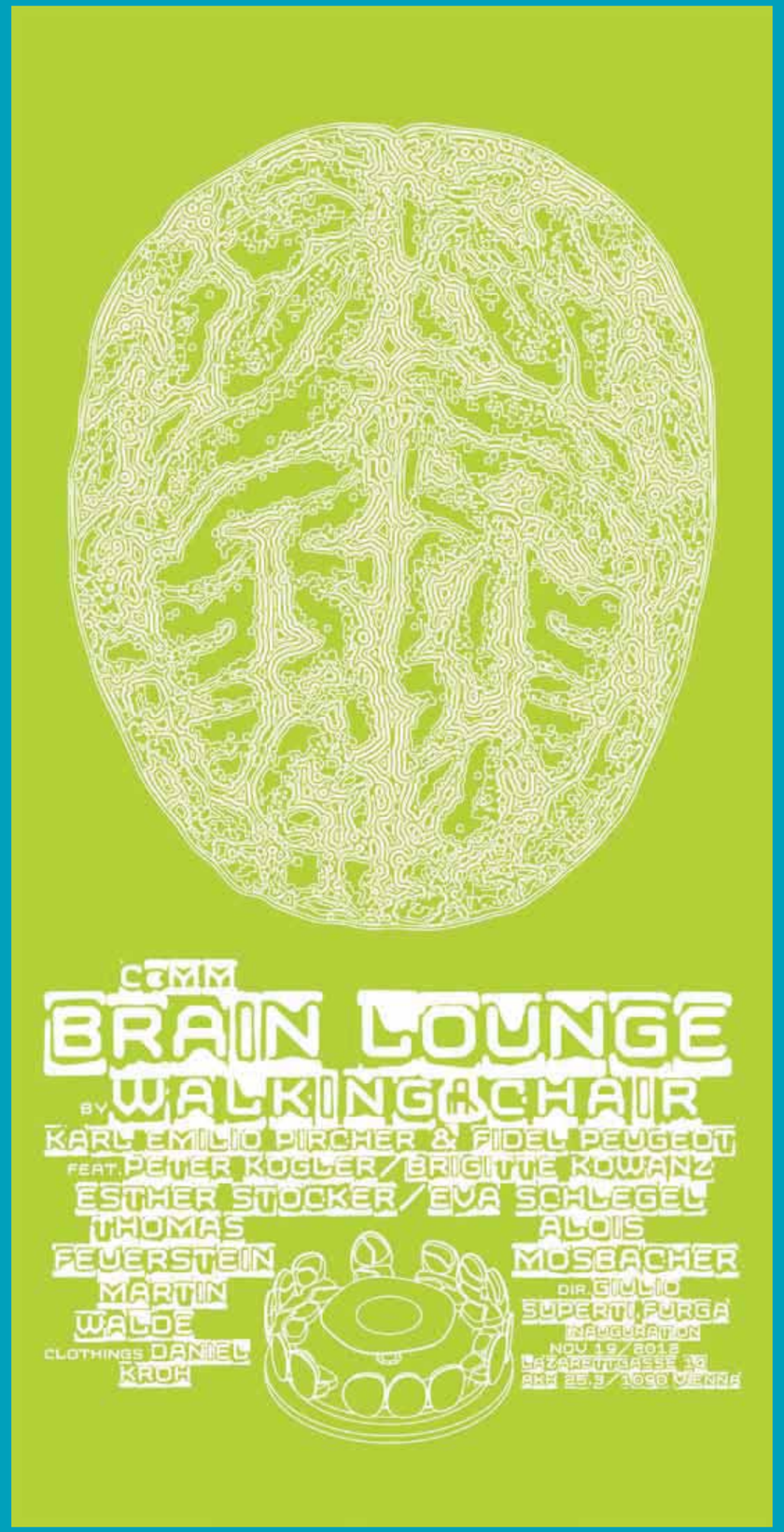
For the sponsorship program please contact Eva Schweng (eschweng@cemm.oeaw.ac.at, +43-1/40160-70 051) or Giulio Superti-Furga directly (gsuperti@cemm.oeaw.ac.at, +43-1/40160-70 001).

We kindly ask for contributions to the following account:
CeMM Forschungszentrum für Molekulare Medizin GmbH
UniCredit Bank Austria AG
Konto: 01270418501
BLZ: 12000
SWIFT: BKAUATWW
IBAN: AT291100001270418501
Reason for Transfer/ Verwendungszweck:
(A) CeMM Brain Lounge
(B) CeMM Projects

(A) Sponsor the CeMM Brain Lounge – Ideas first!
The CeMM Brain Lounge was built to promote new research ideas, ideas for the medicine of the future, and for a better society. We kindly invite everybody who believes in the fertile interplay of science, art, medicine and society to sponsor this on-going project. Every contribution is welcome. For a donation of 1,000 Euro or more, you will receive a signed print by Peter Kogler and Walking Chair titled "Brain Lounge" (limited edition of 100), acknowledgement and privileged access to the Brain Lounge.

Even if it helps to generate only ONE good idea and the idea can change the world, it is worthwhile.

(B) Sponsor CeMM research projects
If you think that the research into future medicines should not be left entirely in the hands of businesses, if you think that society needs to take a better informed and more active role in the health management options of the future, and if you think that knowledge is our biggest asset for the future, then these sponsoring opportunities are for you. We have an entire sponsoring program, with the ability to support individual research projects, professorships, fellowships, training projects or important research instrumentation. It is also possible to give names to rooms, laboratories and even the whole institute ("Your name" Center for Molecular Medicine). At a minimum, for your donation you will receive a symbolic CeMM Health Research Bond certificate that you can treasure or give as a gift.



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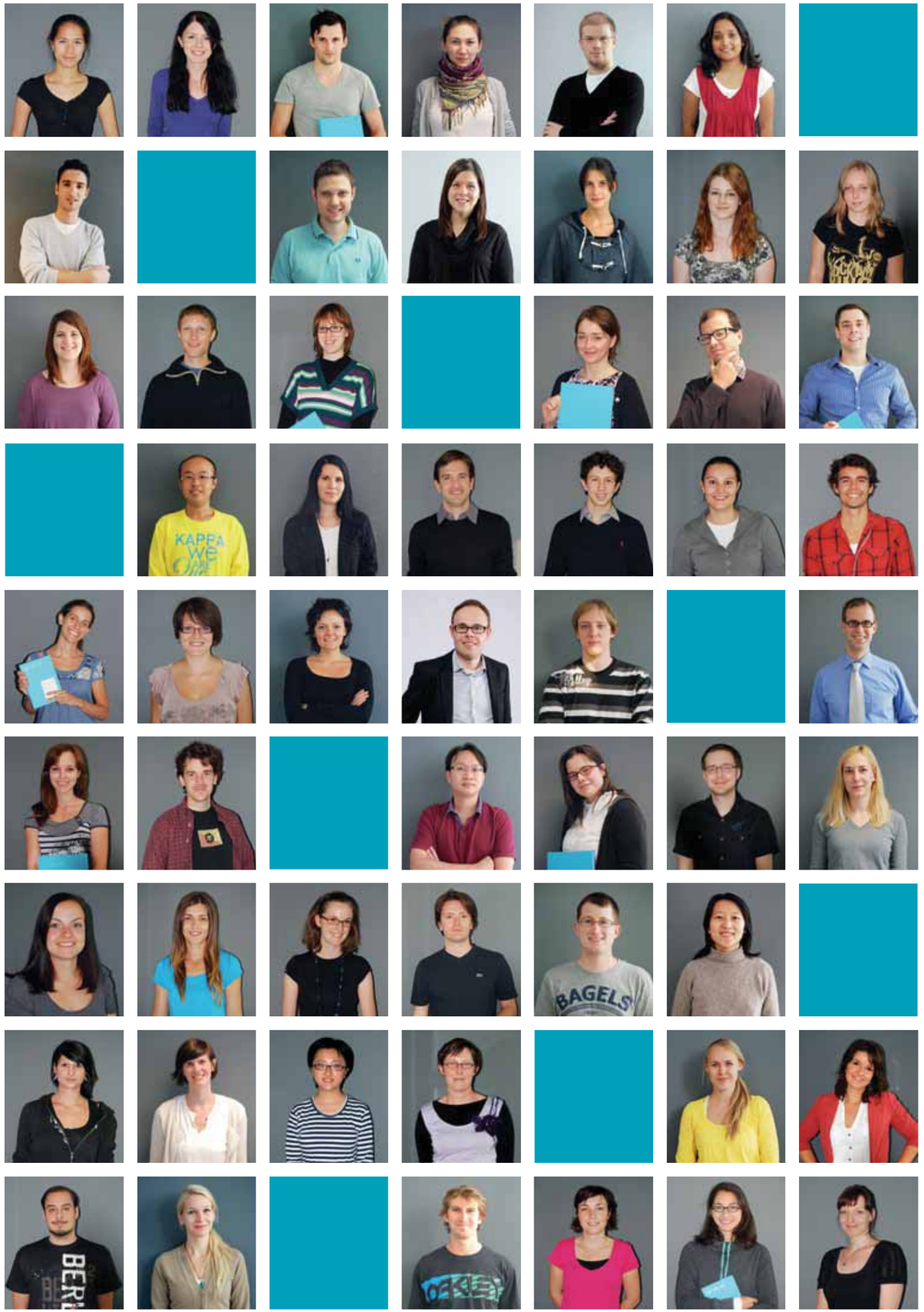
31 Nationalities



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Legend of Grants

Boehringer Ingelheim
Collaboration Project
"Epigenome-wide multiplexed quantification of histone modifications"

EMBO LTF
Long Term Fellowship of the European Molecular Biology Laboratory

ERC AdG I-FIVE
Advanced Investigator Grant
"I-FIIVE: Interferon-focused Innate Immunity Interactome and Inhibitome"

ERC PoC AIRSHIP
Proof of Concept Grant
"AIRSHIP: Acute Inflammation Resolution by Soluble Human Inhibitory Protein"

EU ASSET, EU Project
"ASSET: Analysing and Striking the Sensitivities of Embryonal Tumours"

EU CIG EPICAL
Marie Curie Career integration Grant "EPICAL: Systematic Identification and Validation of Epigenetic Cancer Lesions by Chemical Biology and Functional Genomics"

EU HEM-ID, EU Project
"HEMatopoietic cell IDentity: genetic and epigenetic regulation in normal and malignant hematopoiesis"

EU OPENSCREEN, EU Project
"OPENSCREEN: European Infrastructure of Open Screening Platforms for Chemical Biology"

FWF F43
Special Research Program
"RNA Regulation of the Transcriptome"

FWF I291B09, ERA NET
"PathoGenoMics: Pathogen-Host Metabolomics and Interactomics"

FWF P21768
Stand Alone Project
"Searching for Cancer Achilles' Heels"

FWF P22282
Stand Alone Project
"Regulo-Interactome Modules of Hematopoeitic Stem Cells"

FWF P23257
Stand Alone Project
"Heriditary Predispositions to Myeloproliferative Neoplasms"

FWF P23991
Stand Alone Project
"Role of Oxidative Stress in Viral Hepatitis"

FWF P24217
Stand Alone Project
"Regulation of innate immunity by DEAD box RNA helicase DDX3X"

FWF P24321
Stand Alone Project
"Statistical Modeling ofProtein Modification Regulation"

FWF P24766
Stand Alone Project
"Molecular Characterization of Non-Canonical ATM Signaling"

FWF W1205 DK
Doctoral Program
"CCHD: Cell Communication in Health and Disease"

FWF W1207 DK
Doctoral Program
"Bioinformatics Integration Network III"

FWF Y595
START Grant
"Innate Immunity: Novel Genetic Defects and Pathophysiology"

GEN-AU BIN III,
Austrian Genome Research Program,

GEN-AU PLACEBO
Austrian Genome Research Program
"PLACEBO: PLatform Austria for ChEmical BiOlogy"

GEN-AU EPIGENETIC CONTROL
Austrian Genome Research Program
"Epigenetic gene regulation by imprinted macro non-coding RNAs"

GEN-AU APPIII
Austrian Genome Research Program, "Austrian Proteomics Platform III"

JDRF Grant
Juvenile Diabetes Research Foundation Canada
"Generation of functional ß-cells from alternative pancreatic cell subtypes"

ÖAW Doc Fellowship
Doctoral Fellowship Program of the Austrian Academy of Sciences

ÖNB Jubiläumsfonds
"Resistenz gegen PI3K/m TOR Inhibitoren bei Brustkrebs: Klinische Validierung von Biomarkern"

MPN
Myeloproliferative Neoplasms Foundation USA

WWTF LS09-009
"Searching for Cancer Achilles' Heels"

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Facts and Figures

Inclusiveness at CeMM

CeMM has a strong intellectual environment that stems from the international nature of its employees. Diversity and different cultural backgrounds are a clear advantage to successful research, collaborations, and the day-to-day business, as long as everyone follows a few basic principles, which at CeMM are: Professionalism, Politeness and Persistence. The working language at CeMM is English.

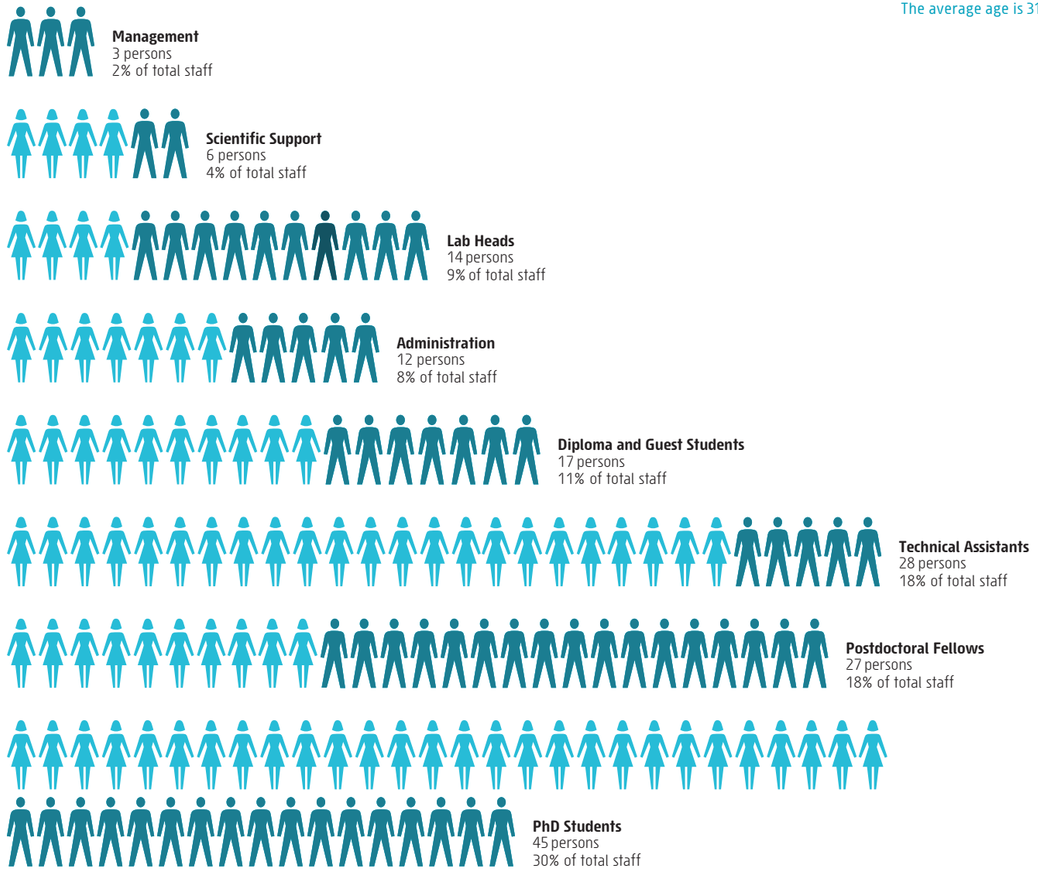
At CeMM, emphasis is given to mentoring independent young investigators and scientists early in their careers, through freedom, availability of infrastructure and a strong support system. A flat hierarchy, where the input of every single person is appreciated and required, leads to an enjoyable work environment and an increase in productivity and ideas.

CeMM is particularly interested in supporting and fostering women scientists in areas where the gender bias is more evident (like chemistry, screening, proteomics, bioinformatics).
In recruiting new scientists, a dedicated effort is made to engage female scientists and foster their career development as much as possible. Among faculty, 30% are female (Denise Barlow, Keiryn Bennett, Sylvia Knapp and Joanna Loizou). Currently the gender balance at CeMM is equitable (54% women in total) as one can see from the statistics in the annual report.

Staff

Listed by number of persons per field of work

CeMM stresses keeping the administration very lean and efficient. We have a very good gender balance, with a small surplus of women (56%). The average age is 31 years.



Management
3 persons
2% of total staff

Scientific Support
6 persons
4% of total staff

Lab Heads
14 persons
9% of total staff

Administration
12 persons
8% of total staff

Diploma and Guest Students
17 persons
11% of total staff

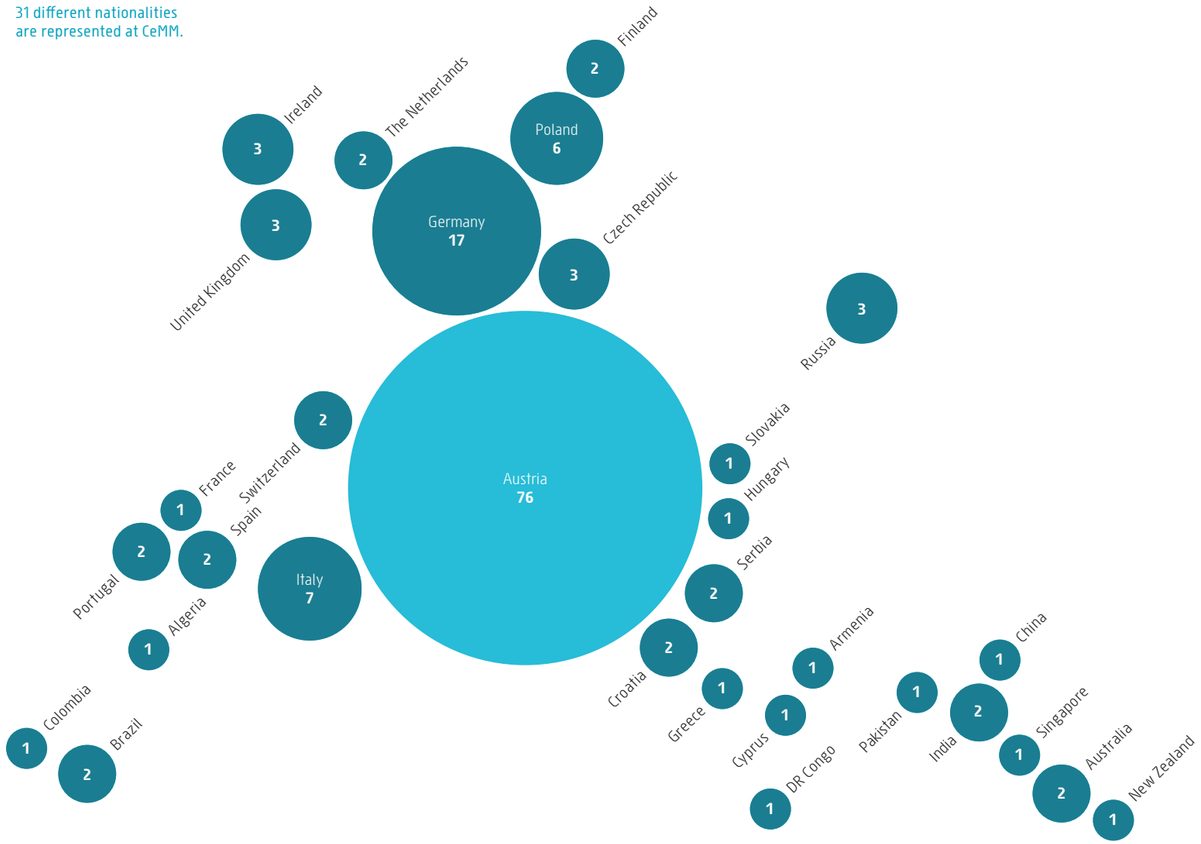
Technical Assistants
28 persons
18% of total staff

Postdoctoral Fellows
27 persons
18% of total staff

PhD Students
45 persons
30% of total staff

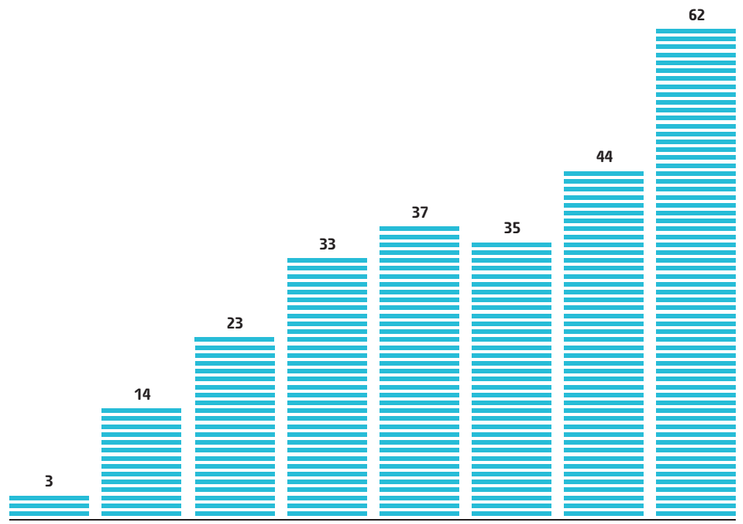
Nationalities at CeMM

31 different nationalities
are represented at CeMM.

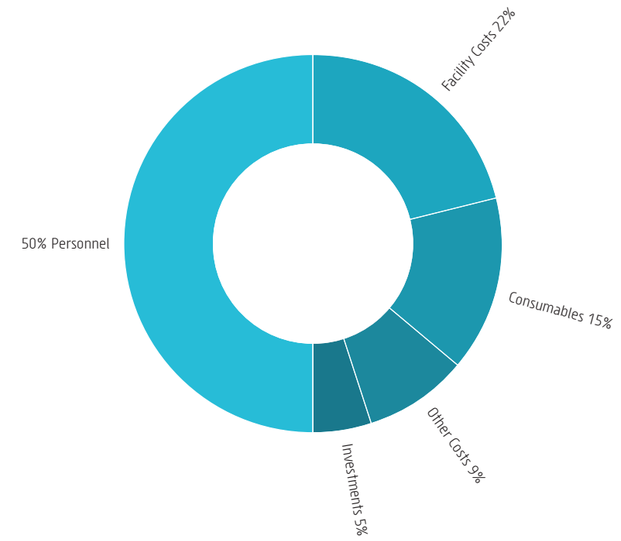


Publications

Includes all publications
by CeMM staff members
from the date of joining
the institute.



Expenses in 2012



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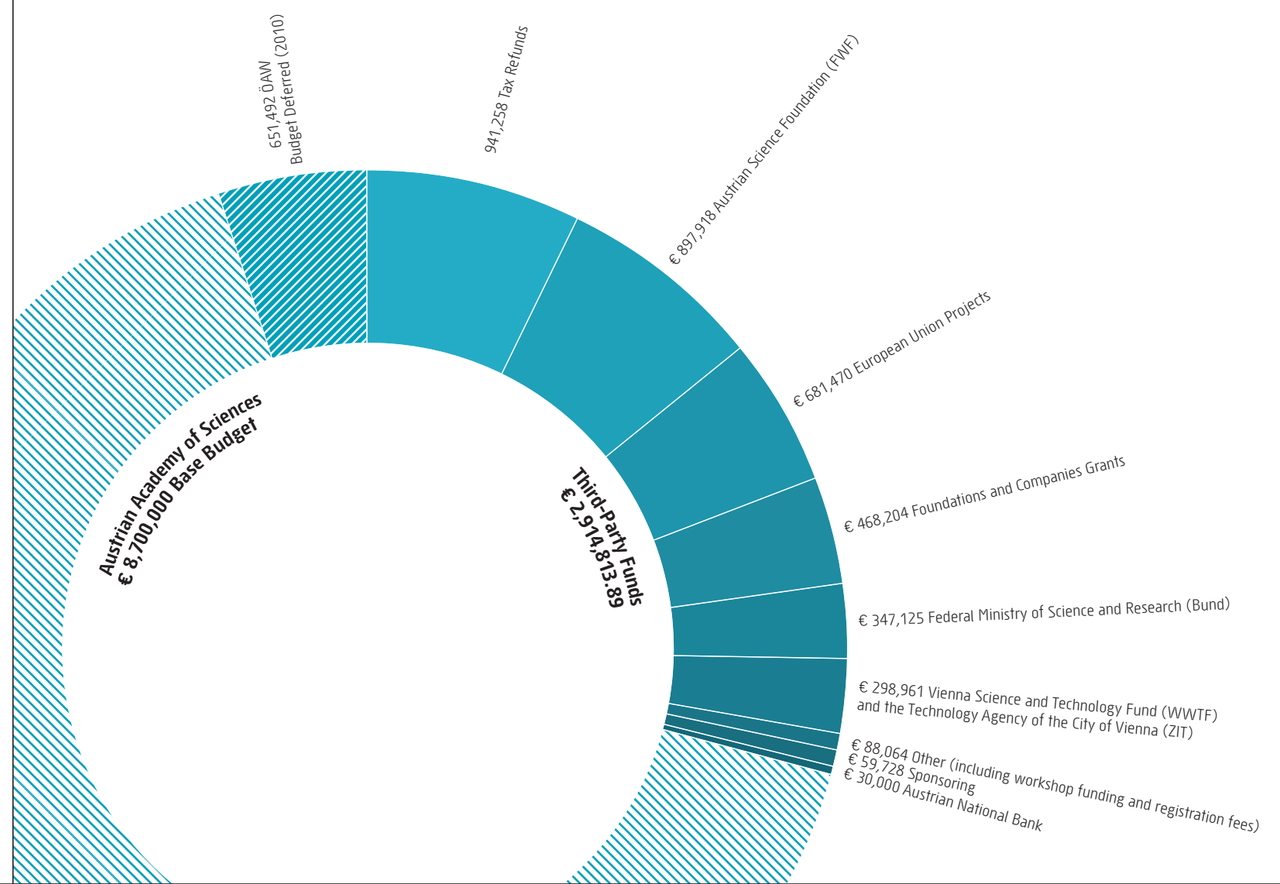

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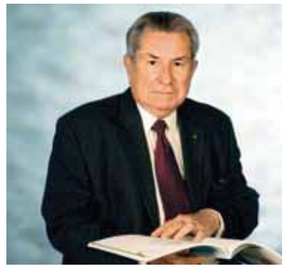

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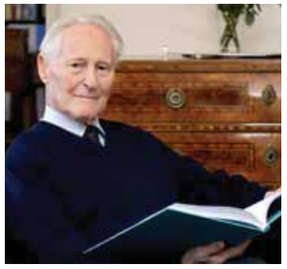

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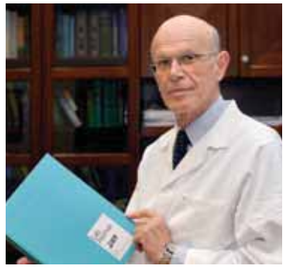

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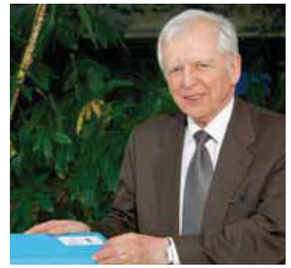

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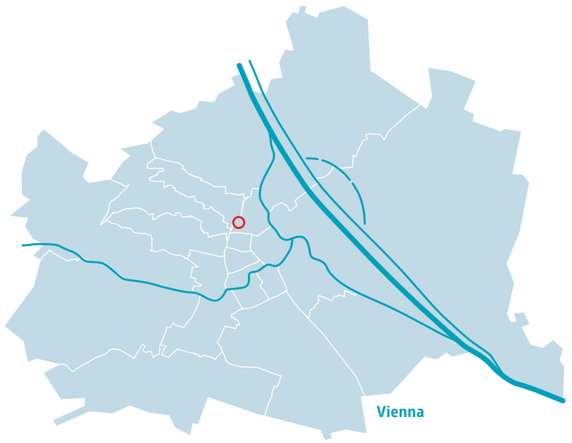

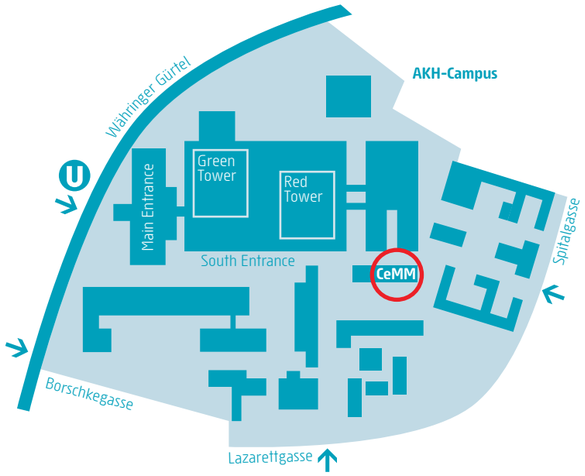

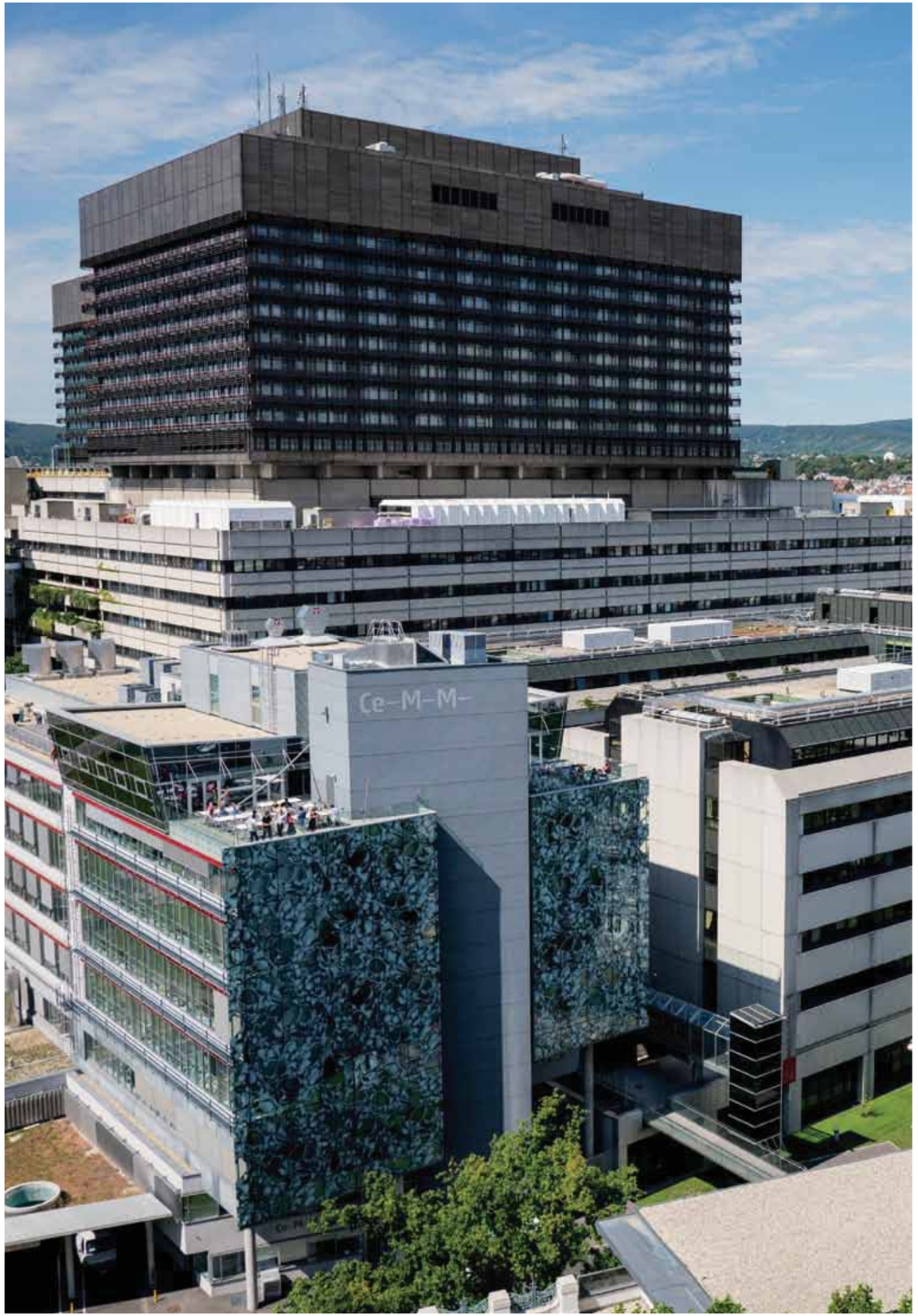

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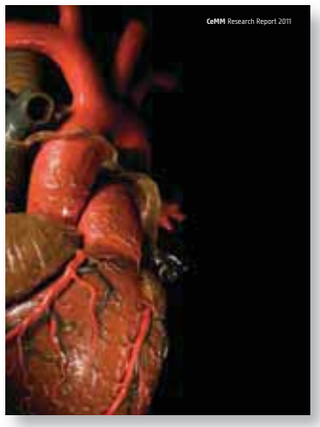

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