Ce–M–M–

Research Center for Molecular Medicine
of the Austrian Academy of Sciences

Research Report 2013

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CeMM Research Report 2013

Introduction by Giulio Superti-Furga

Giulio Superti-Furga
on a "Chair to Share"
by Dorothee Golz

The milestone of the year 2013: At the end of 2013, Robert Kralovics' group, in collaboration with the group of Heinz Gisslinger of the Medical University of Vienna, published the identification of a long-missing piece of a genetic puzzle that he had been trying to assemble for many years. This long sought-after gene is affected in all those patients having one of the several forms of the cancer-like disease of the blood called Myeloproliferative Neoplasms (MPNs), that did not carry a mutation in the other main gene of these disorders, Jak2 that Robert had identified back in 2005 or the thrombopoietin receptor gene. The new gene, encoding the protein called calreticulin, is mutated in an interesting way, not causing a loss of its function, but changing the functionality of the protein. This was entirely unexpected and sheds an entirely new light on fundamental processes of cell biology. So it has a strong impact on basic research. But the finding is particularly remarkable for its immediate impact on medicine. We estimate that hundreds of thousands of patients in the world carry the mutant calreticulin gene and based on Robert's results can now have a molecular diagnosis for their condition. Although targeted therapy for calreticulin will only be possible once we develop further an initial concept that Robert just conceived, the current optimal pharmacological regimen for calreticulin patients is slightly different than from Jak2 positive patients. Thus, personalized therapy through CeMM's research is a reality now. 2013, therefore, can be considered a turn-around year for CeMM, its first translational milestone has been reached. I congratulate Robert Kralovics and the formidable CeMM PhD student Thorsten Klampfl who has persisted in the quest, as well as the entire team involved. But I also wish to congratulate the scientists at CeMM's 7th floor that have contributed to the rapid and professional establishment of genomic sequencing and human mutation mapping, Christoph Bock, Kaan Boztug and their groups and the entire BS facility, operated in collaboration with the Medical University of Vienna.

Another great step towards becoming competent in a translational sense has been the installation of the Christian Doppler Laboratory for Chemical Epigenetics and Anti-Infectives, masterfully set-up and led by Stefan Kubicek and representing a collaboration with the companies Boehringer Ingelheim and Haplogen. We wish to thank the President of the Christian Doppler Research Association, Reinhart Kögerler, for the trust put by the Association into CeMM.

CeMM has been inspired in many ways by the pioneering activities of the Institute for Molecular Pathology IMP that I witnessed from the days of its conception as a "founding student" following Max L. Birnstiel and my mentor Meinrad Busslinger from Zurich to Vienna. The impact that the IMP has had on the Austrian research landscape in the life sciences cannot be overestimated in its immensity. We join the community that expressed its gratitude to Max Birnstiel who celebrated its 80th birthday in the summer and on behalf of CeMM now express once more our admiration for Max and renew our wishes. We also congratulate Jan-Michael Peters on taking the helm of the IMP with auspices of yet more collaboration between the two institutes.

But CeMM also has strong ties to its brother organization of the Austrian Academy of Sciences, the Institute for Molecular Biotechnology IMBA, close to the IMP. Despite some chivalric rivalry that is typical and healthy among loving siblings, mostly taken out on the soccer ground, we are exploiting synergies and collaborations whenever feasible and help each other out as much as possible. CeMM has a deep admiration for its slightly older and larger brother. This peaked as the team of Jürgen Knoblich published the amazing achievement of developing complex human brain tissue in a three-dimensional culture system, popularly called "mini brains". We immediately posted the news on the CeMM web site to congratulate Jürgen and IMBA. It does not happen often that the community perceives that one of its achievements has historical dimension and acknowledges it. This is great for Vienna, Austria and the Academy of Sciences and we feel that 2013, through this work but also Robert Kralovics', can definitely be identified as the year when molecular biology in Austria has reached a truly planetary standing. We feel that it is very appropriate that the community will take the 50th anniversary of the European Molecular Biology Organization and 40th anniversary of the European Molecular Biology Laboratory to celebrate the impact of molecular biology on Austria, on July 7th and 8th 2014.

Besides CeMM's first important steps as translational center, there were other important signs of maturity of CeMM worth highlighting. For some years we have engaged artists, philosophers, historians, economists, physicist and others to help us abandon the intellectual boundaries of our discipline and learn about new territories. Brain Lounge sessions are often unrepeatable little feasts of cerebral exchange and the SMART lectures represent a kind of intellectual challenge that we learned to crave for. On November 25 we had the pleasure of welcoming Fabiola Gianotti (CERN Physics Department, Large Hadron Collider). She gave the 2nd SMART lecture on "The Higgs Boson and Our Life" and fascinated 200 scientists from different fields and interested lay people with her brilliant talk.

We also make a big effort with our Research Reports as we always felt that CeMM has, from its inception, a role that was larger than "just" excellent biomedical research. The genomic era and the accompanying changes in the way humankind understands itself go way beyond the medical revolution it is generating. Thus, our reports are a bit more like cultural manifestos that witness and pay tribute to these pivotal, paradigm-changing years. CeMM's 2013 research report inaugurates a different format. We now offer you information in different coherent sections, to provide for an easier reading of the various components.

To "present" the year we built on a wonderful example of our dialogue with society. One of our befriended artists, Dorothee Golz, who contributed to the CeMM Brain Lounge (see 2012 Research Report), approached me with the idea of having a geneticist collaborate with her to unravel the traits in a particular branch of the body of her oeuvre that allows for a proper "genealogy". What ensued is presented in this report and represents a first-ever formal quantitative representation of the relationship among the works of an artist. The conceptual breakthrough that Dorothee achieved can inspire everybody, also scientists, to create a map of their own creations (ideas, papers, patents, companies, projects, songs, clothes, design objects, brands, products etc). It offers an abstraction of one's own creativity and may predict work of the future. So, the Brain Lounge that we presented to you last year, with its revolving carousel and the interactive community that come to think on it, has created a highly exciting baby. We thank Dorothee Golz for using CeMM to test her idea, for sharing her work with us and for the inspiration that emanates from her creative thrust.

Fostering a whole new quality in the dialogue with other disciplines and in the awareness for the societal impact of biomedical research and the importance of interdisciplinary and cross-cultural approaches, people at CeMM developed a new sense of accountability to society. So instead of doing the yearly CeMM outing in one of the picturesque sites of local cultural heritage, it was time to engage a more serious theatre. 2013 has marked the 75th anniversary of Hitler's "Anschluss" with the Nazi takeover in Austria and the November Pogrom. The Austrian Academy of Sciences has organized a highly interesting symposium on the history of the Academy 1938-1945 on March 11 of this year, during which the president of the parliament Barbara Prammer has unveiled a marble memorial commemorating the victims of the Nazi crimes.

Though CeMM is an institution of the third Millennium, it has its roots in the Academy of Sciences and the Medical Faculty of the University and it felt doubly motivated to engage with the darkest period of its history. At CeMM we are providing for training of young scientists from all over the world and that training includes exposure to knowledge and understanding outside the classical realm of natural science and medicine. It appeared important to convey an understanding of the cultural context of Austria that goes beyond the entertainment and we proposed to the "CeMMies" to visit the Mauthausen concentration camp. The idea was welcomed and we combined the guided visit, in groups of ten, with a seminar in the building of the Academy of Sciences, where undoubtedly some of the racist discriminations and worse deeds had been perpetrated. The entire CeMM team was welcomed by the newly elected President of the Austrian Academy of Sciences, Anton Zeilinger and the seminar was given by journalist and historian Klaus Taschwer on the "Biologische Versuchanstalt", an institute on experimental biological research founded in 1903 by Jewish scientists and philanthropists led by Hans Leo Przibram.

At that time the institute was highly innovative, maybe world-unique in its focus. After the initial twenty years, the research center joined the Academy of Sciences, was then made first Jew-free, then made to host distorted or irrelevant science and, perhaps surprisingly, was not restarted after the damages of the war. Curiously, it also had disappeared from our historical conscience: At least at CeMM we had been oblivious of the existence of this proto-life science institute. It became clear, also from the symposium in the Academy, that crimes against Jewish scientists and non-conformists clearly preceded 1938 and that much of that many post-war failures and omissions were also brutal. The Mauthausen visit sparked a yet new discussion culture at CeMM and we all felt that awareness about the importance of safeguarding key values that should go hand in hand with research endeavors of an international, inclusive and democratic science community. We all felt very privileged to live in Austria and in the 21st century.

CeMM is a community conscious of its social responsibility regarding the past, the present but also the future. For example, of the roughly 140 individuals who every day come to work in the CeMM building, nobody takes a car. A third takes bicycles, scooters or walks and the rest takes public transport. It saddens me to see that people entering the AKH campus on Spitalgasse have no pedestrian crossing and as they step out of the trams are de-routed to a complex and time-costing system of traffic lights. We still have the hope that the city will invest in a new traffic control and information system on the campus which will be of the benefit of thousands of students, employees and patients.

This year has seen one of the key people to turn the CeMM idea into reality, Gerhard Schadler, its administrative director, move on to fresh challenges. He assumed a new role in the Academy of Sciences to help the newly elected Board to manage the Academy. While Gerhard maintained some responsibilities until the end of 2013, the responsibility for administration went entirely to Anita Ender. Anita has been ultimate decision-maker on so many administrative issues for so long that sanctifying this role appeared long due and well deserved. We are very much indebted with Gerhard for all these years of work for CeMM and, on behalf of everybody at CeMM, wish him all the best in the new function. I also wish Anita good fortune in her enlarged role. This has been a year of great structural and organizational changes, so next to a new Board of the Academy and a new chief administrator, we also have, most importantly, a new Minister of Science, Research and Economy, Dr. Reinhold Mitterlehner, whom we welcome and wish wisdom, far-sight and deep pockets.

Beyond our regular Scientific Advisory Board visits, 2013 was a year in which CeMM's research has been evaluated twice. First, on behalf of the Austrian Academy of Sciences, by a panel of international experts lead by Adriano Aguzzi of the University of Zurich. Later we were also evaluated by Technopolis, a professional group providing advice to policy makers, that reviewed the entire genomics program Gen-AU for the Research Ministry (Gen-AU unfortunately already ended). While we have not received any written reports from the two evaluations, we received a very positive oral feed-back, enjoyed the discussions with the various experts thoroughly and profited very much from the advice. We wish to thank both teams.

Finally I would like to thank Stefanie Lichtwitz, Kriso Leinfellner and their team for conceptually insightful and beautiful graphics and Helen Pickersgill for once again skilfully writing the scientific part of the report. Over again, it has been Eva Schweng, the editor and coordinator of all this effort, that deserves my and CeMM's applause. I hope you will enjoy this new account of the intellectual journey we are doing together with our readers and supporters. This, ladies and gentlemen, was our 2013.

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PX 66

Bezeichnung PX66
Wichtigkeit normal
Generation 5
Bruderpaar nein
Aehnlichkeit nein
Groesse gross
Haptik hart
Position_allgemein steht
Position_detail steht
Material Papierpaste
Aufbau gebaut
Aufbau_detail gebaut
Farbe weiss
Farbbasis Materialfarbe
Farbkombination nein
Zweites_Material nein
Einsatz_allgemein nein
Einsatz_detail1 nein
Einsatz_detail2 nein
Ironie nein
Biomorph biomorph
Biomorph_detail biomorph_tailliert
Schnorchel_allgemein nein
Schnorchel_detail1 nein
Schnorchel_detail2 nein
DUO_Gruppe single
Oeffnung_allgemein geschlossene_Form
Oeffnung_detail geschlossene_Form
Formmerkmal nein
Halbkugel nein
Gereiht nein
Konvex nein
Konkav nein
Voluminoes voluminoes
Oberflaeche glatt
Struktur nein
Sockel nein
Beine nein
Zusatztitel ja

Dorothee Golz, 2006
Paper pulp, white chalk
85 x 125 x 148 cm

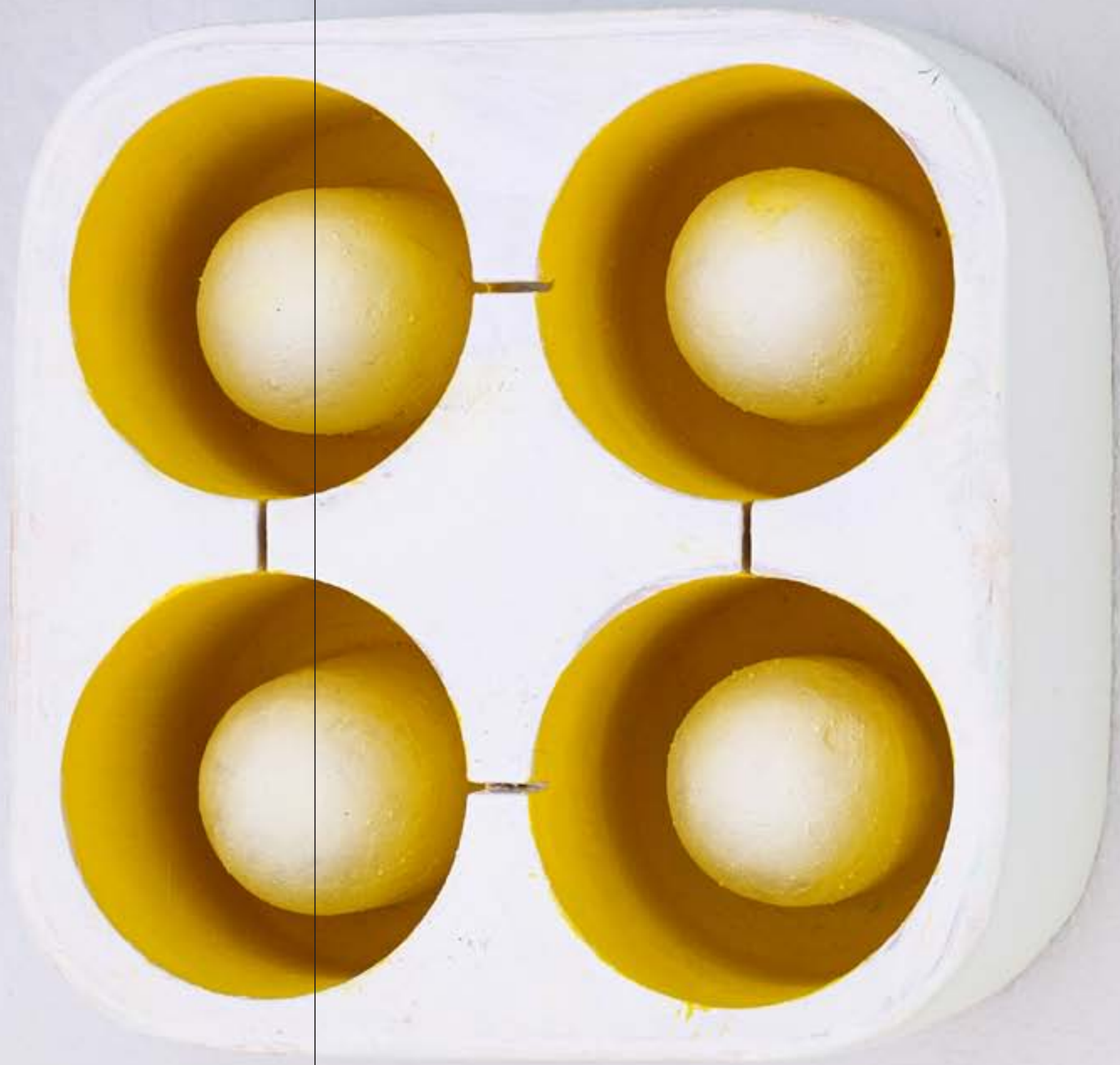
PX 70

Bezeichnung PX70
Wichtigkeit normal
Generation 5
Bruderpaar nein
Aehnlichkeit Aehnlich_PX29
Groesse klein
Haptik hart
Position_allgemein steht
Position_detail steht
Material Paste
Aufbau gebaut
Aufbau_detail gebaut
Farbe rot
Farbbasis Farbauftrag
Farbkombination nein
Zweites_Material Plexiglas
Einsatz_allgemein nein
Einsatz_detail1 nein
Einsatz_detail2 nein
Ironie nein
Biomorph nein
Biomorph_detail nein
Schnorchel_allgemein nein
Schnorchel_detail1 nein
Schnorchel_detail2 Schnorchel_Aufsatz
DUO_Gruppe single
Oeffnung_allgemein geschlossene_Form
Oeffnung_detail geschlossene_Form
Formmerkmal Z_Spoiler
Halbkugel nein
Gereiht nein
Konvex nein
Konkav nein
Voluminoes flach
Oberflaeche glatt
Struktur nein
Sockel Sockel
Beine nein
Zusatztitel nein

Dorothee Golz, 2013
Acrylic plaster, distemper, acrylic glass
33 x 25 x 8 cm

PX 74

Bezeichnung PX74
Wichtigkeit normal
Generation 5
Bruderpaar nein
Aehnlichkeit nein
Groesse klein
Haptik hart
Position_allgemein haengt
Position_detail haengt_ohne_Abstand
Material Gips
Aufbau abgegossen
Aufbau_detail abgegossen
Farbe gelb
Farbbasis Farbauftrag
Farbkombination gelb/weiss
Zweites_Material nein
Einsatz_allgemein nein
Einsatz_detail1 nein
Einsatz_detail2 nein
Ironie nein
Biomorph nein
Biomorph_detail nein
Schnorchel_allgemein nein
Schnorchel_detail1 nein
Schnorchel_detail2 nein
DUO_Gruppe single
Oeffnung_allgemein geschlossene_Form
Oeffnung_detail geschlossene_Form
Formmerkmal Loch
Halbkugel Halbkugel
Gereiht gereiht
Konvex konvex
Konkav nein
Voluminoes flach_voluminoes
Oberflaeche glatt
Struktur nein
Sockel nein
Beine nein
Zusatztitel nein



Dorothee Golz, 2013
Acrylic plaster, distemper, acrylic glass
12,5 x 12,5 x 6,5 cm

PX1

PX2

PX3

PX4

PX5

PX6

PX7

PX8

PX9

PX10

PX11

PX12

PX13

PX14

PX15

PX16

PX17

PX18

PX19

PX20

PX21

PX22

PX23

PX24

PX25

PX26

PX27

PX28

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PX40

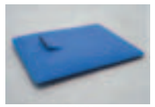
PX41

PX42

PX43

PX44

PX45


PX46

PX47

PX48

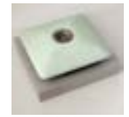
PX49

PX50

PX51

PX52

PX53


PX54

PX55

PX56

PX57

PX58

PX59

PX60

PX61

PX62

PX63

PX64

PX65

PX66

PX67

PX68

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PX74

PX75

PX76

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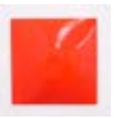
PX84

PX85

PX86

PX87

PX88


PX89

PX90

PX91

PX92

PX93

PX94

PX95

PX96

PX97

Freie Form A

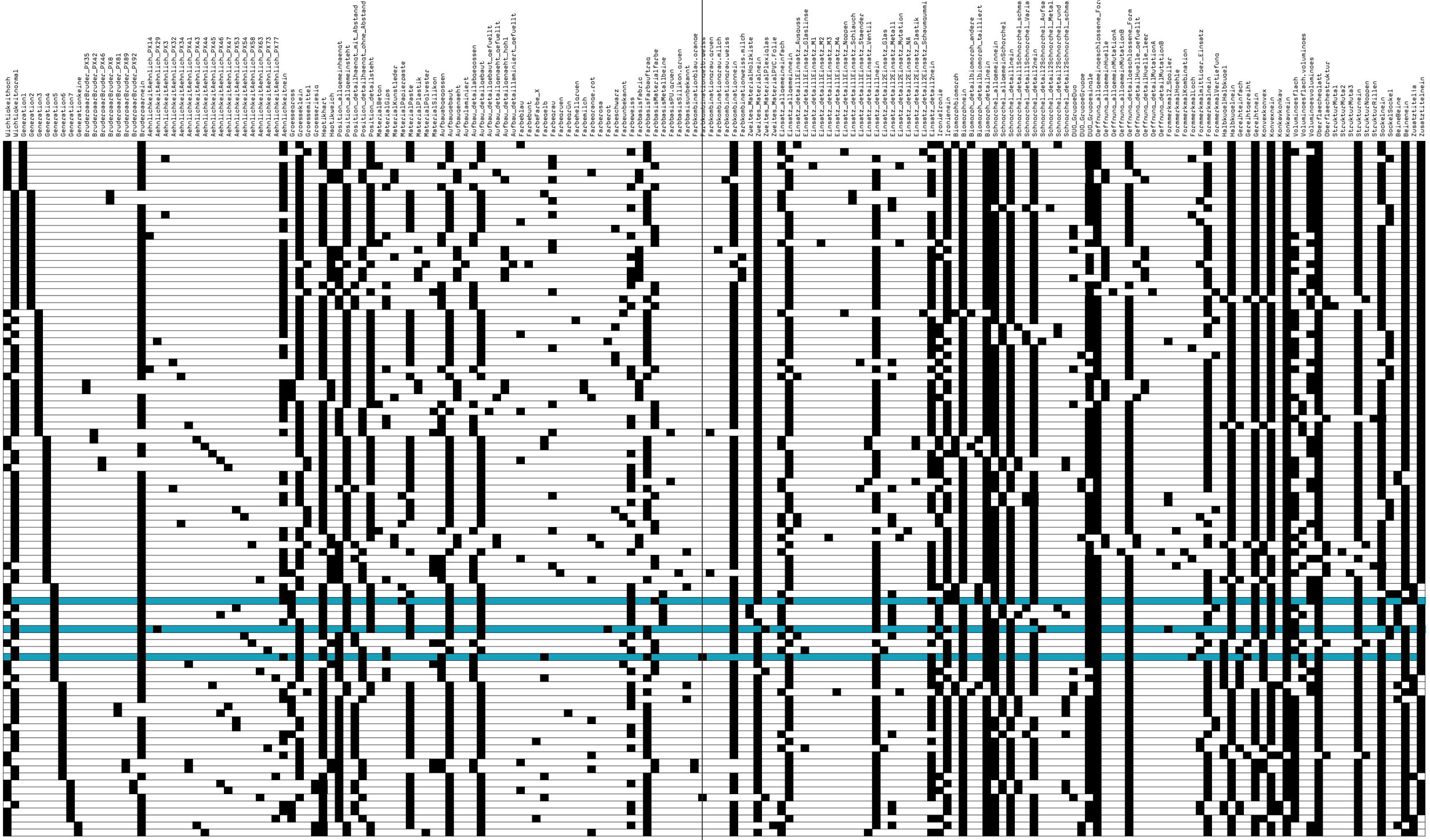
Freie Form B

PX Series
Dorothee Golz
1989–2013

Quantitative Encoding of Art

Encoding the Characteristics of the PX Objects in a High-Dimensional Matrix

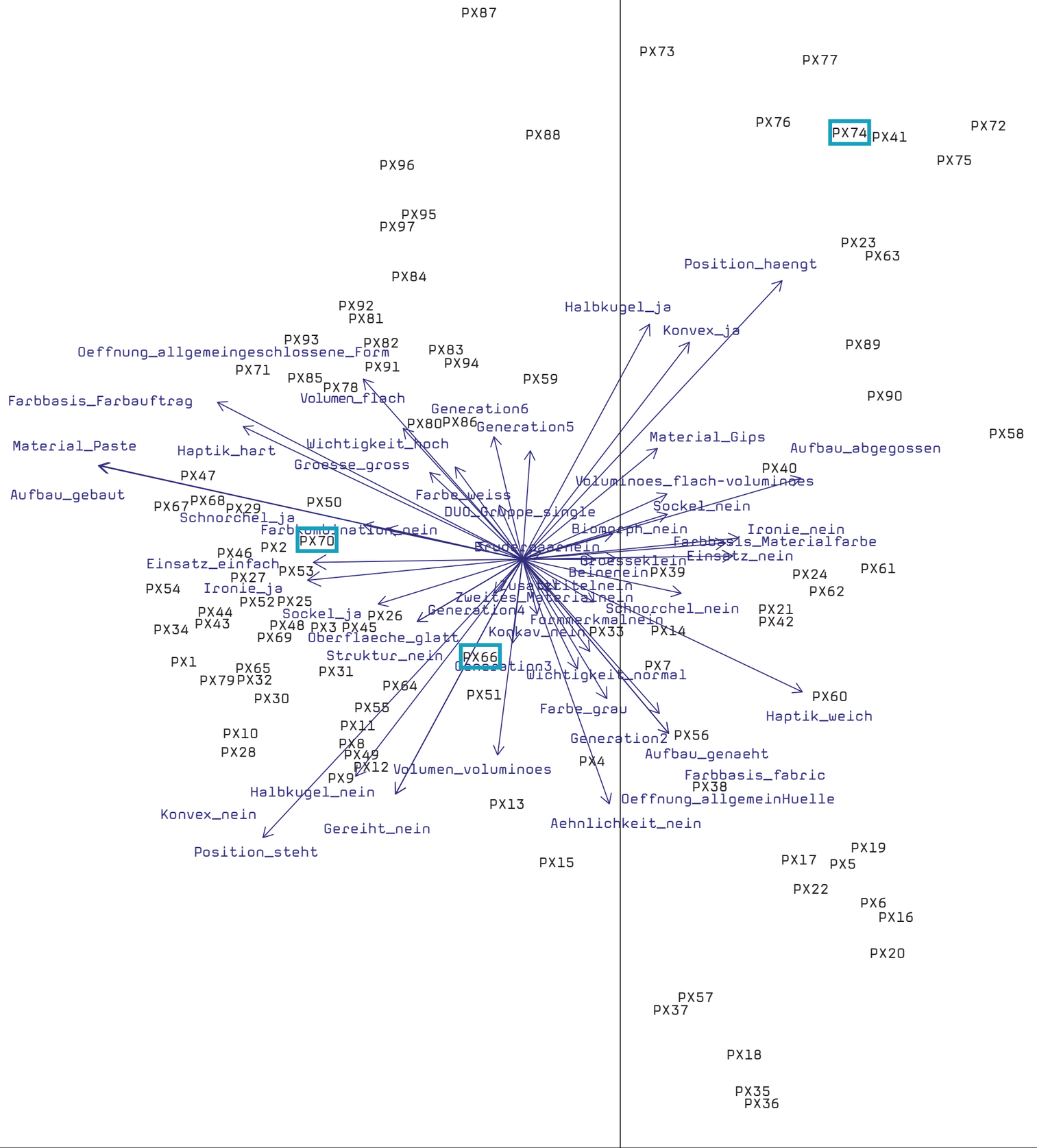
Similar to biologists who study fossils and genetic fingerprints to understand natural history, evolutionary analysis can illuminate principles and processes involved in the creation of art. The PX series of sculptural objects by Dorothee Golz is particularly suited for an evolutionary analysis because the artist explicitly embraces the concepts of mutation and recombination that is also at the core of biological evolution. To prepare for a quantitative analysis, all 99 PX objects were first encoded in feature vectors, resulting in the binary matrix that is depicted here.



Hidden Patterns

Detecting Implicit Patterns in the PX Object Series through Statistical Analysis

The binary matrix (depicted on the previous page) defines the position of each PX object in a 179-dimensional hypercube – a hypercube is the generalization of three-dimensional cubes to arbitrarily high dimensions. While hypercubes are not easy to imagine visually, they are straightforward to analyze by statistical methods and helpful for uncovering hidden patterns in the data. Using a method called "singular value decomposition", a two-dimensional mapping of trends and associations was obtained, which is shown here. This "biplot" identifies expected and new insights into the PX sculpture series. For example, the arrows indicate that objects from recent generations (Generation5, Generation6) are essentially all wall-mounted and flat, in contrast to earlier generations – suggesting a recent increase of evolutionary pressure to produce wall-mounted sculptures.



Predicted Objects

Predicting New Objects that Fill Holes in the Space of PX Objects

Having constructed a statistical model that describes the inherent characteristics of the PX series as it stands today, it becomes possible to predict new objects that could extend the series in a consistent and complementary manner. 1000 potential PX objects were generated by the computer and are visualized (in grey) relative to the 99 existing PX objects (in black). Furthermore, all objects were computationally ranked by their expressiveness and novelty, and the top-50 potential objects are highlighted in red. These top-ranking predictions, the basic design has been reported back to the artist, who will use this information to potentially extend the PX series in directions that may not have been obvious otherwise and thereby increase the density of this sculptural language.

Discussion on Art and Science

You Really Call it DNA?

A round table with Dorothee Golz, Peter Pakesch, Christoph Bock and Giulio Superti-Furga

Dorothee Golz, a sculptor and digital painter who also contributed to the CeMM Brain Lounge approached Giulio Superti-Furga with the idea of studying part of her oeuvre using scientific methods. The goal was to map genealogical relationships in the "PX" series of her sculptures and to discover connections that might not be readily apparent to the viewer or even to the artist herself. Part of the analysis was performed by Christoph Bock, who is a Principal Investigator at CeMM and works on the high-throughput analysis of genomes and epigenomes. Peter Pakesch joined a discussion round at CeMM in spring 2014, which focused on the results of this collaboration between arts and sciences. He is one of Austria's most accomplished experts in contemporary art, pioneer gallery owner, curator and director of the Universalmuseum Joanneum in Graz.

Golz: What was the aim of the project? I started the PX project almost 25 years ago. At the time, I was interested in developing an artistic formal vocabulary, and I asked myself how to go about it. I started with a few basic objects, built them and then recombined the forms with one another. On the basis of the first generation of these objects I then developed a second generation of objects, which combined properties that had already appeared in the first generation. New characteristics, new features then began to arise, and I subsequently carried these over into a third generation.

Superti-Furga: Did you have the concept of generations in mind from the beginning?

Golz: Yes. That is why I called the sculptures PX from the beginning, and numbered them according to a certain system. For example, PX1204: One thousand means first generation, two hundred means the second branch of the family. Four means the fourth member of this second family. My thought was that nature is creative, and in a way, also artistic. When thinking in terms of generations, the artistic process overlaps with natural processes. Nature doesn't invent things all of a sudden either, but always adds on, is evolutionary. Adds to something that has developed, which has emerged from genetic variations and mutations. Nature uses these to develop new forms. In a sense, evolution also has a language; perhaps life forms can also be compared to words. I tried to develop an artistic language with vocabulary.

Superti-Furga: Did creating generations motivate you and help in the creative act, or was it also a bit limiting? Did continuing the generations feel like a chore, or was the presence of a vocabulary liberating?

Golz: It was liberating. It gave me the feeling that I have an incredible range of possibilities. And if I want to incorporate something new, I can do that in the next generation, as a kind of mutation. Recesses, structures, colors that I haven't used before, even dimensions in which I previously might not have worked. So in that respect I wasn't limited at all. The established vocabulary helped me carry the project further. For me, it served to remove the randomness from artistic creativity. I created a framework within which I could work, and upon which I could also orient myself.

Christoph Bock, Peter Pakesch, Giulio Superti-Furga and Dorothee Golz in CeMM's Brain Lounge

As an artist works, there are processes of mutation, selection, recombination and evolution that take place.

Superti-Furga: A creativity machine?

Golz: More like coordinates along which I could orient myself.

Superti-Furga: How did you think of asking CeMM for help?

Golz: I've always seen a scientific analogy in my work. So when we got to know each other, the idea of actually looking at it on a scientific basis emerged. I saw it as a consequence of my work that through science I might confirm to some degree that the system I've developed works.

Superti-Furga: What was it that you asked of Christoph, and how did you both approach it?

Golz: I showed Christoph the work, explained the system of designations to him, and asked him to apply the laws or formulas used in biology to find or calculate genealogical relationships, in order to then render the whole thing in the form of a diagram. At that point I didn't know how the diagram could or should look. Christoph was very open to this rather unusual, unconventional subject matter that he now had to work with. The fact that these are art objects, and not…

Superti-Furga: …humans or life forms.

Bock: As an artist works, there are processes of mutation, selection, recombination, and evolution that take place. This happens continuously, but mostly unconsciously. The significant new step we took in this project was that we were looking for a way to visualize these processes and to make them transparent by analyzing them through quantitative methods. It is not enough, of course, to take pictures of sculptures and to load the photos into a computer. We aren't at the point yet, and we might never be, where a computer can look at a picture and recognize its essential characteristics. In principle, the essential properties of these objects can be only be adequately identified by the artist herself.

Superti-Furga: That was Dorothee's job?

Bock: I asked Dorothee to define the main characteristics and to categorize each object on that basis, which resulted in an Excel spreadsheet with 100 PX objects and 38 attributes for each single object. In doing so, she didn't just include actual physical features such as "large," "standing," "cast in concrete," in the catalog, but also non-material values such as irony, or how important an object was to her personally or to the series. We began the quantitative analysis using this table as a starting point. The first step was to translate it into a binary matrix. Each row is an object and each column is an attribute. A black dot indicates the presence of the attribute in a multidimensional space within which the objects relate to one another.

Superti-Furga: Dorothee, were you surprised by anything you discovered?

Golz: I was actually more surprised by how conclusive the representation is. I was somewhat amused to see that objects that are "ironic" are usually standing. There are hardly any ironic pieces among my hanging work. Based on the diagram, I've discovered that other criteria are important, that aesthetics takes precedence over originality.

Superti-Furga: Peter, what are your first associations regarding this science-art project?

Pakesch: I find the approach fascinating and above all impressive. If you look at it from the perspective of art, though, one could also say "so?" There is this ambivalence that comes up again and again in the history of art. Even in the baroque period there was speculation as to the degree to which art is calculable. What fascinates me is that the genealogy of patterns and textures could put us on track to analyze larger structures. In and of itself, that could already be an artistic as well as a scientific principle. There is something really attractive about it, but at the same time I see that the appeal or the quality of art lies precisely in the fact that systems come up again and again, reappear, and yet art always manages to outsmart these systems.

Superti-Furga: There are a number of approaches here. Essentially, it is an artistic undertaking, in which the artist tries to comprehend her own work in its entirety by taking a superordinate perspective. The description is more than the sum of its parts, and new questions arise: whether the fathers, mothers, and children were in the same place at the moment of creation, if there was cross-fertilization, etc. Dorothee's sculpture series is a straightforward story, but can this method of analysis be applied to other artwork, to music, to poetry? Could the Joanneum be represented in a network that has its own logic? And does the act of analyzing demystify things, or does it give rise to entirely new contexts or dimensions?

Bock: I think we need to make sure that we keep the art historians' and the artist's applications of this methodology separate. In an art history context, any reasonably coherent group of works could be described and analytically mapped using meaningful criteria identified by art historians. But Dorothee's intention was a different one: to her, my methods were ultimately a means to an end, namely to create new art. To follow and to break with the results provided by the computer; to become aware of certain implicit limits to one's own imagination, in order to overcome them.

Golz: That's quite insightful and true. No computer could calculate the objects or build them the way I made them. Not even using the information it might gather through the analysis. The ingredients, the list of characteristics come from me, after all, I made them up. For me, the genealogy is also a way to find out how the act of artistic creation works. How does it work inside an artist? What processes take place there?

Pakesch: I can't make any general statement here. For me, great quality arises where there is the greatest idiosyncrasy. This is a principle, the originality principle, which has sometimes been more and sometimes less pronounced in the arts over the years. The natural sciences, if I naively understand it correctly, aim for reproducibility of results, that experiments must be repeatable, that processes must be computable. While in the arts there is often a demand for the unexpected, the original, the unique. Though that isn't upheld overall, of course. I see a methodological conflict there.

Superti-Furga: I have the feeling that's a myth. I see the scientists and the artists here approach their work in a very similar way. The methodology is indeed different, but even among scientists it's about who has the coolest new idea. And that has to do with creativity. Couldn't one also argue the reverse, that if the genealogy of an idea can't be traced, then it's been falsified or perhaps doesn't even exist? It can also be liberating to say, as an artist or a scientist, I work within a certain context. For example, in music. You often hear pieces or parts of song that are completely referenced, and yet you don't know how aware of this the artist was. Wouldn't a real genealogy be much more interesting here, to know how connected the influences actually are? We believe that we are free and can invent things without context. But at least since people like Marx explained it to us in the 19th century, we know: "We are constantly in some sort of context." When I think of my own scientific oeuvre, it would certainly be very beneficial to recognize the connections, to see where something new has really come up, and where this new thing came from. I wouldn't consider that to be restrictive, or counter to the creative act, but rather as enlightening and interesting.

Pakesch: Perhaps we've misunderstood each other. These references exist, of course, and we are talking about a system that is both very large as well as very well defined. But it is also the case that art operates within a state of strong ambivalence, in a state of contradiction, constantly questioning this system and in part working against it. So it really is like being within two systems. On the one hand, within this large referential landscape, while on the other hand art – at least in our Western notion of art – is expected to exhibit this very, very massive sign of individuality. It must live up to the maxim that, in Western art, the individual and individual thought are considered to be very important. And this is a source of constant friction. For me, that is also a part of the inherent energy that results. So art very much depends upon operating within these contradictions. At the same time, it also makes the claim of representing something universal. I simply see the advantages in an extremely high degree of heterogeneity, both in the methodology and the results, which have been very strongly cultivated in the outgoing 20th century and beginning of the 21st century. Unlike in other periods, where a much stronger mainstream was developed.

Superti-Furga: This brings to mind fashion; one could probably apply this methodology very nicely to fashion.

Pakesch: I like the idea to not reproduce creative-thinking processes, but rather to work with them. Conventional art history is to some degree utterly overwhelmed in this regard and just trying to keep up. Artistically and scientifically, it is also important to keep these somewhat separate. I would be interested to see this mirrored in the work of other artists, or applied to fashion and or creative products. I wonder: To what extent is the sum of an individual's thoughts embedded in a context? To what degree is there a matrix in place that I can comprehend? But I also know plenty of examples of artists who have managed to break through their own matrix. Take the artist Picabia, for example. He was very good at knowing how to break repeatedly with his own matrix, so that his work is not readable as an oeuvre. This is also a huge issue, right up to Kabakov and others, where an artist has deliberately introduced multiple personalities.

Golz: I didn't apply the scientific analysis to my work as a whole. I used the PX series to develop a very individual formal language, which I then applied to other subjects. My basic motivation was, as an artist, to someday have a signature style that I can use as a metaphor. It's not about taking things that exist one-to-one and recombining them, and thereby to perhaps create a kind of tableaux. I wanted to translate the language of things, of the physical world that surrounds us, into a very personal, subjective, individual language. I started with five basic forms, then expanded on them with new features, new characteristics. The properties weren't pulled out of thin air, they weren't things that I just suddenly thought up. I took utilitarian objects, objects with which we humans surround ourselves, that were created by us humans, and looked at them closely. I stripped them of everything that they need to fulfill their function and then looked at what was left. If you leave a humidifier with only those characteristics that aren't necessary for it to function, you are left with just a color, a basic form, and a volume. A formal language is left behind, angular, soft, geometric, or biomorphic. I distilled these words out of utilitarian objects created by human beings and reapplied them to art objects, which have no functional significance.

Superti-Furga: Is there a future for the PX series? If so, to what extent will it be influenced by this scientific analysis?

Golz: I find that an incredibly interesting thing to explore. Christoph has given me a table of a thousand possible PX objects. The computer specifies what each object would look like. The description might be "medium size, flat, blue, made of plaster." I would like to give this description to three or four different people. Once I would make one object from this description, once another artist, once a skilled craftsman who can imagine and build something according to this description. And maybe also a person who has seen my objects, isn't an artist herself, but who would try to feel what matters to me as an artist. I would look at how similar or how different these objects are. And analyze why they are similar or why they are different. Where am I necessary as an artist?

Peter Pakesch Artistic Director, Universalmuseum Joanneum, Graz
Giulio Superti-Furga Scientific Director, CeMM
Christoph Bock Principal Investigator, CeMM
Dorothee Golz Sculptor and Digital Painter

Bock: One possible outcome might be that the lay person or the craftsman produces something plausible, at which point one could say that the story of the PX objects has achieved such momentum or inherent qualities that it has started to emancipate itself from the artist. Or it could be that this experiment might end up as a failure, which would suggest that this structure, these objects, and this story have no life of their own beyond that supplied by the creating artist.

Pakesch: There are artists who constantly reinvent themselves. But there are also artists who create instructions and scenarios for action, which they then pass on to others and thereby are able to achieve certain qualities; who rather consciously bring their art into the realm of the robotic, of the absolutely reproducible. But this is always just a part of a patchwork, an overall system in which the one can't live without the other. In today's art world, I need extremely individualistic-romantic art just as much as very calculated, very conceptual art, because one doesn't work without the other. And that might distinguish the system of art from that of actual nature.

Superti-Furga: You are interested in neuro-biology. Suppose we were able to have a record of everything that a person thinks in their life, and could rewind to the moment when artist X got the idea to depict something entirely new. They, the artist, will inevitably – but that's an interesting debate itself – have taken inspiration from their environment, because they know no other formal language. They couldn't talk before language existed. They couldn't draw before seeing forms. So if you were to take the whole Joanneum, the whole Kunsthalle, and all the modern work, and if you were really able to map these connections, don't you think that in a temporal, as well as artistic, scientific, literary dimension one would recognize networks that in some way are no different than what Dorothee and Christoph have done?

Pakesch: But with the limitation that it is my map. Mapping has been very popular for a long time; it's been used to investigate influences. There is general agreement that first comes Cubism and then abstract painting; that is, that developments have certain references. But usually it's most interesting when the mapping is subjective; it no longer has the same degree of validity, but it is very productive. That's why it would be a worthwhile thought experiment to apply such a method to various works, including intellectual history. How do the collected works from the life of a particular philosopher look like? How much did the work evolve, where are there breaks or continuities?

Bock: Our analytical method isn't an attempt at objectivity either; there is, after all, still the step in which an artist or an art historian categorizes a group of works. This step remains a subjective and often an intuitive one. The advantage of our analysis in comparison to the existing forms of mapping is that we insulate the categorization from the mapping, such that three, ten, a hundred people, perhaps even the original artist and art historian, can categorize the same group of work and create maps that can be directly compared. The categorization by the artist might look very different from that of the art historian.

Pakesch: I would like to come back to a question for the scientist: Does the analysis, the mapping, reveal anything like a DNA? Are there serious parallels to the material with which you usually work?

Bock: I think yes, the concept of mutation and selection, the double step between generating and selecting what will go into the next generation. I think this concept underlies all artistic production. If you look at a very complex piece of art that has been developed over the course of years, it's only the final product that ends up in the museum. In some cases, we are lucky to have some preliminary versions surviving. If we had all the drafts, and maybe even a map of the artist's brain, then we could basically show this process of mutation and selection, and the genesis of the artwork, in every work of art. In Dorothee's PX pieces, we are fortunate that the various steps and the moment of their occurrence are preserved as artifacts. With quantitative methods we can gain a bit of an insight into the synthesis of art as a process of mutation and selection.

Superti-Furga: I can very well imagine that there are considerable variations. There are artists who use a very broad language, and then there are those who use a much narrower language. That might be something that is visible in the work's DNA.

Bock: I think that the concept of DNA is helpful as a metaphor. In biology, there is the principle of separation of genotype and phenotype. We have developed methods through which we can take the phenotypes that we see today and, using a genealogical analysis, can reconstruct how they evolved into that. In biology, just as in the arts, there are jumps that can be difficult to explain. In biology, we are increasingly capable of dealing with a chaotic element and an element that wants to evade predictability.

Pakesch: Yet the question that science doesn't really ask itself is whether that will make it possible to produce art robotically. That's all good and well, but for me it raises the question: what's the point?

Superti-Furga: Are the maps that one creates always so trivializing? Or do they have their own soul, and one can recognize patterns and regularities that have an even deeper meaning than the artists, architects, or fashion designers intended? Are there any secrets or big questions that might be unraveled through such a genealogy? Do we recognize flashes of inspiration that we might not have identified as such without a map?

Pakesch: I rather think that the genealogy is an added tool for tracing one's own creative process and for making that process itself a subject.

Golz: Christoph said earlier that, on the one hand, this genealogical method can be applied in an art historical sense to understand retro-spectively what happened. In the sense of my project, I was just aware that creativity and evolution are related. Even an artist's personal generation of ideas has a history. It develops and develops from an initially manageable number of basic ideas and then grows increasingly complex as these ideas are combined with one another, because these ideas also serve to inspire and create new ideas.

Superti-Furga: Thank you all for the interesting conversation.

Science at CeMM

+ Cancer
+ Infectious Diseases
+ Immune Disorders and Inflammatory Diseases
+ Post-Genomic Technologies
+ Diagnostics and Therapeutics

Cancer

Understand Cancer and Taming it
Cancer has long been recognised as a major cause of death, particularly in Western populations although this is now spreading throughout the developing world. From the so-called "war on cancer", which was launched by then President of the United States, Richard Nixon we have come a long way. Cancer is not just an enemy, a foreigner. It is more an unwanted state of internal affairs. A new perspective may help us develop new ideas on how to come to grip with it.

A lot has happened in the last forty years, particularly from the beginning of this century when the human genome was sequenced. Cancer is essentially a genetic disease being caused by alterations in the DNA sequence of certain genes, which leads to the transformation of a normal cell into a fast growing and invasive cancer cell. Having at hand the full sequence of all the genes in the human body has empowered researchers to uncover more of the molecular complexity underlying this highly heterogeneous disease. Once the genetic cause of a cancer type has been identified, in principle specific drugs can be designed to target it and hopefully cure the disease. But the rapidly growing knowledge allows researchers to also find new vulnerabilities of cancer cells, such as particular metabolic idiosyncracies or dependency on a specific cellular process, such as protein folding.

Reducing the Impact of Cancer by Changing Policies and with Smarter Research
Unfortunately, the effect of all this research on reducing total cancer deaths has not yet been fully realized and there is still a lot of work to do. Global cancer cases have recently reached 14 million, leading the WHO to claim that we are facing an impending "tidal wave" of cancer. Preventing cancer should remain a top priority for policy-makers, and banning smoking in all workplaces, restaurants and bars, with no exceptions, in countries like Austria and China, as has been done successfully in many other countries, would go a long way to reducing cancer incidence.

In the laboratory, there are many battles being fought, and notable successes are leading to victories in the clinic, which is also helping to reduce the impact of cancer. At CeMM, there is a huge drive towards understanding the biology of cancer and developing more effective treatments. In 2013, one significant battle was won against myeloproliferative neoplasms in the group of Robert Kralovics at CeMM. In the laboratories of Denise Barlow, Christoph Bock, Stefan Kubicek, Joanna Loizou, and Giulio Superti-Furga there is a strong focus on understanding the biological basis of cancers such as leukemia, as well as on the role of epigenetics, which is a relatively recent phenomenon and could lead to a new generation of treatments. Finally, scientists at CeMM, particularly in the laboratories of Sebstian Nijman, Stefan Kubicek and Giulio Superti-Furga are using different approaches to identify new drug targets for cancers including lung cancer. Together these efforts should provide new paradigms in the process of tweaking cancer cells into a harmless state.

A Battle Won in 2013

2013 saw a significant advance against myeloproliferative neoplasms (MPN) in the laboratory of Robert Kralovics at CeMM, in collaboration with the group headed by Heinz Gisslinger at the Medical University of Vienna. MPN is a group of blood disorders characterized by the inappropriate growth of one or more of the myeloid blood cell lineages. MPN includes chronic myeloid leukemia (CML), polycythemia vera, essential thrombocythemia, and primary myelofibrosis, and the overall number of MPN patients in the EU is estimated to be around 300,000. The genetic cause for CML was identified over thirty years ago as the protein translocation BCR-ABL, which led to the development of drugs that have dramatically improved long-term survival rates. In contrast, identifying the genetic cause of some of the other major MPNs has lagged far behind.

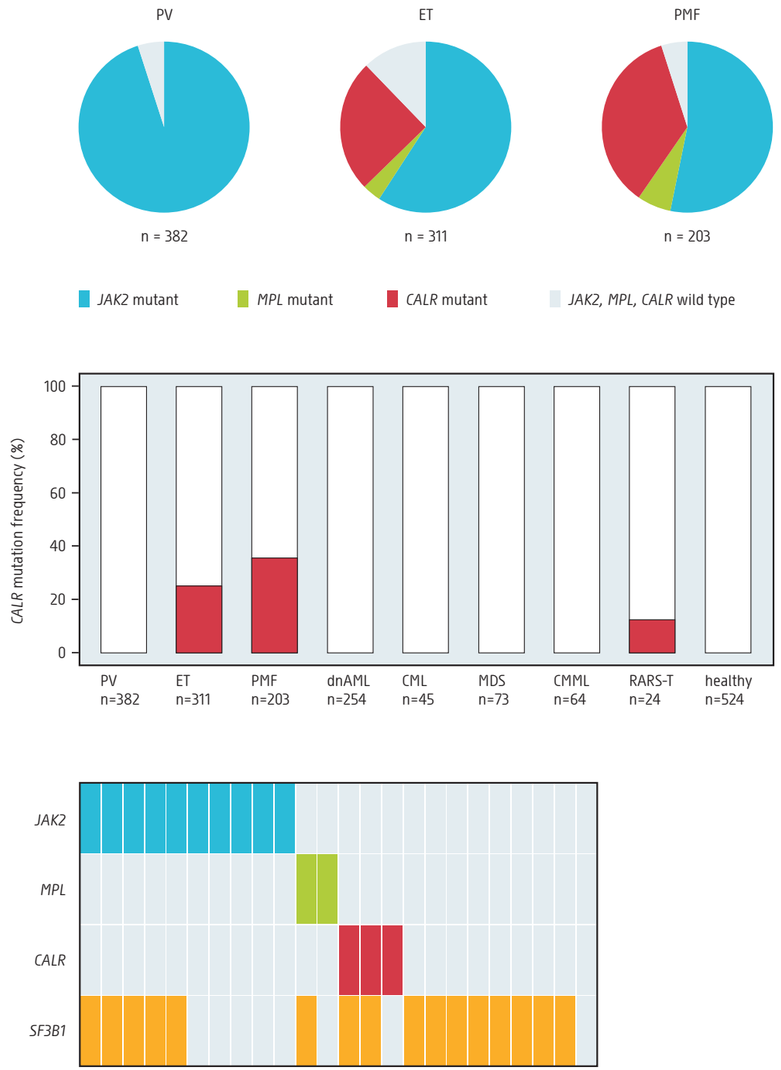


Fig. 1 Frequency of *CALR* Mutations in Myeloid Neoplasms: pie charts show the distribution of *JAK2, MPL,* and *CALR* mutations in the three classical myeloproliferative neoplasms. The bar graph shows frequency of CALR mutations in myeloid cancers with total numbers of patients analysed for a specific disease entity. The matrix underneath visualizes the distribution of mutations in *JAK2, MPL, CALR,* and *SF3B1* among patients with refractory anemia with ring sideroblasts associated with marked thrombocytosis (RARS-T). AML: acute myeloid leukemia, CML: chronic myeloid leukemia, CMML: chronic myelo-monocytic leukemia, MDS: myelodysplastic syndrome.
Adapted from Klampfl et al, New England Journal of Medicine, 2013.

Kralovics and Colleagues: Myeloproliferative Neoplasms

In 2005, CeMM's Robert Kralovics was then working at the University Hospital Basel in Switzerland. Along with Radek Skoda and colleagues, and a team headed by Mario Cazzola at the University of Pavia Medical School in Italy, he made a significant breakthrough by identifying a gain-of-function mutation in the gene called JAK2 in around 75% of patients with MPN. This eminent discovery led to the development of JAK2 inhibitors, which have now been clinically approved. Their success drove the search for other common mutations in the remaining patients, which, in 2013, led Robert and his PhD student Thorsten Klampfl, along with Mario and a new team to victory number two.

They used a technique called whole exome sequencing at the Biomedical Sequencing Facility, which was set up by CeMM and the Medical University of Vienna and is run by CeMM PI Christoph Bock. By sequencing six patients with primary myelofibrosis who did not have a JAK2 mutation they found a second common mutation in the gene encoding for Calreticulin. The high frequency of this mutation was then discovered upon sequencing the gene in a further 1107 MPN patients. This work was published in the prestigious New England Journal of Medicine (Klampfl et al., 2013). Exactly how this mutation causes MPNs awaits further work, but the discovery itself is a significant win for scientists as it contributes to a much better understanding of disease pathogenesis, and as such will lead to improved diagnosis and disease management.

Towards Personalising Cancer Therapy

Christoph Bock's group at CeMM is utilizing the hematopoietic system and the development of leukemia to study the role of epigenetic modifications, particularly DNA methylation, with a view to improving patients diagnosis and treatment. The team combines biochemical assays with next generation sequencing to map the dynamic epigenetic changes that occur throughout the genome during cell differentiation and cancer progression.

These data are then used to dissect the interplay between epigenetics, genetics and transcriptional elements by exploiting bioinformatics algorithms that the group have developed. This work will give rise to a dynamic and potentially predictive computational model of the deregulation of cell states in leukemia, which will help to predict personalised therapies for any given individual cancer patient.

Epigenetics and Cancer

Others at CeMM have been working on alternative approaches for tackling many different cancers, including leukemia, breast and lung cancer. A relatively new phenomenon that has entered the cancer arena is epigenetics, which is defined as heritable changes in gene activity that are not encoded in the DNA (in contrast to genetics). Global epigenetic changes, such as DNA methylation, are now recognised as one of the classic hallmarks of cancer, along with such well-established characteristics as immortality and uninhibited growth. Scientists are slowly beginning to understand that deregulated epigenetic mechanisms play a significant role in causing many different cancers. New discoveries in this field may make important gains in the war on cancer, as they could lead to the development of urgently needed and more effective anti-cancer treatments.

Denise Barlow's group has been working for many years on the mechanisms of epigenetic regulation. More recently they have been focusing on understanding how long non-coding RNAs (lncRNA for short) silence or switch off imprinted genes, which have one copy silenced in a parent-specific manner. Genomic imprinting is a classic example of epigenetics, and the study of imprinted genes has uncovered many unexpected findings about what controls the on/off state of a gene, which are likely to be relevant for understanding how epigenetics plays a role in cancer. PhD student Aleksandra Kornienko is using a recently developed RNA sequencing pipeline to identify a set of lncRNAs expressed in normal human granulocytes, which will later be used to screen haematological malignancies for possible biomarkers, in collaboration with Robert Kralovics' group.

In a landmark paper published in the journal *Science* in 2012, the Barlow laboratory discovered that a special class of lncRNA is able to silence imprinted genes by the act of their transcription (Latos et al., 2012). Following on from this work, PhD student Federica Santoro and Post-doc Florian Pauler, along with others in the Barlow group, developed a system that enabled them to turn off the expression of a specific lncRNA, *Airn,* at different times during the differentiation of mouse embryonic stem cells. Using this system, and supporting their previous results, they found that Airn lncRNA expression is both necessary and sufficient to silence the overlapping *Igf2r* gene. This important work was published in the journal *Development* (Santoro et al., 2013).

Detecting Histone Modifications

While aberrant DNA methylation patterns have long been associated with cancer, mutations and amplifications of histone modifying enzymes have only recently been detected in cancer cell lines and primary tumour material. In some cases, these genetic aberrations result in altered histone modification levels. For example, activating mutations in the histone methyltransferase EZH2 have been detected in diffuse large B cell lymphomas. The subsequent increase in enzymatic activity results in a global increase in the levels of histone H3 lysine 27 trimethylation, which is thought to promote tumourigenesis. In 2013, the first small molecule inhibitors of EZH2 have entered clinical trials in patients with B cell lymphomas and advanced solid tumours.

In the context of the Christian Doppler Laboratory for Chemical Epigenetics and Antiinfectives, researchers in Stefan Kubicek's group at CeMM have been developing fast, robust assays to quantify all histone modifications in cancer cell lines and primary tissues. Using a panel of 104 differently modified synthetic histone peptides they have already extensively characterized the binding specificities of 132 monoclonal antibodies directed against different histone modifications, of which 33 were found to be highly specific. These important tools will allow them to quantify changes in specific histone modifications and study their role in cancer initiation and progression, which could ultimately lead to the development of valuable diagnostic tools.

Cancer and DNA Damage

In addition to deregulated epigenetic mechanisms, another important cause of cancer is the failure to repair damaged DNA. This can occur when specific DNA repair proteins are mutated, rendering them non-functional. Joanna Loizou's group at CeMM is building an understanding of the mechanisms and pathways that repair DNA damage generated by replicative stress and in a programmed manner in B and T cells. This should help them to find out how this might go awry and lead to cancer development.

The group has recently discovered that an important DNA damage kinase, known as ATM, is activated upon DNA replication stress. Using a technique that allows for a global snapshot of ATM targets they have shown that it phosphorylates over 250 proteins upon DNA replication damage. The activity of this kinase and its ability to activate a downstream signaling network is essential for maintaining genomic integrity, protecting against the development of cancer.

Mutations in ATM also lead to an inability to repair DNA breaks that occur in a programmed manner during the development of B and T cells, which are important cells of the immune system. Indeed, patients carrying functionally inactive ATM are immunocompromised. The group has shown that for ATM to carry out its function in the resolution of programmed DNA breaks it requires two co-factors, ATMIN and NBS1. Loss of these two co-factors, or of ATM itself, leads to an inability to form normal, functional T cells. Hence, development of a functional immune system requires a functional DNA damage response.

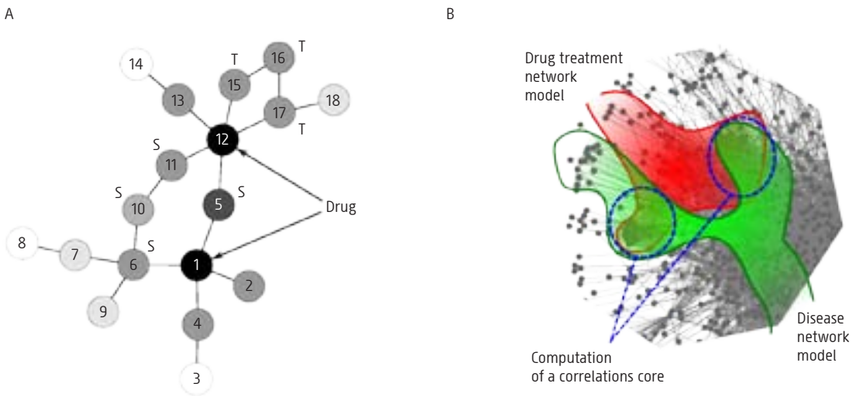


Fig. 2 Target-Disease Network Model (A) Schematic representation of a diffusion process in a "toy" network, proteins displayed as nodes, labelled 1 to 12. Proteins are drug targets and assigned with probabilities (black = maximum, white = minimum) so that proteins residing close to targets receive higher probabilities and synergistic effects are obtained for proteins close to several targets ("S") or linked in multiple ways to a single target ("T"). (B) Scoring principle illustrated in a part of the actual network (grey): two diffusion processes performed separately on the network yield a model of the drug treatment effect (red) and of disease influence on the network (green). Combination of these two sets of scores allows for computation of a correlation score (blue) measuring adequacy of a drug treatment. *Adapted from Rix et al., PLoS ONE 2013.*

Innovating Anti-Cancer Therapeutics

Once the genetic or epigenetic abnormalities that cause cancer have been discovered, targeted therapies can be developed to exploit them. A handful of these are now available in the clinic, and many result in dramatic therapeutic responses, substantially extending patient survival. However, many abnormalities cannot be targeted with small molecule inhibitors, and other approaches are needed. In addition, even with the successful drugs cancers are fighting back by developing resistance, which has become the next big battle. Several groups at CeMM are looking to boost the development of more effective anti-cancer drugs and overcome the challenge of drug resistance.

Scientists in Sebastian Nijman's group have been creating alternative, so-called isogenic models of cancer cells by engineering them to carry defined mutations. These isogenic cancer cells are being used in genetic and chemical screens to identify so-called synthetic lethal interactions. These interactions can be exploited for treating specific cancer subtypes carrying genetic abnormalities that cannot themselves be directly targeted with inhibitors. They have recently developed an isogenic model for one of the most common and deadly lung cancer subtypes. This led them to the identification of a clinically approved compound that may be useful for treating patients with a specific and common set of genetic mutations. Lung cancer is the leading cause of global cancer deaths, therefore there is an urgent need for new and more effective treatments.

Together with the teams around Jacques Colinge and Keiryn Bennett, scientists in the laboratory of CeMM's scientific director Giulio Superti-Furga have over the years become proficient at the identification of the target proteins actually engaged by drugs (see also *Diagnostics and Therapeutics*). This strategy, rather than starting from a defined genetic lesion and then look for a matching chemical agent, reverses the process and uses the chemical agents to go fishing. This "follow the drug" approach has shown that many therapeutic agents exercise their effects on multiple protein targets, often spread across different cellular processes within the interlinked molecular network that forms the inner workings of cancer cells. At CeMM, this knowledge is accrued to identify new possibilities to employ single drugs or combination of drugs. Also, it was used to predict the efficacy of therapies in cellular models of leukemia (Rix et al., *Plos One* 2013).

Infectious Diseases

Getting Ahead of Pathogens
Infectious diseases, those caused by pathogenic bacteria, viruses, fungi and parasites, and transmitted between humans, have had a dramatic influence on all of our lives. They spectacularly altered human history, for example by wiping out 3-5% of the world population in the 1918 flu pandemic, shaped human evolution by driving the development of an entirely new type of immune system (adaptive immunity), and their interminable presence influences our every-day activities, mostly without us realising it (you did remember to wash your hands today didn't you?).

There are hundreds of different types of infectious diseases, ranging from relatively minor infections such as the common cold, to more life-threatening diseases like polio and tuberculosis. New infectious diseases are continually emerging as pathogens jump species barriers and/or quickly evolve to become more virulent.

Fortunately we have several powerful tools for preventing and treating at least some infectious diseases. Antibiotics, which were first discovered accidentally by Alexander Fleming in 1928, trans-formed medicine by curing patients with both minor and life-threatening bacterial infections. However, irresponsible use has led to the emergence of antibiotic resistant bacteria, and there is now an urgent need to develop alternatives.

Vaccinations have also proven to be invaluable for preventing infectious diseases, with the most notable success against smallpox, which was declared completely eradicated in 1979. Vaccines have also almost eradicated polio, which is another devastating infectious disease. In 2013, only 400 global cases were reported, which were limited to a handful of countries. Disinfectant and antiseptic procedures have also played a substantial role in reducing the incidence of infectious diseases that were once rife, particularly in hospitals and other clinical settings.

Even with these precious tools, we will never completely eradicate infectious diseases. However, staying one step ahead of the bugs is critical, particularly if we are to avoid another pandemic of potentially epic proportions. At CeMM, several groups have recently made significant discoveries that are helping us get ahead of infectious diseases. Sylvia Knapp and her group are now one step ahead of the bug that causes bacterial pneumonia by discovering how cells of the immune system help to fight the infection. Scientists in Giulio Superti-Furga's group, in collaboration with Bhushan Nagar and his group at McGill University in Canada, have recently discovered how the body's immune system recognises a group of disease-causing viruses, and Andreas Bergthaler and his team have uncovered a novel mechanism for how liver cells are protected from oxidative damage caused by viral hepatitis.

How to Beat Infections: New Lessons Learnt from Our Own Immune Systems

Finding new ways to treat infectious diseases isn't easy, but one powerful approach is to learn from the experts. Our immune systems have evolved over millions of years into complex machines that work to eradicate many different types of infections. By studying the molecular and cellular details of the immune response to infectious diseases, scientists at CeMM are hoping to open up new therapeutic avenues.

One successful project, published in 2013, focused on IFIT antiviral proteins, which act as foot soldiers to guard the body against viral infections such as those caused by influenza and vesicular stomatitis virus. In 2011, Andreas Pichlmair and colleagues in Giulio Superti-Furga's laboratory at CeMM discovered that IFIT proteins unexpectedly interact directly with viral ribonucleic acid (RNA) and inhibit its replication, thereby stopping the infection. Now, following on from this, scientists in the Superti-Furga group along with a team led by Bhushan Nagar, a professor at McGill University Faculty of Medicine in Canada, have together discovered the molecular blueprint of the IFIT protein.

The multidisciplinary team investigated exactly how RNA is recognised by the IFIT proteins by protein crystallography. The crystal structures revealed a new helical domain in the IFIT protein that houses a positively charged cavity designed to specifically engage only single stranded viral RNA bearing a 5' triphosphate group. This explains at the molecular level how IFIT proteins capture only foreign viral RNA, and how they distinguish it from host RNA molecules. This mode of action sets the IFIT proteins apart from the other known canonical cytosolic sensors of double-stranded viral RNA, RIG-I/DDX58.

Additional biochemical and functional assays further demonstrated the mechanism by which IFIT proteins selectively recognize viral RNA and thus how they block viral infections. This work validates new paradigms for how this family of proteins protects us against viral pathogens, and was published in the prestigious journal *Nature* (Abbas et al., 2013). It also makes a promising step towards the development of new drugs for combatting a wide range of virus-borne immune system disorders.

Learning From the Immune Response to Lung Infections

Elsewhere at CeMM, Sylvia Knapp's group has been focusing on *Streptococcus pneumoniae (pneumococcus),* which is the most prevalent respiratory pathogen and one of the most common causes of community-acquired pneumonia and bacterial meningitis, both of which can be deadly diseases. This bacterium is particularly dangerous for children and elderly people. Once it infects the body, the immune system responds by launching a powerful pro-inflammatory response to destroy it. This is followed by an anti-inflammatory response, which acts to limit tissue damage. These responses are predominantly effected by innate immune cells, particularly macrophages, which are found in the infected lungs.

In the Knapp laboratory, PhD student Joanna Warszawska and her colleagues discovered that lung macrophages must be re-activated in order for the host to successfully eliminate a pneumococcal infection. They identified a key player, the protein LCN2, which keeps macrophage deactivated via IL-10 induction in the respiratory tract. While this helps prevent unnecessary inflammation in healthy lungs, this protein – that can be further induced by glucocorticoids – also prevents the required activation of lung macrophages upon pneumococcal infection. The work was published in *The Journal of Clinical Investigation* (Warszawska et al., 2013). These results are the first to describe a role for inactivated macrophages in the progression of an infectious disease, along with the molecular mechanism involved, and are likely to be important when treating patients with serious lung infections caused by S. pneumoniae.

In a related study in the Knapp group, a project led by Post-doc Omar Sharif sought to elucidate the potential role of the cell surface receptor, CD36, in pneumococcal pneumonia. CD36 binds to a wide range of extracellular ligands, which enables it to function in a variety of cellular processes ranging from angiogenesis to sensory perception. It is also found on the surface of macrophages and is known to help fight infection by the bacterium *Staphylococcus aureus*.

The group now shows that CD36 is also expressed on alveolar macrophages and respiratory epithelial cells, placing it in the right location to also tackle respiratory pathogens such as *S. pneumonia*. To test this directly, they used mice lacking CD36, and found that it indeed plays a role in S. pneumonia infection by influencing both the early innate immune response and bacterial clearance from the lungs. These data were published in *The Journal of Immunology* (Sharif et al., 2013), and provide an important new look into the immune response to bacterial pneumonia. This could help in the search for new therapies to tackle the recent emergence of virulent serotypes that are resistant to current treatments.

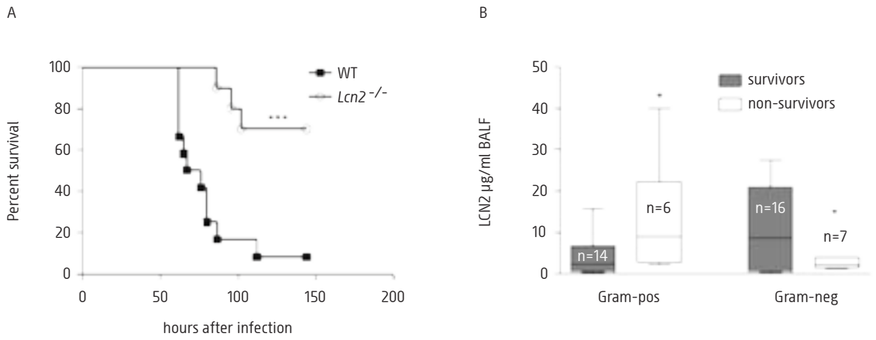


Fig. 3 Lipocalin 2 (LCN2) is detrimental during pneumococcal pneumonia in mice and humans: (A) Survival comparison of wildtype (WT) and Lcn2-knockout (Lcn2-/-) mice upon infection with *S. pneumonia*. (B) Levels of LCN2 in bronchoalveolar lavage (BAL) of intensive care unit (ICU) patients with bacterial pneumonia, caused by Gram-positive or Gram-negative pathogen. *Adapted from Warszawska et al., The Journal of Clinical Investigation 2013.*

Towards a New Therapy for Sepsis

In a third project, which was also published in 2013, scientists in Sylvia Knapp's laboratory discovered a critical modulator of the innate immune response to bacterial peritonitis, another potentially deadly disease caused by infection of the peritoneum by different types of bacteria. This project, led by PhD student Ulrich Matt, uncovered an unanticipated role for the protein WAVE-1 in the innate immune response to this infectious disease. Previously, WAVE-1 was only known as a protein that regulates another protein complex, Arp2/3, which has several cellular functions that are managed by regulating the actin cytoskeleton. They now show that WAVE-1 plays a crucial role also in macrophages as it mediates anti-phagocytic effects induced by lipid-derived danger molecules in Gram-negative sepsis. Their discovery, which was published in *The Journal of Clinical Investigation* (Matt et al., 2013), presents WAVE-1 as an important new therapeutic target for developing drugs to treat severe bacterial infections and sepsis, for which there is currently no effective therapy.

How the Liver Deals with Infections

Persistent viral infections with hepatitis B and hepatitis C affect more than 500 million people. However, treatment options are limited due in part to the complex pathogenesis of these infectious diseases as well as a lack of suitable tools with which to study them in detail in the laboratory. At CeMM, Andreas Bergthaler and his group employ a model approach by exploiting a tiny mouse virus called lymphocytic choriomeningitis virus (LCMV), which shares hallmark features with human viral hepatitis but allows them to study it far more easily.

The team recently uncovered a novel mechanism for how the host protects liver cells from virus-induced oxidative damage. They used an array of genetic and pharmacological tools to identify and delineate the molecular players and signaling pathways involved. Their results reveal potential new targets to improve the treatment of hepatitis patients.

In another project, in collaboration with Keiryn Bennett's group at CeMM, the Bergthaler group has been studying global protein and RNA perturbations in the liver upon viral infection. By employing quantitative protein mass-spectrometry as well as transcriptional profiling by RNAseq, they were able to capture the dynamics of the liver proteome and transcriptome over 100 days of persistent viral infection. This provides a map, in unprecedented detail, of how the liver reacts to viral infection. It has led them to poorly understood areas of metabolism, pathogen-inflicted cellular stress, and inflammation, which appear to be interconnected. To gain further insights into these host-virus interactions they are currently collaborating with basic scientists as well as clinicians with their invaluable perspectives from the bedside.

Immune Disorders and Inflammatory Diseases

The Protective and Destructive Properties of the Immune System

The human immune system is a specialized internal defence system. It is highly complex, consisting of many different types of cells and molecules, such as macrophages, white blood cells, antibodies and cytokines, which are all activated in different ways and under specific disease-causing conditions. Some parts of our immune system act as a first line defence and become activated by an initial infection or by tissue damage, whereas others act in chronic disease settings. There is also a dedicated division for remembering a certain infectious agent and preventing reinfection.

Without our immune systems we simply wouldn't survive. When we do expose ourselves to damaging agents or infectious diseases, which happens on a daily basis and mostly without us realising it, our immune systems are immediately activated and work hard trying to restore us to a healthy state. How our immune systems function can tell us a lot about how to fight diseases such as cancer and infections, and can be studied in patients with immune system disorders. At CeMM, Kaan Boztug and his group have been studying the genetic mutations underlying immune deficiency disorders in order to tease apart the molecular mechanisms involved and find new ways of treating patients.

The immune system is also immensely powerful because it needs to be able to destroy infectious pathogens and cancer cells, and neutralise toxic agents. In addition, the inflammatory immune response, which can be triggered by tissue damage, is strong enough to cause us to experience localised pain, redness and swelling. Its main purpose is to respond to the trigger of inflammation and resolve it. To keep this powerful system under control and functioning well there are a large number of regulatory mechanisms in place. This is critical also because continuous stimulation of this part of the immune system can cause chronic inflammation, which can lead to severe conditions such as atherosclerosis. Atherosclerosis is a chronic disease characterized by damage of blood vessel walls, and is a major cause of heart attack and stroke. Christoph Binder and his team at CeMM have been investigating the role of the inflammatory immune response in driving the progression of atherosclerosis, and how other components of our immune system, specifically so-called natural antibodies, work to prevent it.

The Causes of Immune System Malfunction

Primary immunodeficiency disorders are a rare group of childhood diseases that are characterised by an increased predisposition to infection. They are caused by the inheritance of specific genetic mutations that impair the immune system and lead to a defective infection-fighting capacity, and are often associated with other characteristics such as autoimmunity. Indeed, severe autoimmunity in childhood can indicate a primary immunodeficiency disorder. Knowledge of the underlying mechanisms, which are currently mostly unclear, could lead to the development of much needed new therapies. Kaan Boztug's group analyses patients with immunodeficiency disorders using state-of-the-art genomic approaches available at CeMM including exome sequencing. This enables them to identify the causative genetic mutations, which they then use to analyse their molecular functions and dissect the underlying mechanisms involved.

In 2013, PhD student Elisabeth Salzer and her colleagues in the Boztug group, in collaboration with the University Department of Paediatrics and Adolescent Medicine, discovered a new molecular cause for a primary immunodeficiency in a 12-year-old patient who was suffering from autoimmunity and immune dysfunction. They identified abnormal numbers of specific subsets of B cells, which produce antibodies. To pinpoint the genetic mutation causing the disease the team undertook single nucleotide polymorphism array-based homozygosity mapping and exome sequencing on DNA from the patient and compared it to that of close family members and healthy individuals. This revealed candidate causative mutations in two genes. One of these genes, *PRKCD,* was known to play a role in B cell signalling making it the prime candidate as the disease-causing gene in this patient.

Further analyses revealed that the protein product of *PRKCD* was absent in the patient's B cells, as was the activation of known down-stream effectors. These events are likely to have caused the malfunction in B lymphocytes and the development of autoimmunity. This important discovery of a new genetic mutation that can cause human immunodeficiency was published in the journal *Blood* (Salzer et al., 2013). It significantly enhances our understanding of B cell function, and could help in the diagnosis and development of treatments for patients with related autoimmune disorders.

In a related project on B cell deficiency and autoimmunity, also led by Elisabeth Salzer in Kaan's group and in collaboration with research-ers from Ankara University, Turkey, the Center of Chronic Immunodeficiency, Freiburg, Germany and the Medical University of Vienna, and using similar sequencing techniques, the team identified a homozygous mutation in the *IL-21* gene, which is a well known regulator of different parts of the immune response. Their novel discovery that this mutation causes early onset inflammatory bowel disease and is associated with defects in B cell numbers and function has important implications for IL-21-inhibitor treatment strategies that have been proposed for autoimmune diseases.

How a Protective Immune Response Can Lead to a Deadly Disease

While the absence of a functional immune system can cause severe immune disorders, a fully functioning immune response in certain settings can also cause diseases, such as the chronic inflammatory disease atherosclerosis. Atherosclerosis is caused by high levels of cholesterol in the blood leading to the presence of low density lipoproteins in the blood vessel walls. These low density lipoproteins become oxidised and are subsequently recognised by the immune system leading to a chronic inflammatory response. Over several decades this process results in the formation of atherosclerotic plaques containing the oxidised low density lipoproteins and immune cells. These plaques can eventually rupture, triggering the formation of a blood clot (thrombus) that can block the vessel and lead to a myocardial infarction or stroke. Scientists in Christoph Binder's group at CeMM have recently been studying the role of microparticles in inflammation and thrombosis formation, and how this relates to disease progression.

Microparticles are small (0.1 – 1 µm) vesicles released by cells, including those of the immune system, and have diverse functions including promoting inflammation. Christoph Binder's group has recently discovered that microparticles display so-called malondialdehyde (MDA) adducts, which are oxidation specific epitopes, on their surface. These MDA adducts mediate an inflammatory response, which can be blocked by naturally occurring IgM antibodies and complement factor H. They are now testing whether these MDA-adducts on microparticles also mediate thrombosis upon atherosclerotic plaque rupture, which could lead to novel diagnostic biomarkers and the development of therapies.

In addition, the Binder group is currently studying how the recognition of oxidation specific epitopes by natural antibodies helps to protect against chronic inflammation, which could be involved in a wide range of different diseases including pulmonary, renal and liver disease, as well as Alzheimer's disease and multiple sclerosis. PhD students Dimitrios Tsiantoulas and Sabrina Gruber from Christoph Binder's group presented this topic in a recent review published in the journal *Frontiers in Immunology* (Tsiantoulas et al., 2013). The aim of these projects is to identify disease-relevant molecular mechanisms, which could be exploited to provide novel therapeutic approaches for these pathological conditions.

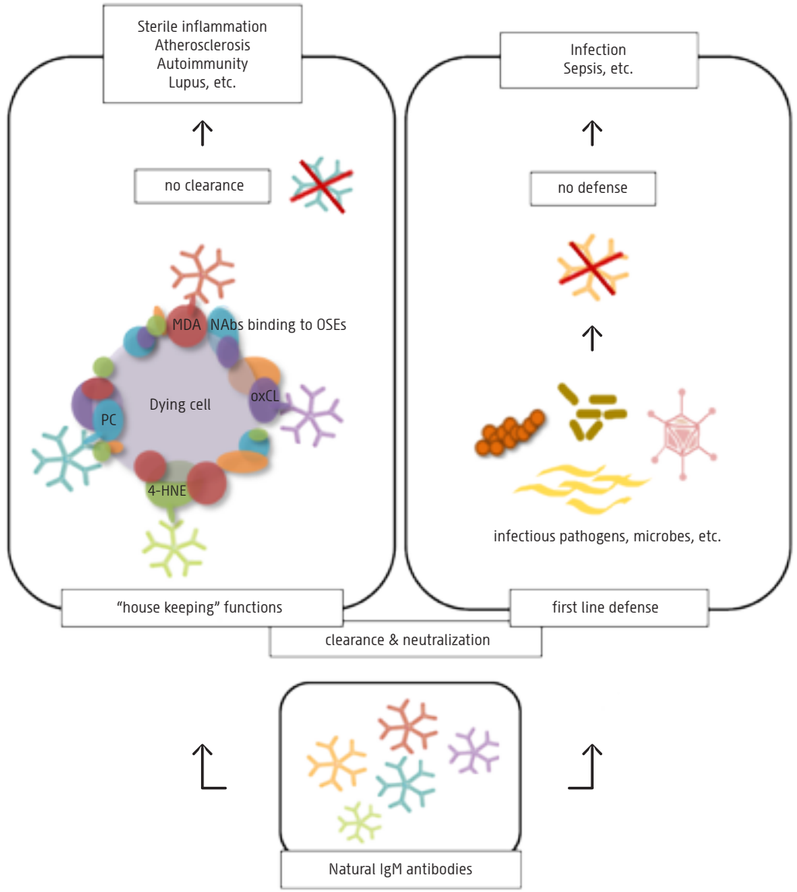


Fig. 4 Cartoon outlining protective properties of natural antibodies (NAbs) specific to oxidation-specific epitopes (OSEs). NAbs exhibit housekeeping and host defence functions by targeting OSEs on the surface of apoptotic cells, cells undergoing programmed cell death (apoptosis), self antigens, and microbial agents. Insufficient NAb titers may lead to impaired clearance of cellular debris and reduced protective capacity from invading pathogens. Accumulating apoptotic material can trigger auto-immune responses and promote chronic inflammatory disease. *Adapted from Tsiantoulas et al., Frontiers in Immunology 2013.*

Post-Genomic Technologies

The Major Drivers of New Scientific Discoveries
Technological advance has always been a significant driver of scientific discovery. Once tools are developed that enable scientists to answer questions that were previously considered inaccessible, substantial gains can be made in established fields, sometimes leading to dogmas being overturned or the birth of completely new fields. As an institute operating in the post-genomics era (i.e., at a time when entire genomes, both healthy and diseased ones, can be relatively easily accessed and explored), CeMM has invested heavily in the development of a suite of modern tools and technologies to promote its own disease relevant research as well as to provide tools and technologies for the local and international scientific community.

Next Generation Sequencing
CeMM's technology suite includes the Biomedical Sequencing Facility (BSF), which is hosted at CeMM and coordinated by CeMM PI Christoph Bock. This is Austria's first technology platform dedicated to next generation sequencing in biomedicine, and is part of the joint genomics core facility of the Medical University of Vienna and CeMM. The facility offers sequencing using the Illumina HiSeq platform, which is currently the preferred technology for many applications, as well as advice for other sequencing technologies. Sequencing performed at the BSF has featured in several prominent CeMM publications in 2013, including work from Robert Kralovics' group (Klampfl et al., NEJM 2013), and Kaan Boztug's group (Salzer et al., Blood 2013), as well as in the collaborative project on Haploid Genetics with Haplogen (Bürckstümmer et al., Nature Methods 2013). For more details on these projects, see the chapters on cancer and immune system disorders in this report, and below.

Mass Spectrometry and Proteomics
Another technology central to many CeMM projects is mass spectrometry, which has helped to generate high resolution protein interactomes, identify drug-protein interactions, perform comparative quantitative analysis of global proteomes, and monitor the role of post-translational modifications in cell signalling pathways. Keiryn Bennett is the head of the Mass Spectrometry and Proteomics research group at CeMM, and manages a laboratory equipped with four mass spectrometers. Each mass spectrometer is coupled to a nano-high performance liquid chromatography (HPLC) system for on-line liquid chromatography mass spectrometry. An additional HPLC is available for peptide and protein fractionation.

Bioinformatics

Helping to manage and exploit some of the large datasets generated by mass spectrometry are the bioinformaticists, headed by Jacques Colinge, who have developed tailored statistical and computational frameworks to enable users to sort through complex data and make novel discoveries. Recent work performed in the Superti-Furga, Bennett and Colinge groups led to a publication in the high profile journal *Nature Methods* (Varjosalo et al., 2013), see below for more details. Further computational work led to the innovative mapping of non-sequence specific nucleic acid-protein interactions (Dürnberger et al., *Genome Biology* 2013) as well as the development of advanced statistical tools to identify and quantify posttranslational modifications in mass spectrometry data (Breitwieser & Colinge, *J Proteomics* 2013).

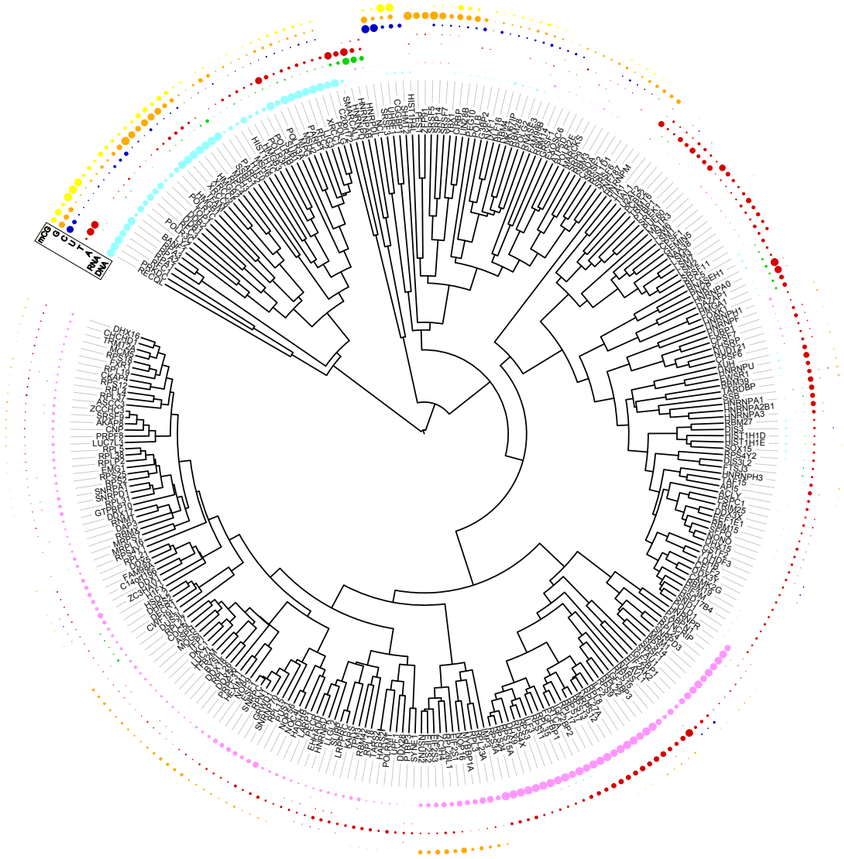


Fig. 5 Experimental characterization of the human non-sequence-specific nucleid acid interactome. 219 proteins were assigned binding preferences for at least one nucleic acid subtype and clustered by binding preference similarity in an affinity fingerprint dendrogram. Most protein families show similar binding preferences, while H1FX, for instance, was found to be RNA-specific as opposed to the family members H1F0 and HIST1H1C, which are DNA-specific. *Adapted from Dürnberger et al., Genome Biology 2013.*

Chemical Biology Resources

Also based at CeMM is the Platform Austria for Chemical Biology (PLACEBO); a comprehensive chemical screening platform that enables the identification and characterisation of small molecules for studying biological processes and developing drugs. It was initiated as a partnership between CeMM and seven other Austrian research groups, and funded under the Gen-AU program of the Austrian Ministry of Science and Research. The project is now open on a collaborative basis to the wider scientific community. PLACEBO is headed by Stefan Kubicek and provides chemical biology resources including a 92,000 compound library, and high-throughput and high-content screening.

Haploid Genetics Tools

And finally to haploid genetics, which has recently emerged as an important new tool in human cells that can be used to make scientific discoveries that were unobtainable with previous methods. This technology was originally developed by CeMM adjunct PI Thijn Brummelkamp who won the prestigious EMBO Gold Medal in 2013. It has now been used to produce a haploid cell library in a joint effort by CeMM and the biotechnology company Haplogen, which was published in the journal *Nature Methods* (Bürckstümmer et al., 2013). See below for more details.

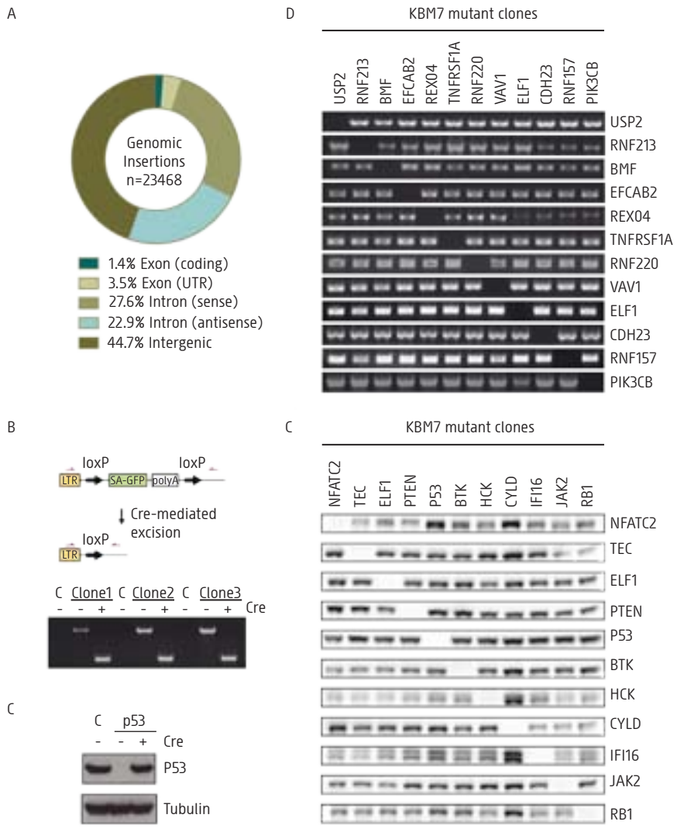


Fig. 6 Gene-trapped mutants are reversible and can resemble gene knock-outs. (A) Summary of the distribution of all gene-trap integration sites mapped in the high-throughput sequencing pipeline. (B) Schematic of the retroviral gene-trap vector and PCR analysis of genomic DNA from three clones is shown. (C) Western blot of KBM7 cells with a gene trap disrupting p53 expression, with and without Cre recombinase treatment and parental KBM7 cells as negative control. (D-E) Overview of RT-PCR and Western blot analysis of the indicated clones, respectively. *Adapted from Bürckstümmer et al., Nature Methods 2013.*

Developing Haploid Genetics Tools for the Scientific Community

Scientific research hugely benefits from collaborative efforts between different laboratories, as illustrated by the study above. It also benefits from the development and sharing of valuable tools. In another project, performed as a partnership between scientists at CeMM and Haplogen, a powerful new human genetics tool has recently been developed, which will benefit groups at CeMM as well as the broader scientific community.

Over the past three years, as part of a public-private partnership, Haplogen and CeMM have been developing a large collection of human cell lines that are deficient for single genes. Classical human cell lines are highly heterogeneous, making them very difficult to control when performing genetic experiments. This limits their value particularly for drug discovery efforts and studying gene function. This new collection circumvents this problem as each cell line carries only a single, known, gene mutation in an otherwise identical genetic background. Obtaining human cells where an individual gene is inactivated had previously been difficult because they carry two copies of each gene (i.e. are diploid). Thijn Brummelkamp, founding member of Haplogen and Adjunct PI at CeMM, presented a solution with the invention of haploid genetics technology.

This technology was further developed by Haplogen and subsequently used to create the haploid collection, which is the largest human cell line collection available to date. At Haplogen this collection is being used as an indispensable tool for the research and development of antiviral medications for treating a wide range of harmful infectious diseases. It is also expected to fuel academic research in molecular medicine where the vast majority of human genes await functional characterization. Indeed, several groups at CeMM are using it to study host-pathogen interactions and mechanisms of drug action.

As an indication of things to come, scientists in the laboratory of CeMM adjunct PI Thijn Brummelkamp, in collaboration with scientists at the Radboud University (Netherlands) and Harvard University (US), used haploid cell lines to identify genes required for coupling sugar groups to the dystroglycan protein. Defects in these genes make cells insensitive to infection by Lassa Fever virus, which causes hemorrhagic fever, but they also cause a severe hereditary disease called Walker-Warburg syndrome, which is characterized by brain, muscle and eye defects. The identification of these genes using this approach, which was published in the prestigious journal *Science* (Jae et al., 2013), further highlights the value of haploid genetics technology, and could lead to the development of new treatments.

The haploid cell collection was made possible by the partnership between academic research at CeMM and private investment by Haplogen, along with financial support from ZIT (Technology Agency of the City of Vienna). The technological advances involved in the development of this collection were recently published in the journal *Nature Methods* (Bürckstümmer et al., 2013). At that time, the collection included cell line clones covering 3,000 different human genes, which represents about one third of all the genes that are active in these cells. Haplogen is continuing to expand its repertoire of mutant haploid cell lines. The current collection can be explored at clones.haplogen.org.

CeMM and Haplogen have been developing the largest haploid human cell line collection available to date.

Pushing the Limits of a Technology

Testing the reliability and pushing through the boundaries of new technologies is critical for seeing their potential realised. This was done in a recent joint research project between CeMM and ETH Zurich, and has made the golden goal of mapping all protein interactions within the human proteome readily achievable. Researchers in Giulio Superti-Furga's group at CeMM and Matthias Gstaiger's group at the Institute of Molecular Systems Biology, ETH Zurich, together demonstrated the high intra- and inter-laboratory reproducibility of a standardized affinity purification-mass spectrometry protocol. The study would not have been feasible without the integral involvement of the laboratories of Keiryn Bennett and Jacques Colinge at CeMM, and of Ruedi Aebersold, director of the institute at ETH.

A comprehensive understanding of how proteins interact with each other is a Rosetta stone for the interpretation of the genome. Only then can the role of individual gene products be fully understood, as each one's function is intimately connected with the function of others. Previously, the focus had been on studying the function of individual genes and proteins. More recently it has become clear that studying the functional organization of the entire human proteome is required to decipher the orchestration of cellular processes at a systems level. Considering that only a tenth of the more than half a million protein-protein interactions in human cells have been experimentally observed so far, it has become clear that a complete characterization of the human interactome can only be achieved by a collaborative scientific effort.

The success of this project was critically dependent upon the recent progress in sensitivity, throughput and specificity of a technique known as affinity purification coupled to mass spectrometry (AP-MS). Having been successfully used in yeast and *Drosophila,* this technique has become ideal for the large-scale analysis of human protein complexes. However, there are important technical limitations, in particular in reproducibility between different groups. The available public data revealed that on average only 25% of an individual protein's interactions were reproduced in an independent experiment, highlighting differences between experimental systems and/or data processing pipelines.

To address this shortcoming, the team conducted a large-scale comparative study in two separate laboratories (and countries) by each analysing the protein interactions of 32 human protein kinases using affinity purification and AP-MS analyses. The experiment took three years and involved the standardization of experimental parameters and cross-laboratory training of scientists. The project was performed maintaining most of the mass spectrometry instrumentation settings typical of the individual laboratories, to mimic as much as possible realistic conditions for future multi-laboratory efforts.

The final network produced from these experiments is composed of 488 protein interactions, 364 of which were novel. This represents the largest AP-MS data set on the human kinome published to date. The data generated were highly reproducible in the partner laboratory (81%), with the biochemical experiments being the largest cause of data variation. The study was published in *Nature Methods* (Varjosalo et al., 2013). This unique Zurich-Vienna effort demonstrated that this technology is highly robust, and can now be confidently used in an inter-laboratory effort to map the entire protein machinery of a human cell.

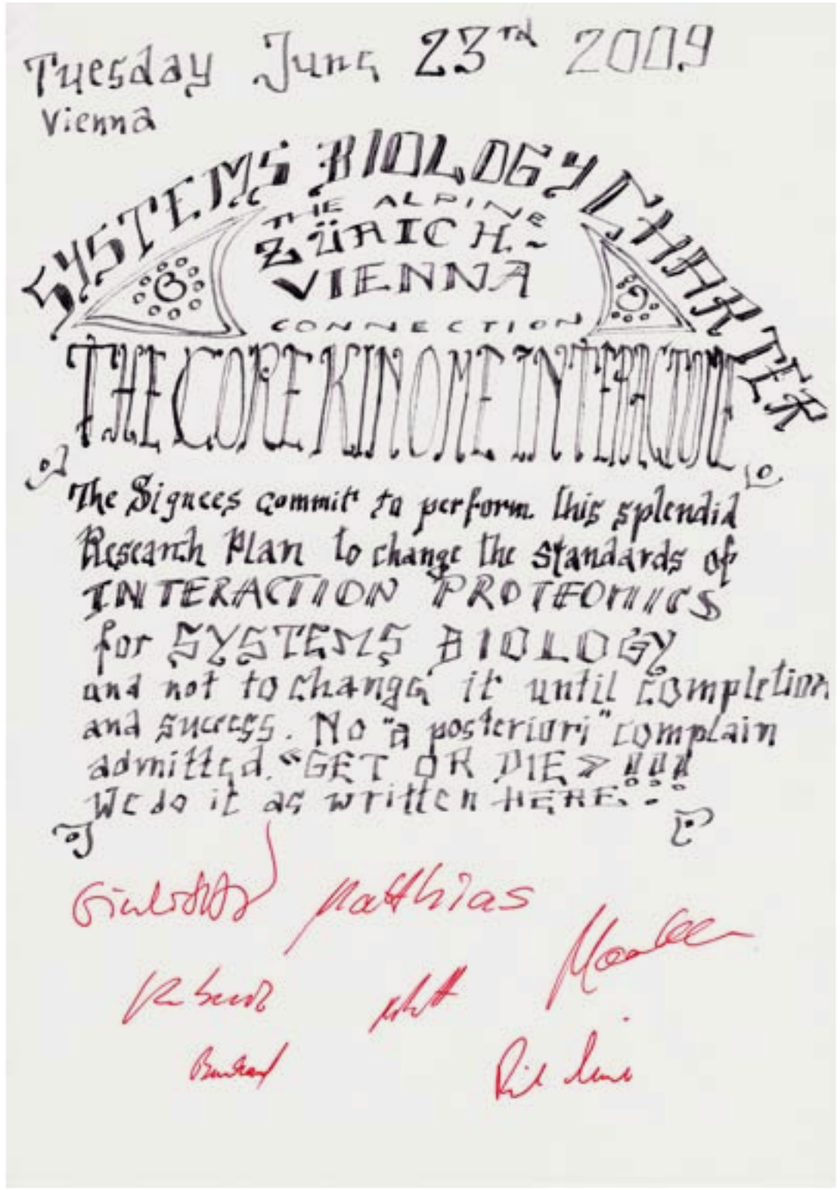


Fig. 7 Systems Biology Charter establishing the "The Core Kinome Interactome" project alliance known as "The Alpine Zurich – Vienna Connection". A joint research effort between CeMM and the ETH Zurich demonstrates in a systematic study of the intra- and interlaboratory reproducibility of a standardized affinity purification-mass spectrometry protocol, that high reproducibility can be achieved, providing a hint at the feasibility of a large-scale human interactome project through interlaboratory efforts. The charter testifies the a priori commitment of the signees to perform this research strategy towards a change in the standards of interaction proteomics for systems biology, not to change it until completion and success and not to criticize "a posteriori". *Artwork by Giulio Superti-Furga.*

Diagnostics and Therapeutics

From the Clinic to the Clinic
The research conducted at CeMM tackles significant biomedical challenges with an emphasis on cancer, immune disorders and infectious diseases. In keeping with CeMM's mission "From the clinic to the clinic", there are several projects that are specifically focused on the development of innovative diagnostics and therapeutics, some of which could have an immediate impact in the clinic.

An accurate diagnosis is absolutely required for optimal clinical management of any disease. Biological markers identified through scientific research have been highly valuable for supporting the medical profession in making accurate diagnoses, as well as providing important new understanding of the mechanisms underlying diseases, which can lead to the development of new treatments. Disease biomarkers are also crucial for tailoring specific therapies to the individuals most likely to benefit from them, which is known as personalised medicine. This is also important for the success of candidate drugs undergoing clinical trials. Unfortunately, there have been some notable failures of drugs that have not been clinically approved because of the absence of a biomarker, which meant that the patients were not stratified during the trial, and not because the drug was ineffective. However, identifying useful biomarkers for diseases can be quite challenging.

The Hunt for New Biomarkers and Drugs

Defects in the incidence of epigenetic marks such as DNA methylation tend to occur early during cancer development and are thought to correlate with disease severity and response to treatments. This makes them promising targets for biomarker development. In Christoph Bock's group at CeMM, researchers have established an epigenetic biomarker platform that they are using to systematically derive, prioritize and validate DNA methylation biomarkers in cancer as diagnostics for personalised medicine. Their work is performed in the context of the European BLUEPRINT project and the International Human Epigenome Consortium.

For many diseases, the hunt is also still on for effective drugs. Classical drug screening approaches have yielded important but too few successes. To address this shortfall, scientists at CeMM have been developing and utilising novel technologies and tools as alternative drug target discovery approaches. These include PLACEBO (Platform Austria for Chemical Biology), which provides chemical biology tools for high-throughput and high-content screening. This technology is being used in the Christian Doppler laboratory, which is a public-private partnership between CeMM, Boehringer Ingelheim, and Haplogen, headed by CeMM's Stefan Kubicek, in order to identify potential new drugs and diagnostics for a variety of different diseases.

Another alternative approach has been developed in Sebastian Nijman's group, where scientists are using isogenic cancer models and haploid genetics that they have been developing to identify synthetic lethal interactions. These genetic interactions can potentially be exploited to develop new drugs targeted to certain types of cancers. And together with long-time CeMM collaborator Eric Haura and colleagues from the H. Lee Moffitt Cancer Center and Research Institute in the US, the groups of Keiryn Bennett, Jacques Colinge and Giulio Superti-Furga have together been harnessing the power of systems biology to discover novel therapeutics for treating patients with lung cancer, including those that have developed resistance to known drugs. See below for more details.

Even when drugs are available, it is surprising how little is understood about how they actually work, particularly on the molecular level. Scientists in Giulio Superti-Furga's group are working on characterizing the mechanism of action of known drugs. They use systems-level approaches comprising transcriptomics, haploid cell genetics and chemical proteomics, which are established at CeMM, to elucidate how a specific drug, such as an anti-cancer drug, can target cancer cells and inhibit molecular processes that result in cell death. This information is important for the development of new generations of potentially more effective drugs, and for understanding the development of drug resistance, which is a major clinical problem.

A Systems Approach to Drug Discovery

Most cellular processes, such as growth and differentiation, are controlled by complex intracellular signaling pathways, which are composed of many different types of molecules. For example, when a cell should be proliferating, extracellular growth factors such as the epidermal growth factor (EGF) are produced that bind to their cognate receptors on the surface of the target cell, triggering a cascade of activity inside that cell. This activity involves many different proteins, including kinases and phosphatases, which can chemically modify and thereby alter the activity of a select group of target proteins. The cascade eventually reaches the cell nucleus and leads to the activation and repression of a gene expression program. This program is designed to produce an array of specialized proteins such as those involved in biosynthesis to enable the cell to grow.

The capability of signaling pathways to control a cell makes them vulnerable to mutation during the development of diseases such as cancer. For example, the receptor for EGF, known as EGFR, is often found mutated or aberrantly expressed in several different types of cancer including lung cancer. Lung cancer is one of the most deadly cancers, and treatment options are severely limited. Although EGFR inhibitors have worked to a certain extent in the clinic, they do lead to the development of drug resistance, necessitating the identification of alternative treatment approaches. Scientists in the groups of Giulio Superti-Furga, Jacques Colinge and Keiryn Bennett at CeMM, together with the group of Eric Haura in the US, hypothesised that if they could comprehensively map all the proteins that bind to the mutated forms of EGFR, which are found in lung cancer, this may help to identify new anti-cancer drug targets, and alternative treatment strategies to overcome drug resistance.

They began by using tandem affinity purification to identify all the proteins that bound to a cancer-associated EGFR mutant and wild type EGFR protein expressed in two selected lung cancer cell lines. Bound proteins were identified by liquid chromatography mass spectrometry (LC-MSMS). To expand this initial protein-protein interaction network (i.e., 'interactome') they selected some of the newly identified proteins and repeated the process. These experiments were also complemented by identifying all of the proteins that were modified by tyrosine phosphorylation in one of the lung cancer cell lines treated with an EGFR inhibitor.

Collectively, the data could be assembled into a coherent interactome. Selected proteins in the interactome were then depleted using RNA interference to identify those that are required for viability of three different lung cancer cell lines. Finally, to uncover new combinations of drugs that could be more effective for treating lung cancer, particularly EGFR inhibitor resistant lung cancer, they went on to identify drugs that are known to interact with some of the core components of their interactome and generated a drug network, which they also tested for efficacy in vitro. This large body of work was published in the journal *Molecular Systems Biology* (Li et al., 2013), and has provided many new avenues for future research. By following a systems approach, the team has uncovered new insights into EGFR inhibitor resistance mechanisms and suggested feasible and urgently needed treatments that could be used to overcome this resistance in lung cancer patients.

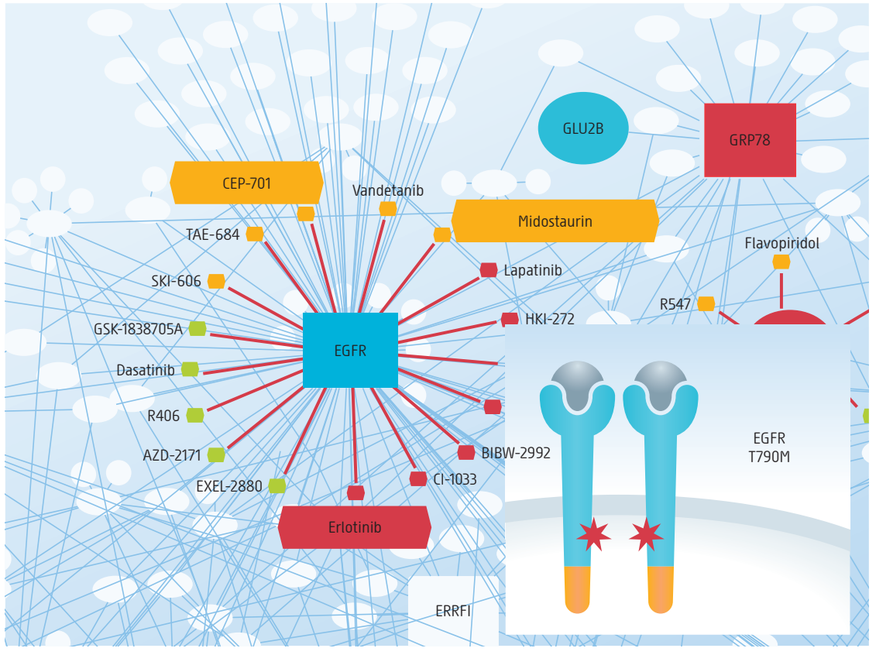


Fig. 8 Perturbation of the mutated Epidermal Growth Factor Receptor (EGFR) interactome identifies vulnerabilities and resistance mechanisms. A graphic rendition of the coherent drug network derived from the core physical EGFR interactome integrated with kinase inhibitors derived from competition binding assays is shown. Midostaurin and lestaurtinib (CEP-701) can overcome drug resistance in EGFR-mutated lung cancer cells through direct EGFR inhibition, when combined with erlotinib. Blue nodes (proteins) highlight EGFR-specific core proteins for cell survival, red nodes highlight non-specific core proteins. Rectangles and ellipses are bait and prey proteins, respectively, identified by tandem affinity purification or phosphoproteomics. Red lines indicate inhibitor – protein interactions, Hexagons are inhibitor drugs and their colour is related to inhibitor Kd. *Figure adapted based on Fig. 6B from Li et al., Molecular Systems Biology 2013.*

Principal Investigators

Denise P. Barlow

Epigenetic Mechanisms in Development and Disease

Denise Barlow is a British national who joined CeMM in 2003 and is an Honorary Professor at the University of Vienna. She 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. She 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. Her group's 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 uses the model of genomic imprinting to dissect how lncRNAs epigenetically silence genes, and together with high throughput sequencing technology is extending these results into the mouse and human genome with the goal of understanding how lncRNAs play a role in human diseases such as cancer.

Main Research Interests

+ Moleular 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

Relevant/Important Publications

Barlow DP, et al. Genomic imprinting in mammals. *Cold Spring Harb Perspect Biol.* 2014 Feb 1;6(2). pii: a018382.

Kornienko AE, et al. Gene regulation by the act of lncRNA transcription. *BMC Biol.* 2013 May 30;11:59. Review.

Latos PA, et al. Airn transcriptional overlap, but not its lncRNA product, induces imprinted Igf2r silencing. *Science.* 2012 Dec 14;338(6113):1469-72.

Santoro F, et al. Imprinted Igf2r silencing depends on continuous Airn lncRNA expression and is not restricted to a developmental window. *Development.* 2013 Mar;140(6):1184-95.

Keiryn L. Bennett

Mass Spectrometry and Proteomics

Keiryn Bennett 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. She spent 2½ years as a post-doctoral fellow in the laboratory of one of the forefathers 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). She is respected worldwide in the field of protein mass spectrometry and proteomics, with more than 17 years of experience including 4 years managing a high-throughput industrial proteomic laboratory. She joined the laboratory of Giulio Superti-Furga in 2004 and established the mass spectrometry/proteomic research group at CeMM. Since 2009, Keiryn Bennett has had an independent group leader position and currently the laboratory consists of a total of 4 people. The mass spectrometry research group is currently focused on: monitoring the phosphorylation events of kinase substrates; understanding the role of HDAC1 and HDAC2 in T-cell proliferation; and investigating the cellular pathways involved in oxidative stress. These research areas are supplemented by technological advancements in protein-protein and drug-protein interactions, chemical crosslinking, quantitative-, and post-translational modification proteomics.

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

Relevant/Important Publications

Giambruno R, et al. Affinity purification strategies for proteomic analysis of transcription factor complexes. *J Proteome Res.* 2013;12(9):4018-4027.

Rudashevskya EL, et al. 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. *Nat. Protoc.* 2013;8, 75-97.

Bürckstümmer T, et al. An efficient tandem affinity purification procedure for the characterisation of protein complexes in mammalian cells. *Nat. Methods.* 2006;3, 1013-1019.

Ho Y, et al. Systematic identification of protein complexes in *Saccharomyces cerevisiae* by mass spectrometry *Nature.* 2002;415: 180-183.

Andreas Bergthaler

Viral Pathogenesis and Immunopathologies

Andreas Bergthaler, born 1977, joined CeMM in 2011. He studied veterinary medicine at the University of Veterinary Medicine in Vienna and spent clinical and research stays at the Royal (Dick) School of Veterinary Studies, Edinburgh, the University of Tokyo, the University of Zurich and the Danish Veterinary Institute, 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 basis of how viral infections cause disease and immunopathology. 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 bear patho-physiological relevance to human disease and provide defined experimental systems to gain mechanistic insights through targeted perturbations. 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 human viral diseases such as hepatitis, immunosuppression and superinfections.

Main Research Interests

+ Viral pathogenesis
+ Antiviral immune responses
+ Mouse infection models
+ Systems biology

Relevant/Important Publications

Kreutzfeldt M*, Bergthaler A*, et al. Neuroprotective intervention by interferon-γ blockade prevents CD8+ T cell-mediated dendrite and synapse loss. *J Exp Med.* 2013 Sep 23;210(10):2087-103.

Litvak V, et al. A FOXO3-IRF7 gene regulatory circuit limits inflammatory sequelae of antiviral responses. *Nature.* 2012 Oct 18;490(7420):421-5.

Bergthaler A, et al. Viral replicative capacity is the primary determinant of lymphocytic choriomeningitis virus persistence and immunosuppression. *Proc Natl Acad Sci U S A.* 2010 Dec 14;107(50):21641-6.

(* equal contribution)

Christoph Binder

Atherosclerosis and Immunity

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, in 2006 he joined CeMM. He is a specialist in Laboratory Medicine and leads a research group focusing on the role of immune functions in atherosclerosis and how these can be exploited for therapeutic interventions. He first described the atheroprotective effect of pneumococcal vaccination 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). He has won numerous prestigious fellowships and awards and has authored >70 publications in important journals, including Nature Medicine and Nature.

Main Research Interests

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

Relevant/Important Publications

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

Weismann D, et al. Complement factor H binds malondialdehyde epitopes and protects from oxidative stress. *Nature.* 2011 Oct 5;478(7367):76-81.

Chou MY, et al. Oxidation-specific epitopes are dominant targets of innate natural antibodies in mice and humans. *J Clin Invest.* 2009 May;119(5):1335-49.

Binder CJ, et al. Pneumococcal vaccination decreases atherosclerotic lesion formation: molecular mimicry between Streptococcus pneumoniae and oxidized LDL. *Nat Med.* 2003 Jun;9(6):736-43.

Binder CJ, et al. Innate and acquired immunity in atherogenesis. *Nat Med.* 2002 Nov;8(11):1218-26.

Christoph Bock

Medical Epigenomics and Next Generation Sequencing

Christoph Bock is a Principal Investigator at CeMM, a guest professor at the Medical University of Vienna's department for laboratory medicine and the coordinator of the Biomedical Sequencing Facility at CeMM. His research focuses on medical epigenomics, studying the role of DNA methylation in cancer and developing methods for rational design of epigenetic cancer therapies. He graduated from the Max Planck Institute for Informatics and Saarland University in 2008, and there he has been an adjunct group leader for computational epigenetics since 2009. As a postdoctoral research fellow at the Broad Institute of MIT and Harvard, Christoph Bock contributed to the work of the Roadmap Epigenome Mapping Consortium. He joined CeMM in 2012, and his lab is involved in the International Human Epigenome Project and in several EU project consortia aimed at dissecting the role of epigenetics in cancer through large-scale epigenome mapping. In 2009, Christoph was awarded an Otto Hahn Medal by the Max Planck Society for pioneering work in computational epigenetics.

Main Research Interests

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

Relevant/Important Publications

Bock C., et al. Analysing and interpreting DNA methylation data. *Nature Reviews Genetics.* 2012; 13: 705-719.

Bock C, et al. Managing drug resistance in cancer: lessons from HIV therapy. *Nature Reviews Cancer.* 2012; 12: 494-501.

Bock C, et al. DNA methylation dynamics during in vivo differentiation of blood and skin stem cells. *Molecular Cell.* 2012; 47: 633-647.

Bock C, et al. Reference Maps of human ES and iPS cell variation enable high-throughput characterization of pluripotent cell lines. *Cell.* 2011; 144, 439-452.

Bock C, et al. Quantitative comparison of genome-wide DNA methylation mapping technologies. *Nature Biotechnology.* 2010; 28: 1106-1114.

Kaan Boztug

Genetics and Molecular Pathophysiology of Inborn Errors of the Immune System

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 M.D. 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). He is the director of the newly established CeRUD Vienna Center for Rare and Undiagnosed Diseases.

Main Research Interests

+ Molecular genetics of primary immundefiencies and congenital bone marrow failure syndromes
+ Molecular genetics of malignant hematological disorders of childhood

Relevant/Important Publications

Boztug K, et al. A syndrome with congenital neutropenia and mutations in G6PC3. *N Engl J Med.* 2009; 360: 32-43.

Glocker E-O*, Kotlarz D*, Boztug K*, et al. Early-onset inflammatory bowel disease caused by loss-of-function mutations in the IL10-receptor genes. *N Eng J Med.* 2009; 361: 2033-45.

Salzer E*, Santos-Valente E*, et al. B cell deficiency and severe autoimmunity caused by deficiency of protein kinase C delta. *Blood.* 2013 Apr 18;121(16):3112-6.

(* equal contribution)

Thijn Brummelkamp

Genetics of Cancer and Infectious Diseases

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

Main Research Interests

+ Cancer research
+ Infectious diseases
+ Drug action

Relevant/Important Publications

Jae, LT, et al. Deciphering the glycosylome of dystroglycanopathies using haploid screens for Lassa virus entry. *Science.* 2013 Apr 26;340(6131):479-83.

Carette JE, et al. Ebola virus entry requires the cholesterol transporter Niemann-Pick C1. *Nature.* 2011; 477(7364):340-3

Carette JE, et al. Haploid genetic screens in human cells identify host factors used by pathogens. *Science.* 2009; 326(5957):1231-5.

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

Jacques Colinge

Bioinformatics

Jacques Colinge was born in Switzerland and heads CeMM's bioinformatics group 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 Ph.D., Jacques Colinge 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 bioinformatics from TU Graz. The bioinformatics lab does research to develop data analysis methods aimed at unraveling the functions and structure of biological networks. The group also develops statistical models and maintains data processing pipelines to analyze and manage mass spectrometry data.

Main Research Interests

+ Computational proteomics
+ Protein interaction network analyses
+ 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

Relevant/Important Publications

Colinge J, et al. Building and exploring an integrated human kinase network: global organization and medical entry points. *J Proteomics.* 2014. pii: S1874-3919(14)00150-X.

Duernberger G, et al. Experimental characterization of the human non-sequence-specific nucleic acid interactome. *Genome Biol.* 2013, 14:R81.

Pichlmair A, et al. Viral immune modulators perturb the human molecular network by common and unique strategies. *Nature.* 2012. 487:486-490.

Colinge J, et al. Systems biology analysis of protein-drug interactions. *Proteomics Clin Appl.* 2012 Jan;6(1-2):102-16.

Breitwieser FP, et al. General statistical modeling of data from protein relative expression isobaric tags. *J Proteome Res.* 2011 Jun 3;10(6):2758-66.

Sylvia Knapp

Innate Immunity and Bacterial Infections

Sylvia Knapp studied Medicine at the University of Vienna and the Free University in Berlin. She obtained her M.D. 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 Internal Medicine at the Medical University of Vienna. After several residencies, mostly in areas like Infectious Diseases, AIDS and Intensive Care, 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. She 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 immune response to clinically relevant pathogens and on the role of bacterial virulence factors and their interactions with host structures and pathways. Her most important achievements include the functional characterization of lung macrophages as well as the biological function of several pattern recognition receptors during Streptococcus pneumoniae pneumonia. Sylvia Knapp maintained her responsibilities at the Intensive Care Unit at the Medical University Vienna and was appointed Professor of Infection Biology in 2012.

Main Research Interests

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

Relevant/Important Publications

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

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

Baumann CL, et al. CD14 is a coreceptor of Toll-like receptors 7 and 9. *J Exp Med.* 2010. 207: 2689-2701.

Robert Kralovics

Genetics of Hematological Disorders

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, he was a project leader with Radek Skoda in Basel. Kralovics' 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 Kralovics 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.

Main Research Interests

+ 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

Relevant/Important Publications

Klampfl T, et al. Somatic mutations of calreticulin in myeloproliferative neoplasms. *N Engl J Med.* 2013.Dec 19;369(25):2379-90.

Harutyunyan A, et al. p53 lesions in leukemic transformation. *N Engl J Med.* 2011 Feb 3;364(5):488-90.

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

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

Stefan Kubicek

Chemical Biology and Epigenetics

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. Since 2013 Stefan Kubicek also heads the Christian Doppler Laboratory for Chemical Epigenetics and Antiinfectives, a public-private partnership between CeMM, Boehringer Ingelheim, and Haplogen. The Kubicek lab is working on the role of chromatin in the definition of cell types and cell states. 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 with the aim of generating new insulin-producing beta cells.

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

Relevant/Important Publications

Mair B, et al. Exploiting epigenetic vulnerabilities for cancer therapies. *Trends Pharmacol Sci.* 2014; 35; 136-145.

Kubicek S, et al. Compounds targeting chromatin modifying enzyme induce specific cell-type independent transcription signatures in the endocrine pancreas. *Proc Natl Acad Sci U S A.* 2012; 109; 5364-5369.

Fomina-Yadlin D*, Kubicek S*, et al. Small-molecule inducers of insulin expression in pancreatic alpha-cells. *Proc Natl Acad Sci U S A.* 2010;107(34):15099-104.

Kubicek S, et al. Reversal of H3K9me2 by a small-molecule inhibitor for the G9a histone methyltransferase. *Mol Cell.* 2007 Feb 9; 25(3):473-81.

(* equal contribution)

Joanna I. Loizou

DNA Repair and Genomic Stability

Joanna Loizou joined CeMM in 2011. She 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 she 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 Loizou made the fundamentally important finding that cells utilize 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. She 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 Loizou's group investigates the mechanisms by which cells respond to, and repair, DNA damage in order to maintain genomic stability and suppress tumorigenesis. She 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 and suppression of cancer, but also for the maturation of immune cells.

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

Relevant/Important Publications

Loizou JI, et al. ATMIN is required for maintenance of genomic stability and suppression of B cell lymphoma. *Cancer Cell.* 2011; 19: 587-600.

Murr R*, Loizou JI*, et al. Histone acetylation by Trrap-Tip60 modulates loading of repair proteins and repair of DNA double strand breaks. *Nat Cell Biol.* 2006; 8: 91-99.

Loizou JI, et al. The protein kinase CK2 facilitates repair of chromosomal DNA single-strand breaks. *Cell.* 2004; 117: 17-28.

(* equal contribution)

Sebastian Nijman

Functional Cancer Genomics

Sebastian Nijman was born in the Netherlands in 1979. He studied medical biology at Utrecht University and specialized in Molecular Biology and Biochemistry in the labs of Hans Bos and René Medema. He 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 René 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. 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 in 2007, Sebastian Nijman's research is mostly focused on the identification and understanding of cancer vulnerabilities using chemical genetic screens.

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

Relevant/Important Publications

Nijman SM, et al. Cancer. Potential of the synthetic lethality principle. *Science.* 2013 Nov 15;342(6160):809-11.

Bürckstümmer T, et al. A reversible gene trap collection empowers haploid genetics in human cells. *Nat Methods.* 2013 Oct;10(10):965-71.

Muellner MK, et al. A chemical-genetic screen reveals a mechanism of resistance to PI3K inhibitors in cancer. *Nat Chem Biol.* 2011 Sep 25;7(11):787-93.

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

(* equal contribution)

Giulio Superti-Furga

Pathological Networks and the Mechanism of Action of Drugs in Infection and Cancer

Giulio Superti-Furga is an Italian molecular and systems biologist. He performed his studies at the University Zurich, Genentech, and IMP/Vienna. He was a Post-doctoral fellow at EMBL and later became a Team Leader. He co-founded the biotech companies Cellzome and Haplogen. Since 2005 he directs CeMM. He is a member of EMBO, Austrian Academy of Sciences, German Academy of Sciences Leopoldina, European Academy of Cancer Sciences, and chair of the EMBL Alumni Association. He obtained an Advanced Investigator ERC Grant and was made Knight Officer Order of Merit of the Republic of Italy. In 2011 the received the Prize of the City of Vienna for Natural Sciences, and became "Austria's scientist of the Year". Among his major achievements to date count the elucidation of basic regulatory mechanisms of tyrosine kinases in human cancers, the discovery of fundamental organization principles of the proteome of higher organisms and the development of integrated approaches to understand the mechanism of action of drugs at the molecular level. His recent work focuses on studying and understanding the time-resolved molecular impact of perturbations, such as drugs or viruses, on the human system.

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

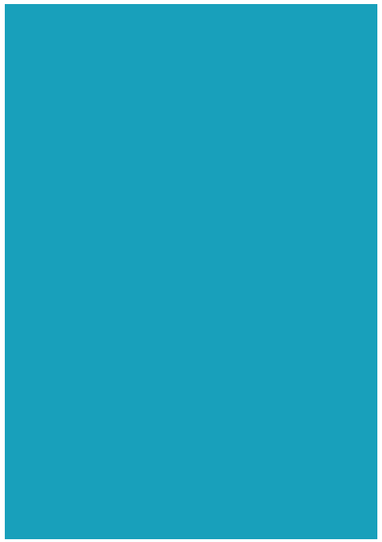
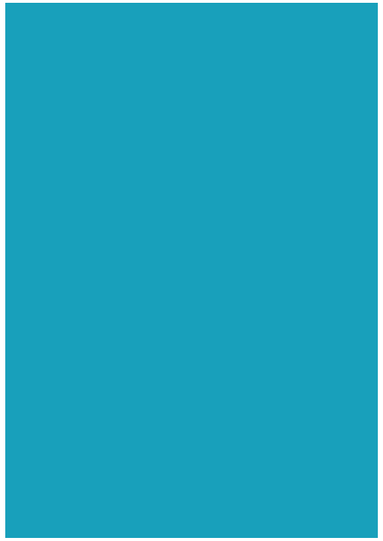
Relevant/Important Publications

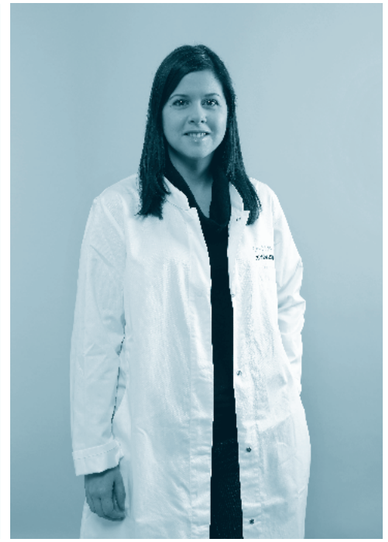
Huber KVM, et al. Stereospecific targeting of MTH1 by (S)-crizotinib as anticancer strategy. *Nature.* 2014 Apr 10;508(7495):222-7.

Winter GE, et al. Systems-pharmacology dissection of a drug synergy in imatinib resistant CML. *Nat Chem Biol.* 2012, 8(11):905-12.

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

Bürckstümmer T, et al. An orthogonal proteomic-genomic screen identifies AIM2 as a cytoplasmic DNA sensor for the inflammasome. *Nat Immunol.* 2009 Mar;10(3):266-72.



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Denise P. Barlow, Keiryn L. Bennett, Andreas Bergthaler, Christoph Binder, Christoph Bock, Kaan Boztug, Thijn Brummelkamp, Jacques Colinge, Sylvia Knapp, Robert Kralovics, Stefan Kubicek, Joanna I. Loizou, Sebastian Nijman, Giulio Superti-Furga

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72	5,8310	6	6,1644	5,6569	5,8310	6	5,8310	6	4,2426	4,2426	4,6904	5,2915	4,8990	5,2915	5,6569	4,8990	6,3246	6,1644	5,6569	6,4807	6,3246	5,6569	6	6
26	4,6904	4,8990	5,0990	4,6904	4,6904	4,8990	3,4641	4,6904	4,8990	4,8990	5,0990	3,4641	4,2426	3,7417	4,2426	4,4721	5,2915	5,0990	4,2426	5,4772	5,0990	4,2426	4,6904	5,2915
17	4,6904	4,4721	5,0990	4,2426	4,2426	3,7417	5,0990	4,2426	5,0990	5,0990	5,4772	4,6904	4,6904	5,2915	5,6569	5,0990	4,2426	4,2426	4	4,8990	5,0990	4	4	4,4721
00	5,0990	4,8990	5,2915	4,2426	4,4721	3,7417	5,4772	4,2426	5,4772	5,4772	5,8310	4,8990	5,0990	5,6569	6	5,2915	4,6904	4,6904	4,4721	5,2915	5,4772	4,4721	4,2426	4,4721
21	4,4721	3,4641	4,2426	4,4721	4,4721	4,2426	5,0990	4	5,8310	5,8310	6	5,2915	5,2915	5,6569	6	5,8310	5,2915	5,0990	4,4721	4,8990	4,8990	4,4721	4,4721	4,6904
41	4,6904	4	4,2426	2,8284	3,4641	4,2426	4,4721	4,2426	5,2915	5,2915	5,4772	4,4721	4,6904	5,2915	5,4772	5,0990	5,0990	4,8990	3,7417	4,8990	5,0990	4	4,6904	4,8990
23	4,4721	3,4641	4,2426	3,1623	3,1623	4,2426	4,4721	4,2426	5,0990	5,0990	5,2915	4,4721	4,2426	5,0990	5,4772	5,0990	5,0990	4,8990	3,7417	4,6904	5,0990	3,7417	4,4721	4,8990
41	4,2426	4,2426	4,8990	4	3,4641	4	4	4,6904	4,8990	4,8990	5,0990	3,4641	4	4,6904	5,0990	4,8990	5,0990	4,8990	3,7417	4,8990	5,0990	3,7417	4	4,6904
26	5,0990	5,2915	5,2915	4,6904	4,4721	5,0990	2	5,2915	5,2915	5,2915	5,0990	3,1623	4,4721	3,7417	4,2426	4,6904	5,8310	5,6569	4,4721	5,2915	5,2915	4,2426	4,8990	5,2915
90	5,2915	5,0990	6	4,6904	5,2915	4,2426	4,6904	4,6904	5,4772	5,4772	5,2915	3,7417	4,8990	4,8990	5,2915	4,8990	5,0990	4,8990	5,0990	5,6569	5,8310	4,6904	4,6904	4,8990
15	6	6,1644	6,3246	5,4772	5,4772	6,1644	5,2915	6,4807	4,2426	4,2426	4,6904	4,8990	4,8990	5,0990	5,6569	4,8990	6,7823	6,6332	5,8310	6,3246	6,4807	5,4772	6	6
15	5,6569	5,8310	6,3246	5,2915	5,6569	5,8310	5,4772	6	4,4721	4,4721	4	5,4772	4,8990	4,8990	5,4772	5,0990	6,4807	6,3246	5,6569	6	6	4,8990	6	5,6569
90	5,8310	5,6569	6	5,2915	5,2915	5,6569	5,4772	6	4,2426	4,2426	4,2426	5,0990	5,2915	5,6569	6	5,6569	6,3246	6,1644	5,2915	5,8310	6	5,2915	5,6569	6,1644
90	5,8310	6	6,1644	5,4772	5,4772	6	5,2915	6,1644	4	4	4,4721	5,2915	4,6904	4,6904	5,2915	4,8990	6,6332	6,4807	5,4772	6,1644	6,1644	5,0990	5,8310	5,8310
72	6,1644	6	6,4807	5,8310	5,6569	6	5,2915	6,1644	4	4	4,8990	5,0990	4,8990	5,0990	5,4772	5,0990	6,6332	6,4807	5,4772	6,4807	6,4807	5,4772	5,6569	5,6569
21	5,2915	5,0990	5,6569	4,8990	4,8990	5,0990	3,7417	5,2915	5,0990	5,0990	5,2915	3,7417	3,7417	3,1623	3,7417	4	5,8310	5,6569	4,4721	5,6569	5,6569	4,4721	4,8990	4,6904
04	5,8310	5,8310	6	5,0990	5,0990	5,8310	4,8990	6,1644	4,8990	4,8990	4,8990	4,0000	4,6904	5,0990	5,2915	4,6904	6,4807	6,3246	5,4772	5,8310	6	5,2915	5,8310	6,3246
15	6	5,8310	6,3246	5,6569	5,6569	5,8310	5,2915	6,1644	6	6	6,1644	5,0990	5,0990	4,2426	4,2426	5,0990	6,4807	6,3246	5,4772	6,3246	6,4807	5,4772	6	5,6569
90	5,6569	5,4772	6	5,2915	5,2915	5,4772	4,2426	5,6569	5,4772	5,4772	5,6569	4,2426	4,2426	2,8284	4,2426	4,4721	6,1644	6	4,8990	6	6	4,8990	5,2915	5,0990
	4,4721	5,0990	4,8990	4,4721	4,4721	4,2426	5,2915	4,2426	5,8310	5,8310	5,6569	5,0990	5,0990	5,4772	6	5,6569	4,2426	3,7417	4,2426	5,4772	5,2915	4,4721	4,6904	5,0990
	3,7417	4	4	2,8284	2,4495	4	4,2426	4,4721	4,8990	4,8990	4,6904	4	4	4,4721	5,0990	4,6904	5,0990	4,8990	3,7417	4,4721	4,6904	3,1623	4,4721	4,8990
17	0	3,1623	3,7417	3,7417	4	4,2426	5,0990	4,4721	5,6569	5,6569	5,0990	4,8990	4,8990	5,2915	5,8310	5,4772	5,0990	4,8990	4,6904	3,7417	3,4641	3,7417	5,2915	5,2915
	3,1623	0	3,7417	3,4641	4	4,2426	4,8990	4,2426	5,4772	5,4772	5,2915	4,8990	4,6904	5,4772	5,8310	5,4772	5,2915	5,0990	4,4721	4	4,4721	4	5,0990	5,0990
	3,7417	3,7417	0	4	4	5,0990	4,8990	4,6904	6	6	5,8310	5,2915	5,2915	5,6569	6	5,8310	5,6569	5,4772	4,8990	4,6904	4,4721	4,6904	5,6569	5,8310
84	3,7417	3,4641	4	0	2,8284	4	4,2426	4	5,2915	5,2915	4,6904	4,2426	4,4721	4,8990	5,4772	4,8990	5,0990	4,8990	4,2426	4,4721	4,6904	3,1623	4,8990	4,8990
95	4,0000	4	4	2,8284	0	4,2426	4	4,4721	5,2915	5,2915	5,0990	4,2426	4,4721	4,8990	5,4772	5,0990	5,4772	5,2915	4,2426	4,8990	5,0990	3,7417	4,4721	4,8990
	4,2426	4,2426	5,0990	4	4,2426	0	5,0990	3,1623	5,4772	5,4772	5,2915	4,8990	4,8990	5,4772	5,6569	5,4772	4,2426	4	4,2426	4,8990	5,0990	4	4,2426	3,1623
26	5,0990	4,8990	4,8990	4,2426	4,0000	5,0990	0	4,8990	5,2915	5,2915	5,0990	3,1623	4,4721	3,7417	4,2426	4,6904	6	5,8310	4,6904	5,4772	5,4772	4,4721	5,0990	5,4772
21	4,4721	4,2426	4,6904	4	4,4721	3,1623	4,8990	0	5,8310	5,8310	5,6569	5,2915	5,2915	5,6569	5,8310	5,8310	4,2426	4	4,4721	5,2915	4,8990	4,2426	4,4721	4
90	5,6569	5,4772	6	5,2915	5,2915	5,4772	5,2915	5,8310	0	0	3,7417	4,8990	5,0990	5,4772	5,8310	5,2915	6,1644	6,1644	5,2915	5,8310	6	5,2915	5,6569	6,1644
90	5,6569	5,4772	6	5,2915	5,2915	5,4772	5,2915	5,8310	0	0	3,7417	4,8990	5,0990	5,4772	5,8310	5,2915	6,1644	6,1644	5,2915	5,8310	6	5,2915	5,6569	6,1644
04	5,0990	5,2915	5,8310	4,6904	5,0990	5,2915	5,0990	5,6569	3,7417	3,7417	0	4,8990	5,0990	5,2915	5,8310	5,4772	6,1644	6	5,4772	5,4772	5,6569	4,6904	5,8310	6
	4,8990	4,8990	5,2915	4,2426	4,2426	4,8990	3,1623	5,2915	4,8990	4,8990	4,8990	0	3,7417	4	4,2426	3,7417	5,8310	5,6569	4,6904	5,4772	5,6569	4,4721	4,8990	5,4772
	4,8990	4,6904	5,2915	4,4721	4,4721	4,8990	4,4721	5,2915	5,0990	5,0990	5,0990	3,7417	0	3,7417	4	3,4641	5,8310	5,6569	4,6904	5,2915	5,6569	4,4721	5,0990	5,0990
21	5,2915	5,4772	5,6569	4,8990	4,8990	5,4772	3,7417	5,6569	5,4772	5,4772	5,2915	4	3,7417	0	3,7417	4	6,3246	6,1644	5,0990	5,8310	5,8310	4,6904	5,4772	5,4772
90	5,8310	5,8310	6	5,4772	5,4772	5,6569	4,2426	5,8310	5,8310	5,8310	5,8310	4,2426	4	3,7417	0	4,2426	6,4807	6,3246	5,2915	6,1644	6,1644	5,2915	5,8310	5,6569
04	5,4772	5,4772	5,8310	4,8990	5,0990	5,4772	4,6904	5,8310	5,2915	5,2915	5,4772	3,7417	3,4641	4,0000	4,2426	0	6	6,1644	5,2915	5,8310	6	5,0990	5,4772	5,6569
90	5,0990	5,2915	5,6569	5,0990	5,4772	4,2426	6	4,2426	6,1644	6,1644	6,1644	5,8310	5,8310	6,3246	6,4807	6	0	2,4495	4	5,2915	5,0990	4,6904	4,4721	4,6904
90	4,8990	5,0990	5,4772	4,8990	5,2915	4	5,8310	4	6,1644	6,1644	6	5,6569	5,6569	6,1644	6,3246	6,1644	2,4495	0	4	5,2915	5,0990	4,4721	4,2426	4,4721
17	4,6904	4,4721	4,8990	4,2426	4,2426	4,2426	4,6904	4,4721	5,2915	5,2915	5,4772	4,6904	4,6904	5,0990	5,2915	5,2915	4	4	0	4,6904	4,6904	3,4641	4,2426	4,4721
21	3,7417	4	4,6904	4,4721	4,8990	4,8990	5,4772	5,2915	5,8310	5,8310	5,4772	5,4772	5,2915	5,8310	6,1644	5,8310	5,2915	5,2915	4,6904	0	2,4495	4	5,4772	5,2915
04	3,4641	4,4721	4,4721	4,6904	5,0990	5,0990	5,4772	4,8990	6	6	5,6569	5,6569	5,6569	5,8310	6,1644	6	5,0990	5,0990	4,6904	2,4495	0	4	5,4772	5,2915
23	3,7417	4	4,6904	3,1623	3,7417	4	4,4721	4,2426	5,2915	5,2915	4,6904	4,4721	4,4721	4,6904	5,2915	5,0990	4,6904	4,4721	3,4641	4	4	0	3,7417	4,2426
21	5,2915	5,0990	5,6569	4,8990	4,4721	4,2426	5,0990	4,4721	5,6569	5,6569	5,8310	4,8990	5,0990	5,4772	5,8310	5,4772	4,4721	4,2426	4,2426	5,4772	5,4772	3,7417	0	4
90	5,2915	5,0990	5,8310	4,8990	4,8990	3,1623	5,4772	4	6,1644	6,1644	6	5,4772	5,0990	5,4772	5,6569	5,6569	4,6904	4,4721	4,4721	5,2915	5,2915	4,2426	4	0
17	4,2426	4,2426	4	4	4,2426	5,0990	4,6904	5,4772	5,4772	5,4772	5,2915	4,2426	4,4721	4,8990	5,4772	5,0990	5,6569	5,4772	4,4721	4,4721	4,6904	4	4,8990	5,4772
41	4	3,4641	3,1623	3,4641	3,4641	4,8990	4,4721	4,6904	5,6569	5,6569	5,4772	4,8990	4,8990	5,0990	5,6569	5,4772	5,4772	5,2915	4	4,2426	4,2426	3,4641	4,6904	5,0990
23	4,4721	4,4721	4,2426	3,4641	2,8284	4,4721	4,4721	4,6904	5,4772	5,4772	5,2915	4,8990	4,8990	5,2915	5,6569	5,4772	5,2915	5,0990	4	4,2426	4,4721	3,7417	4,8990	5,0990
21	5,0990	4,8990	5,0990	4	4,4721	4	5,2915	3,7417	6,1644	6,1644	5,6569	5,6569	5,6569	6	6,3246	6,1644	4,8990	4,6904	4,8990	4,6904	4,8990	4,2426	4,8990	4,4721
90	5,2915	5,0990	5,8310	4,8990	5,2915	3,7417	5,0990	3,4641	5,6569	5,6569	5,4772	5,0990	5,0990	5,4772	5,6569	5,8310	4,6904	4,4721	4,4721	4,8990	4,8990	4,2426	4,2426	4
26	5,2915	5,2915	5,4772	4,4721	4,6904	5,0990	4,2426	5,4772	5,2915	5,2915	5,2915	2,8284	4,2426	4,4721	4,6904	4,2426	5,6569	5,4772	4,6904	5,4772	5,6569	4,4721	4,8990	5,4772
15	6	6,1644	6,3246	5,6569	5,2915	5,4772	5,4772	5,8310	4,8990	4,8990	3,7417	5,2915	5,6569	5,8310	6,3246	6	6	5,8310	5,6569	6,1644	6,3246	5,2915	4,8990	5,4772
46	6,9282	6,9282	7,0711	6,6332	6,6332	6,7823	6,4807	7,0711	5,6569	5,6569	5,0990	6,1644	5,8310	5,8310	5,4772	6,1644	7,2111	7,0711	6,3246	6,6332	6,7823	6,3246	6,7823	6,4807
90	5,8310	6	6	5,2915	5,2915	5,6569	5,8310	5,8310	6,1644	6,1644	6	5,8310	5,0990	4,6904	5,4772	5,6569	6,1644	6	5,2915	6	6	4,8990	5,2915	5,2915
04	5,6569	5,2915	5,8310	4,8990	5,0990	5,4772	4,6904	5,8310	5,0990	5,0990	5,2915	4,2426	3,7417	4,2426	4,6904	4,2426	6	5,8310	4,8990	5,6569	6	4,8990	5,2915	5,0990
15	5,8310	6,1644	6	5,4772	5,6569	6,1644	5,2915	6,1644	5,8310	5,8310	5,8310	4,4721	4,2426	3,7417	4,8990	4,2426	6,3246	6,1644	5,6569	6,3246	6,1644	5,4772	6	6
15	6	6,1644	6,3246	5,6569	5,6569	6,1644	5,2915	6,4807	5,4772	5,4772	5,2915	5,0990	4,6904	4	5,2915	4,2426	6,6332	6,4807	5,6569	6	6,1644	5,2915	6	6
15	6	5,8310	6,1644	5,6569	5,6569	5,6569	5,0990	6	5,6569	5,6569	5,6569	5,0990	4,8990	4,6904	3,4641	4,8990	6,1644	6	5,0990	6	6,1644	5,2915	5,8310	5,4772
26	4,5826	4,7958	5,3852	4,5826	5	4,7958	5,1962	4,5826	5,5678	5,5678	5,3852	5	5	5,3852	5,7446	5,5678	4,3589	4,3589	3,6056	5,3852	5	4,1231	5	5,1962
62	5,5678	5,3852	5,5678	5,1962	5,1962	5	5,5678	4,3589	5,9161	5,9161	6,0828	5,7446	5,7446	6,0828	6,4031	6,2450	4,7958	4,7958	4,3589	6,0828	5,7446	4,7958	4,5826	5,3852
26	5	5,1962	5,3852	5	5	5,1962	5	5,0000	5,1962	5,1962	5,3852	4,7958	4,7958	5,1962	5,5678	5,5678	4,7958	4,7958	3,6056	5,5678	5,1962	4,5826	5	5,5678
90	4,8990	4,8990	5,2915	5,2915	5,4772	5,0990	6	5,2915	6,4807	6,4807	6	6,1644	6,1644	6,3246	6,6332	6,6332	6	5,8310	5,6569	5,0990	5,0990	4,6904	5,2915	5,4772
69	4,6904	5,2915	5,4772	5,6569	6	5,0990	6,1644	4,8990	6,4807	6,4807	6,1644	6	6	6,4807	6,4807	6,4807	5,6569	5,4772	5,6569	4,6904	4,4721	4,8990	5,2915	5,4772
	4,4721	4,6904	5,2915	4	4,4721	3,7417	4,8990	4	5,6569	5,6569	5,0990	4,8990	4,8990	5,0990	5,6569	5,4772	4,8990	4,6904	4,4721	4,8990	4,8990	2,8284	3,7417	4,2426
17	4,6904	4,4721	3,1623	3,7417	3,7417	4,8990	4,6904	4,8990	5,8310	5,8310	5,6569	5,0990	5,0990	5,4772	5,8310	5,6569	5,6569	5,4772	4,4721	4,8990	5,0990	4,2426	5,2915	5,4772
04	5,2915	5,0990	5,2915	4,2426	4,6904	4,2426	5,2915	3,7417	6,4807	6,4807	6	5,8310	5,2915	5,4772	5,8310	5,8310	5,2915	5,0990	5,0990	5,4772	5,4772	4,4721	5,0990	3,7417
	6,3246	6,6332	6,4807	6,3246	6,3246	6,4807	5,6569	6,4807	6,3246	6,3246	6,3246	5,2915	5,0990	4,8990	4,4721	5,2915	6,7823	6,6332	6,1644	6,7823	6,6332	6,1644	6,6332	6,3246
15	6,1644	6,3246	6,1644	5,6569	5,6569	5,4772	5,4772	5,6569	6,6332	6,6332	6,4807	5,8310	5,0990	5,0990	4,2426	5,8310	6,1644	6	5,6569	6,3246	6,3246	5,4772	5,4772	5,2915
90	6	6	6,1644	5,2915	5,4772	6	5,2915	6,3246	6,1644	6,1644	6,1644	4,8990	4,6904	4,6904	3,7417	4,4721	6,4807	6,3246	5,6569	6,3246	6,4807	5,4772	6,1644	6
69	6	6,3246	6,1644	6	6	6,1644	5,2915	6,1644	6	6	6	4,8990	4,4721	4,8990	3,1623	4,6904	6,4807	6,3246	5,8310	6,4807	6,3246	5,8310	6,3246	6,1644
	6	6,1644	6,4807	6	6,1644	6	4,8990	5,8310	6,4807	6,4807	6,3246	5,0990	5,2915	4,8990	3,7417	5,4772	6,3246	6,1644	5,8310	6,4807	6,1644	5,6569	6,1644	5,6569
62	5,9161	5,9161	6,0828	5,5678	5,5678	5,7446	5	6,0828	6,0828	6,0828	6,0828	4,7958	4,5826	4,5826	3	4,5826	6,2450	6,0828	5,3852	6,0828	6,2450	5,3852	6,0828	5,7446
46	5,7446	5,9161	6,2450	5,7446	5,9161	5,7446	5,9161	5,5678	6,4031	6,4031	6,2450	5,9161	6,2450	6,5574	6,0828	6,7082	5,3852	5,3852	4,5826	6,0828	5,7446	5	5,5678	5,9161
	5,3852	5,1962	6,0828	5	5,1962	4,3589	5,5678	4,5826	6,0828	6,0828	5,9161	5,3852	5,7446	6,0828	6,4031	6,2450	4,5826	4,1231	4,3589	5,3852	5,3852	4,5826	4,5826	4,5826
04	4,4721	4,8990	5,0990	5,0990	5,0990	5,6569	5,4772	5,8310	5,8310	5,8310	5,6569	5,4772	4,6904	4,8990	5,4772	5,2915	6,3246	6,1644	5,0990	4,4721	4,4721	4,2426	5,0990	5,4772
04	4,4721	4,8990	4,8990	5,0990	5,0990	5,4772	5,4772	5,6569	5,8310	5,8310	5,8310	5,6569	5,0990	5,2915	5,6569	5,4772	6	6	4,8990	4	3,7417	4,6904	5,6569	5,0990
04	4,4721	4,8990	4,8990	5,0990	5,0990	5,4772	5,6569	5,8310	5,8310	5,8310	5,8310	5,6569	5,0990	5,4772	5,8310	5,4772	6	6	5,0990	3,7417	4,2426	4,8990	5,8310	5,2915
23	4,6904	4,8990	4,6904	4	3,7417	4,6904	4,8990	5,0990	5,6569	5,6569	5,2915	4,8990	4,2426	4,6904	5,0990	4,8990	5,4772	5,2915	4,2426	4,8990	5,0990	4	5,0990	4,4721
41	4,4721	5,0990	4,4721	4,2426	4	4,8990	4,8990	4,6904	5,8310	5,8310	5,6569	5,0990	4,4721	4,6904	5,0990	5,0990	5,2915	5,0990	4,2426	5,0990	4,6904	4	5,0990	4,4721
04	4,6904	4,6904	4,8990	5,0990	5,0990	4,8990	5,6569	5,0990	6	6	5,8310	5,6569	5,0990	5,2915	5,8310	5,6569	5,8310	5,6569	5,0990	4,6904	4,6904	4,6904	5,0990	4,4721
23	4,4721	4,6904	4,6904	3,7417	3,7417	4,6904	4,8990	5,0990	5,4772	5,4772	5,2915	4,6904	4	4,4721	5,0990	4,6904	5,4772	5,2915	4,2426	4,8990	5,0990	3,7417	4,8990	4,4721
90	5,8310	6	5,8310	5,2915	5,2915	5,0990	5,8310	5,2915	6,6332	6,6332	6,4807	6	5,4772	5,6569	4,8990	6	5,8310	5,6569	5,2915	6	6	5,0990	5,2915	4,6904
04	5,0990	5,6569	5,4772	5,0990	5,0990	5,6569	5,8310	5,6569	6,3246	6,3246	6	5,6569	5,0990	4,8990	5,4772	5,6569	6	5,8310	5,2915	5,8310	5,6569	4,8990	5,8310	5,4772
72	5,8310	6,1644	6	5,8310	5,8310	6,1644	5,0990	6,1644	5,8310	5,8310	5,8310	5,0990	4,4721	4,6904	4,4721	4,4721	6,3246	6,3246	5,8310	6	6	5,6569	6,3246	6,1644
15	6	6,1644	6,1644	5,6569	5,6569	6	4,8990	6,3246	5,6569	5,6569	5,4772	4,8990	4,4721	4,4721	4,2426	4,2426	6,4807	6,4807	5,6569	6	6,1644	5,4772	6,1644	6
30	4,3589	4,5826	5,0000	3,8730	4,3589	4,3589	5	4,7958	5,7446	5,7446	5,1962	5	4,1231	4,5826	5	4,7958	5	4,7958	4,3589	4,5826	4,7958	3,6056	5,1962	4,3589
90	4,2426	5,0990	4,6904	5,2915	5,2915	5,6569	5,6569	5,4772	6,1644	6,1644	6,1644	5,8310	5,2915	5,4772	5,8310	5,6569	5,8310	5,8310	5,0990	4	3,7417	4,8990	5,8310	5,2915
90	4	4,6904	4,8990	5,0990	5,4772	5,4772	6	5,4772	6,3246	6,3246	6	6	5,2915	5,8310	6,1644	5,8310	5,6569	5,6569	5,4772	3,7417	3,4641	4,8990	6,1644	5,2915
21	4,8990	5,4772	5,0990	4,8990	4,6904	5,2915	5,0990	5,2915	6,1644	6,1644	6	5,0990	4,6904	5,0990	5,4772	5,0990	5,4772	5,2915	4,8990	5,4772	5,2915	4,6904	5,4772	5,0990
04	5,6569	5,8310	5,8310	5,0990	5,0990	5,0990	5,8310	5,2915	6,1644	6,1644	6	5,8310	5,2915	5,4772	5,2915	5,8310	6	5,8310	5,2915	5,8310	5,8310	4,8990	5,2915	4,6904
90	5,4772	6	5,6569	5,2915	5,2915	5,2915	6	5,0990	6,3246	6,3246	6,1644	6	5,4772	5,6569	5,4772	6	5,8310	5,6569	5,4772	6	5,6569	5,0990	5,4772	4,8990
26	4,5826	5,1962	5,1962	4,5826	5	5	5,5678	5	5,9161	5,9161	5,3852	5,5678	4,7958	5,1962	5,1962	5,3852	5,3852	5,1962	5	5	4,7958	4,3589	5,7446	5
	5,3852	5,5678	5,5678	5,3852	5	4,5826	5,5678	4,3589	6,0828	6,0828	6,2450	5,5678	5,7446	6,0828	6,2450	6,2450	5	5	4,7958	5,7446	5,3852	4,5826	4,1231	4,5826
	5	5,1962	5,5678	5	5	4,3589	5,5678	4,3589	5,9161	5,9161	5,5678	5,3852	5,5678	6,0828	6,2450	6,0828	4,5826	4,1231	5	5,3852	5,1962	4,7958	4,5826	4,5826

Science

Director's Intro
Discussion on Art and Science
Science at CeMM
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How to Reach CeMM
Imprint

“Austria and Britain share a belief that science and innovation are at the heart of sustainable economic growth. The research undertaken at CeMM is world-leading and could well change all our lives. The environment in which the talented team led by Prof Superti-Furga works is exciting and cosmopolitan. It fosters creative thinking, new approaches to old problems and cross-cutting collaboration. CeMM has already made significant break-throughs in the study of diabetes, something close to my heart as my father has lived with the condition for more than 30 years. Recent developments in cancer research promise even more for the future.”

Susan le Jeune d’Allegeershecque
Her Britannic Majesty’s Ambassador to the Republic of Austria

“I spent a few (regrettably, too few) hours at CeMM, the Centre for Molecular Medicine of the Austrian Academy of Sciences, on a rainy day in November 2013. I was literally dazzled by the highly creative and stimulating atmosphere, the huge number of outstanding, enthusiastic young people, the ingenious vision of the Director and senior scientists, the state-of-the-art instrumentation and infrastructure. A wonderful place, a dream place, to do research. I wish there were more in the world.”

Dr. Fabiola Gianotti
Particle Physicist, CERN, Geneva

“As the chair of the scientific advisory board (SAB), it is a treat to observe the impressive development of CeMM during the past few years. Indeed, under the visionary leadership of its Director, the SAB believe that CeMM has become a new scientific powerhouse in the heart of Europe. It successfully competes with many of the best institutes worldwide. This is well documented by a steady stream of high-impact research, including two remarkable studies in the field of cancer biology in recent days. Given its unique, collaborative spirit and its highly motivated and talented students and scientists, the SAB look forward to the emergence of even more world class science at CeMM and its translational imprint. We believe that the people of Austria are being very well served by this scientific gem!”

Prof. Dr. David Livingston
Deputy Director, Dana-Farber/Harvard Cancer Center, Boston, USA
Chair of CeMM’s Scientific Advisory Board

“I have had the great pleasure to be a Member of CeMM’s Scientific Advisory Board (SAB) since the inception of the Institute. Within this role I have watched CeMM grow from its concept stage to an Institute carrying out world-class science within a remarkably short period! CeMM’s publication record is enviable and despite its small size, its research, focusing on cancer, infection and inflammation and epigenetics, is outstanding.”

Prof. Dr. Nadia Rosenthal
Director, Australian Regenerative Medicine Institute, Melbourne, AU
Member of CeMM’s Scientific Advisory Board

“It is an honor and pleasure to dedicate our bodies to science – even though it’s for the purpose of a picture for now. We fully trust in CeMM to handle our and any other bodies with care. To a better world!”

Stermann & Grissemann
Comedians, TV-Stars, Compéres “Willkommen Österreich”

“As an interdisciplinary research institute of the Austrian Academy of Sciences studying the human system and its molecular inner workings, the mission of CeMM is to assist in preparing the predictive, preventive and personalized medicine of the future.”

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

Life at CeMM

+ Great Lectures
+ Scientific Meetings
+ Great Competitions
+ Great Celebrations
+ Good Scientific Citizenship

Great Lectures

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.

CeMM Karl Landsteiner Lecture

The annual Karl Landsteiner lecture was launched at CeMM in 2007 to honor the Austrian immunologist renowned for discovering the four human blood groups, which earned him the Nobel Prize in Physiology or Medicine in 1930. The recipient of the lectureship is selected by CeMM faculty for his/her outstanding achievements in the area of molecular medicine. This year marked the seventh Karl Landsteiner lecture, which was presented by Dr. Hans Clevers of the Hubrecht Institute in The Netherlands, and President of the Royal Netherlands Academy of Sciences.

Hans Clevers' research has made fundamental breakthroughs in a number of different fields over the course of his career, and his most recent topic, stem cell biology, is no exception. His lecture, entitled "Stem Cells of the Bowel: Bright Side, Dark Side", was presented to a mixed audience of 350 people from all scientific disciplines alongside other interested parties in the *Festsaal* of the Austrian Academy of Sciences on the 6th May, 2013.

The Power of a Single Cell

Using entertaining animations peppered with little known historical insights, Hans Clevers presented the results of several projects performed in his laboratory over the last ten years, all centered around the dynamic lives of intestinal stem cells. He explained that the epithelial cell layer, which lines the 12 meters of the small intestine and helps us digest food, is exposed to one of the most violent biological environments on the planet, i.e. the contents of the gut. As such these cells don't survive very long, and the entire lining of the gut needs to be replaced every four days. This massive cell turnover is made possible by intestinal stem cells, which ensure the continuous supply of new epithelium.

Hans explained how work done by his group led to the breakthrough discovery of the identity of the elusive intestinal stem cell in mice. In an unprecedented next step, they showed how they could use a single one of these stem cells to grow three-dimensional "mini" guts long-term in the laboratory. These mini-guts could even be transplanted back into a mouse with a damaged gut, and function normally. They showed the same thing for liver stem cells. And in another project, they pinpointed the intestinal stem cell niche, which is the cellular microenvironment required to support the stem cells and thereby renewal of the intestine.

Being able to grow healthy, functional tissue in the laboratory in this way could revolutionize regenerative medicine and the ability to cure patients with intestinal and liver damage. And the system will also give scientists a much-needed boost to better model and thereby study associated diseases such as colon cancer, in vitro. Unsurprisingly, there were many questions, particularly on the properties of these stem cells and the many possibilities of using this new model to answer previously intractable biomedical questions.

A Dynamic Lecture
Dutch scientist Hans Clevers presents his research over the last decade on the dynamic life of the intestinal stem cell.

The SMART Lecture Series and the “God Particle”

On Monday 25th November 2013, Dr. Fabiola Gianotti from the Physics Department at CERN, Switzerland, presented a fantastic SMART lecture at CeMM entitled “The Higgs Boson and Our Life”, to a packed audience. The SMART (Science, Medicine, Art, Research & Technology) lecture series is a biannual event hosted by CeMM to address current scientific challenges spanning science, art, and society. The lecture series aims to encourage out-of-the-box-thinking as well as to establish a dialogue with the broader public.

Following a warm introduction by CeMM’s Scientific Director, Giulio Superti-Furga, Dr. Gianotti began her talk by introducing CERN, the world’s largest particle physics laboratory, currently engaging over 11,000 scientists from more than 60 countries. CERN’s primary mission is the study of elemental particles, and Dr. Gianotti went on to describe how an understanding of the ‘very small’ can often help us to understand the ‘very big’.

The Higgs boson is an elementary particle, first discussed in 1964. It’s discovery by CERN, announced on the 4th July 2012, was monumental. During the almost 40 year search for this particle, CERN developed and constructed the Large Hadron Collider over a 20 year period, which was critical for the discovery of the Higgs boson.

Dr. Gianotti explained the three features required to study the behaviour of elementary particles: an accelerator, a detector and computing power. These three features are combined in the Large Hadron Collider, which is a subterranean ring, 27km in circumference, lying across the border between Switzerland and France. Proton streams extracted from hydrogen gas are accelerated in a vacuum around the ring at immense speeds. Upon particle collision, energy is released which can be transformed into matter – in the form of larger, heavier particles. Through this process, the Large Hadron Collider is able to create Higgs bosons and other particles for observation and study. By advancing the frontiers of technology, such discoveries will ultimately prove to be beneficial to society.

Many questions followed Dr. Gianotti’s fascinating lecture, including whether the Higgs boson can help us better understand dark matter, or the origin of the universe. Dr. Gianotti explained that they aim to recreate conditions at the beginning of the universe for study, and then translate these finding back in time.

At CERN there is a strong focus on training the next generation of scientists and more than half of CERN’s collaborative scientists are under the age of 30. In an inspirational take home message for the young scientists in the audience, Dr. Gianotti emphasised that curiosity was essential for research and for driving motivation.

Elementary Particles
Fabiola Gianotti from CERN, Switzerland, describes how studying the behaviour of elementary particles such as the Higgs boson can advance the frontiers of technology.

Overview CeMMinar/Impromptu Series

21.01.2013
CeMMinar
Jiri Lukas
Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark
"Spatial and temporal regulation of the DNA damage response: mechanisms and unexpected limitations of genome surveillance"
Host: Joanna Loizou

11.02.1013
CeMMinar
Tony Green
Department of Haematology, Cambridge Institute for Medical Research, University of Cambridge
"JAK/STAT signalling and malignancy – clonal complexity and stem cell"
Host: Robert Kralovics

25.02.2013
CeMMinar
Frederic Geissmann
Division of Immunology, Infection & Inflammatory Disease (DIIID), King's College London
"In Vivo Differentiation & Functions of Macrophages"
Host: Christoph Binder

27.02.2013
Impromptu
John Castle
TRON - Translational Oncology, University Medical Center, Johannes Gutenberg University, Mainz, Germany
"Next generation sequencing for truly individualized vaccines?"
Host: Robert Kralovics

08.04.2013
CeMMinar
Steve Jackson
Department of Biochemistry & Cancer Research UK Laboratories, The Gurdon Institute, University of Cambridge
"Cellular responses to DNA damage"
Host: Joanna Loizou

29.04.2013
CeMMinar
Georg Wick
Div. for Experimental Pathology & Immunology, Laboratory of Autoimmunity, Biocenter Innsbruck Medical University
"The Immunology of Atherosclerosis"
Host: Giulio Superti-Furga

27.05.2013
CeMMinar
Stephan Beck
Research Department of Cancer Biology, University College London (UCL) Cancer Institute
"Pinball Methylome: Functional insights from multi-dimendional perturbations"
Host: Christoph Bock

06.06.2013
Impromptu
Laura Steenpass
Institute for Human Genetics, University of Duisburg-Essen
"Imprinting of RB1: origin and mechanism"
Host: Denise Barlow

07.07.2013
Special Seminar
Ivan Dikic
Institute of Biochemistry II, Goethe University School of Medicine, University of Frankfurt, Germany
"Ubiquitination in regulation of inflammation and autophagy"
Host: Giulio Superti-Furga

01.07.2013
CeMMinar
Akinori Takaoka
Division of Signalling in Cancer and Immunology, Institute for Genetic Medicine, Hokkaido University
"Innate immune signaling networks during host-microbe interaction"
Host: Andreas Bergthaler

02.07.2013
Impromptu
Roland Arnold
Philip M. Kim Laboratory Terrence Donnelly Centre for Cellular and Biomolecular Research, University of Toronto
"Exploring genetic interactions in E. coli and human cancer cells: enlighting functional cross-talk in bacteria and targeting cancer vulnerabilities"
Host: Jacques Colinge & Sebastian Nijman

09.07.2013
Impromptu
Richard R. Meehan
MRC Human Genetics Unit, Western General Hospital, Edinburgh, Scotland
"5-Hydroxymethylation and the Epigenetics of Identity"
Host: Denise Barlow

24.07.2013
Impromptu
Berend Snijder
CeMM
"Inferring functional interactions between genes from high-content perturbation screens"

26.08.2013
Impromptu
Elke Deuerling
Chair of Molecular Microbiology, University of Konstanz
"Quality Control Processes at the Ribosome"
Host: Giulio Superti-Furga

03.09.2013
Impromptu
Ross Dickins
Walter and Eliza Hall Institute, Victoria, Australia
"Mechanisms of leukemia suppression by the transcription factors Pax5 and Ikaros"
Hosts: Florian Grebien/ Giulio Superti-Furga

10.09.2013
Impromptu
Stephanie Dumon
School of Immunity and Infection, College of Medical and Dental Sciences, University of Birmingham
"The MYB protein in normal and malignant haematopoiesis"
Host: Florian Grebien/ Giulio Superti-Furga

17.09.2013
Impromptu
Natalie de Souza
Senior Editor Nature Methods
"Behind the scenes at Nature Methods"
Host: Giulio Superti-Furga

24.09.2013
Impromptu
Menno C. van Zelm
Dept. Immunology, Erasmus MC, University Medical Center, Rotterdam, the Netherlands
"Build-up of immunological memory in young children"
Host: Kaan Boztug

01.10.2013
Impromptu
Eric Haura
H. Lee Moffitt Cancer Center & Research Institute
"Bringing Network Medicine to the Clinic: Annotating Cancer via Protein Complexes"
Host: Giulio Superti-Furga

21.10.2013
Impromptu
Prof. Dr. Michael Rehli
Department of Internal Medicine III, University Hospital Regensburg
"The regulomes of human monocytes and everything else – Insights from FANTOM5 CAGE-data"
Host: Christoph Bock

28.10.2013
CeMMinar
Ivan Dikic
Goethe University Frankfurt
"Ubiquitin & autophagy networks in regulation of infection & inflammation"
Host: Giulio Superti-Furga

06.11.2013
Joint MUW - CeMM Impromptu Seminar
Paolo Bernardi
University of Padova, Italy
"Mitochondria and cancer: A molecular mechanism for the Warburg"
Hosts: Karin Nowikovsky (MUW) & Keiryn Bennett

11.11.2013
CeMMinar
Adriano Aguzzi
Institute of Neuropathology, University Hospital Zurich
"The biology of mammalian prions"
Host: Giulio Superti-Furga

21.11.2013
Impromptu
Andre Franke
Institute of Clinical Molecular Biology, Christian-Albrechts-University of Kiel
"A systematic analysis to study host-gut microbiome interactions"
Host: Kaan Boztug

28.11.2013
Impromptu
Yinon Ben-Neriah
Lautenberg Center for Immunology, Hebrew University-Hadassah Medical School
"Inflammation from an epithelial perspective"
Hosts: Giulio Superti-Furga, Joanna Loizou and Sebastian Nijman

Scientific Meetings

Communicating scientific results is essential for advancing science, and probably the most efficient and fun way to do this is at a conference. Conferences enable the direct communication and discussion of results between scientists from a certain field, and oftentimes scientists of different disciplines. This provides a breeding ground for new ideas and research directions. CeMM sponsors several national and international conferences each year. In 2013, besides several smaller meetings, two conferences were organised by CeMM scientists and held at the institute. The organisers would like to thank all the speakers and participants who contributed to the success of these meetings.

Next Generation Sequencing Vienna Symposium and Workshop

On April 9, 2013, researchers from around Vienna gathered at CeMM to discuss the latest developments and future perspectives of arguably the hottest technology in biomedicine: Next Generation Sequencing (NGS). NGS has made it relatively routine to determine the DNA sequence of entire human genomes (a procedure that would have cost millions of Euros just a few years ago), providing unprecedented research opportunities in organisms ranging from bacteria and plants to insects and mammals. The symposium provided an overview of NGS-enabled research in Vienna, with scientific talks by Renée Schroeder (MFPL), Sebastian Nijman (CeMM), Julius Brennecke (IMBA), Franco Laccone (MedUni Vienna), Johannes Zuber (IMP) and Renate Panzer (St. Anna CCRI).

Furthermore, a keynote lecture by Prof. Reinhold Schäfer (Vice director of the Charité Comprehensive Cancer Center) highlighted the medical relevance of genome-scale technology for cancer research, and a subsequent technical workshop provided the venue for discussing the challenges of this complex technology in greater depth. The meeting was organized by CeMM Principal Investigator Christoph Bock, who also coordinates the joint Biomedical Sequencing Facility of CeMM and the Medical University of Vienna, and by Andreas Sommer, who is the head of the NGS unit at the Campus Science Support Facilities at the Vienna Biocenter (CSF). Both facilities also presented their sequencing services, which are provided at a significantly subsidized rate to academic researchers in Austria, thus contributing to the wide availability of this breakthrough technology to researchers in Vienna and Austria.

Opening Christian Doppler Laboratory at CeMM, Austrodrugs Meeting

On February 28 and March 1, 2013, more than 130 academic chemical biologists and industrial drug discoverers met at CeMM for a scientific symposium and the third Austrodrugs meeting. Following speeches by the project partners and the president of the Austrian Academy of Sciences, Prof. Helmut Denk, the Christian Doppler Laboratory for Chemical Epigenetics and Antiinfectives was officially opened by Prof. Reinhart Kögerler, President of the Christian Doppler Research Association.

The newly established Christian Doppler Laboratory is a public-private partnership between CeMM, Boehringer Ingelheim, and Haplogen. It aims to develop novel screening technologies and identify chemical probe compounds as a basis for future drug development projects with the corporate partners. In the chemical epigenetics module, the team around CeMM's Stefan Kubicek aims to develop technologies in collaboration with Oncology Research at Boehringer Ingelheim RCV GmbH & Co KG to identify and characterize small molecules and 'druggable' proteins regulating chromatin structure and function. In a second module, their goal is to identify chemical probes for host factors of infectious diseases based on molecular targets derived by a powerful screening approach using human haploid cells implemented at Haplogen GmbH. Bringing these targets together with CeMM's comprehensive compound library and screening expertise will generate novel chemical probes that can be used for proof-of-concept studies.

The opening was celebrated with a scientific symposium on the research topics of the CD Laboratory. Maria M. Mota (Instituto de Medicina Molecular, University of Lisbon) gave a fascinating keynote lecture on "Approaching malaria from the host side but not always". Her lecture, together with Johan Neyt's presentation the following day, represents a role model for targeting host-pathogen interactions with small molecules. The symposium continued with a series of lectures on chemical biology approaches to epigenetics, the second focus of the Christian Doppler lab.

The afternoon of March 1 was dedicated to the third Austrodrugs meeting. Five academic and eight industrial speakers gave updates and presented their tools, resources, and opportunities and needs for collaboration. Discussions then continued informally at a cocktail reception, further strengthening the interactions between Austrian academic chemical biologists and industrial drug discoverers. Based on the success of the meeting, we are sure that additional collaborations will emerge. We are looking forward to learning about their progress at the next Austrodrugs meeting in 2014.

Opening Christian Doppler Lab
CDG President Reinhart Kögerler, Academy President Helmut Denk, Georg Casari, Norbert Kraut and Giulio Superti-Furga at the opening of the Christian Doppler Laboratory for Chemical Epigenetics and Antiinfectives, on February 28th, 2013.

Great Competitions

When it comes to sports, CeMMies are multi-talented, fearless and ambitious team players.

SURF 2013
On September 11th, 2013 the soccer teams of IMP, IMBA, ISTA, MFPL, GMI, the Austrian Academy of Sciences and Companies of the Vienna Biocenter and CeMM met for the SU(mmer)R(esearchers) F(ootball) Tournament. With fancy footwork, elaborate strategy, and a high team spirit spurred on by enthusiastic cheer-leaders the CeMM soccer team carried the day! CeMM won each of its matches with a total score of 17:5. We congratulate all teams and thank coach Mischa Pilz for his very good job and IMBA for the excellent organization of the tournament.

Mountainbike Race
Camillo Sanchez, part of the Colombian national team for the World Championships in Canberra 2010, captained CeMM's mountainbike team with Adriana Goncalves, Ciara Cleary and Lindsay Kosack in the Wien Energie MTB Team Race on April 22nd, 2013. Each participant was required to ride a 7km cross-country trail through forests and vineyards in the beautiful surroundings of Kahlenberg on the outskirts of Vienna. We placed 12th out of 35 teams!

Cancer Research Run
The 7th Cancer Research Run took place on October 5th, 2013. The sports event provides an opportunity to raise awareness of the fight against cancer and establish additional, independent and private research funding. CeMM sponsored 15 runners from the institute who mastered 274 rounds with about 232 kilometers in total. Revenue from the 7th Cancer Research Run will be pumped into a research project aimed at establishing treatments that are specifically co-ordinated towards genetic mutations and protein ex-pressions in tumors.

Vienna City Marathon
Some thirty-six CeMM scientists and administrative personnel participated in the 30th Vienna City Marathon on Sunday, April 14, 2013. Ph.D. student Carol Ann Eberle, ran the half-marathon in 01:27:16, which was the 11th best time out of 4271 women and the second place in her age bracket! On average the CeMM teams needed about 4 hours and 7 minutes for the 42 kilometer distance. CeMM congratulates the nine running teams and wishes them all the best for their next competitions!

Great Celebrations

"Work hard, party hard", is a motto at CeMM, which contributes to a motivating and inspiring work atmosphere and makes this place something special. Following tradition, the first year's students have the task of organizing a Halloween ball and each new generation has big shoes to fill. It seems as if creativity has no limits! Every year the motto is more challenging, the labs get more creative and the costumes get more fanciful! In May 2013 Keiryn Bennett and Lindsey Kosack initiated CeMM's first International Food Festival, which was a big hit and will hopefully become a tradition as well. Another small gourmet festival was a kick-off of the icecream season on CeMM's terrace in June. However, the most pleasant reason for a celebration is the growing number of outstanding publications!

International Food Festival
A culinary world trip at CeMM.

Summer Feeling
Ice cream on CeMM's terrace.

Collaboration I
A joint research project of the CeMM and ETH Zurich, published in *Nature Methods* on March 4th, 2013 not only pointed out the merits of a long-lasting international collaboration, it seems to make the complete mapping of the interactions within the human proteome achievable. While the Viennese contributors were honored by Giulio with the traditional "coronation", the colleagues in Zurich took part virtually via Skype.

Collaboration II
On August 25th, 2013 Nature Methods announced that Haplogen, a spin-off and partner of CeMM, made available their large collection of haploid human cell lines. The study is a best practice model for scientific teamwork. Some 35 scientists from CeMM and Haplogen contributed to the publication and celebrated their huge collaborative success with champagne, wine and cheese.

Translational Success
CeMM and the Medical University of Vienna published the new discovery of a mutation in December 2013 in the New England Journal of Medicine (NEJM) and this mutataion was a main topic at the Annual Meeting of American Society of Hematology (ASH). The findings of Robert Kralovics' group were also presented at a press conference in Vienna and bring hope to millions of Myeloproliferative neoplasm patients.

Undead, Ghosts and Wonderland
Following tradition, the first year's students are in charge of organizing the Halloween ball. The committee met twice a week to ensure perfect entertainment and an extensive supply of food and drinks. The party guests enjoyed a spectacular dance performance and an award ceremony, and demonstrated their incredible talents in front of our expert jury as part of an acting contest. The theme "Rocky Horror Picture Show" was accompanied by a heart-warming piece of music, the lyrics of which were inspired by the life of a PhD student. Among the guests: Andy Warhol and his famous painting, Alice in Wonderland, the English royal family, vampires, skeletons and many more.

Christmas Party
On December 19th, 2013, we celebrated our traditional Christmas Party at the "Aux Gazelles" in Vienna. Santa Claus gave his best and pleased all 26 children of the extended CeMM family. As in previous years, our second year PhD students arranged for the entertainment and – for the first time this year – they organized a charity tombola. Prizes consisted of fantastic activities with sometimes cryptic names such as *Hot Air, Blue Note, Chameleon, Crosstrainer,* or *Meet&Greet* and were exclusively donated by CeMMies. The tombola tickets were sold out quickly, and the amount of 1,010 Euro was handed over to the Sterntalerhof. Later in the evening CeMMies were thrilled by a very special music guest: Diploma student Udo Richson and his brother's band rocked the dance floor.

Good Scientific Citizenship

Clearly CeMM's future vision is one that encompasses a whole new perception of the importance of molecular medicine in the 3rd millennium at the interface with society. CeMM promotes a new and different awareness about the uniqueness of people's genomic identity, the chances of personalized and preventative medicine, and the advocacy of a new responsibility of society towards biomedical research and, symmetrically, of research towards society. Real scientific competence at the international level, measured by traditional bibliometric parameters but also by altmetric views, that include originality of thought, outreach, education, training, patents, commercialization and medical impact, represent the earnestness and credibility that CeMM aspires to.

Openness and Accountability

The level of financial support, the visibility of the CeMM building with its beautiful art facade, and CeMM's research themes and successes represent a new paradigm in terms of social contract and transparency between a research institution and its stakeholders, the taxpayers, the patients and the government. A good example is the yearly CeMM Research Report, which is more than a summary of the ongoing projects and activities. It attempts to address a wider public of culturally interested people by providing interesting artistic insights and provoking new questions. Being aware of the potential impact of the scientific work on society, CeMM is fostering a seriously-meant yet playful and open exchange with the public, emphasizing science and art projects (art façade, special encounters and discussion rounds, think rooms, art projects) but also popular lectures (Landsteiner Lectures, SMART Lectures) and sociological, ethical and health-political debates. The quests we pursue are too important and too close to the key interests of humankind to be tackled by biomedical researchers in isolation. To shape a better, worthwhile future we need to elaborate a common vision, be aware of what is at stake and take on challenges with commitment and courage.

Interacting with Stakeholders

Her Britannic Majesty's Ambassador to the Republic of Austria and the UK Permanent Representative to the United Nations in Vienna, Susan le Jeune d'Allegeershecque and her delegation visited us on April 14th, 2013. Stefan Kubicek gave a lecture on "Epigenetics for Type 1 Diabetes: Making new insulin producing beta cells"– a dynamic discussion developed afterward. Stefan Kubicek's lab is supported in part by the Juvenile Diabetes Research Foundation Canada, which – overall supports research projects in over 17 nations, including the United Kingdom.

On April 14th, 2013, Life Science Austria (LISA) arranged for researchers and biotech representatives from Luxembourg to visit CeMM. This important visit took place in the course of a state visit by the Grand Duke and the Grand Duchess of Luxembourg, underscoring and supporting their continuing venture to establish Luxembourg as a European Biotechnology hot-spot.

The European Forum Alpbach is an international discussion platform attracting politicians, scientists, business people, decision makers and students alike, that convene each summer in the Tyrolean village of Alpbach. A special symposium, dedicated to health-related topics took place from August 16th to 19th 2013, and focused on the question "Who Decides Health". CeMM's Scientific Director Giulio Superti-Furga was invited to chair the discussion "Fair Society, Healthy Lives" following the keynote presentation by Sir Michael Gideon Marmot, the Professor of Epidemiology and Public Health at the University College London. Giulio also led a plenary interview with John P. A. Ioannidis, the Professor of Health Research and Policy at Stanford School of Medicine, on "How Reliable is Evidence in Medicine". Together with Jochen Taupitz, an expert in Medical Ethics, Giulio Superti-Furga moderated the breakout working group "Creating Knowledge: The freedom of research". In his opening statement, Giulio emphasized that demographic developments and emerging diseases require dedicated funding for medical research. The existing scientific expertise in infections, cardiovascular and metabolic diseases, as well as cognitive, psychiatric and neurological disorders in Austria, represents a strong strategic value. To this effect, Giulio Superti-Furga proposed a dedicated health science research model, to complement basic research funding programs, in the style of an Austrian "National Institute of Health".

On October 29th, 2013, we were honored by a visit from the new Board of the Austrian Academy of Sciences, President Anton Zeilinger and Vice-President Michael Alram. Giulio Superti-Furga gave a general introduction on the research strategy at CeMM followed by three short presentations by Sylvia Knapp, Robert Kralovics and Christoph Bock. To round up their first official visit to CeMM, President Zeilinger and Vice-President Alram received a special tour of CeMM, including our PLACEBO lab, the Mass Spectrometry unit as well as the Next-Generation Sequencing Facility.

Interacting with the Local Scientific Community

CeMM's research attitude takes a cooperative mindset into consideration by fostering a highly collaborative, open-minded and interactive research strategy. We work beyond boundaries of labs and departments to educate and encourage our students to follow this path. Our research facilities are strategically and conveniently located in the heart of the campus of the Medical University of Vienna and the Vienna General Hospital, a leading European medical research and training center. We are privileged to closely interact and collaborate with a number of accomplished scientists and clinicians from the Medical University of Vienna. To nurture an open and integrative atmosphere, we jointly organize quarterly get-togethers with the neighboring Anna Spiegel Research Building of the Medical University of Vienna.These events consist of scientific presentations, followed by social get-togethers. Some 80 people from CeMM and Anna Spiegel join each of these events, which so importantly foster interactions and build a foundation of trust.

The Medical University of Vienna is CeMM's most important partner, and the home academic institution of its Ph.D. Program, but CeMM also has numerous personal and institutional ties to the more basic research institutions at the Vienna Biocenter, most notably IMBA (Institute of Molecular Biotechnology), IMP (Institute of Molecular Pathology) and the Max Perutz Laboratories.

On May 16th, 2013, organized by CeMM PI Andreas Bergthaler and a team from the Institute of Science and Technology (IST Austria), a delegation from CeMM visited IST Austria at their beautiful institute just outside of Vienna. Our host, President Thomas A. Henzinger, joined the scientific presentations and discussions, which were followed by a social program. We have current collaborative ventures with IST Austria and look forward to a long relationship. As a show of friendship, CeMM presented President Henzinger and his staff with an original print from Peter Kogler, representing the graphical elements portrayed by CeMM's glass façade.

Interacting with Students and Pupils

In April 2013, CeMM in conjunction with Christine Mannhalter, the Vice-President of the Austrian Science Fund (FWF) and Professor of Molecular Diagnostics hosted thirty pharmaceutical students from The Netherlands. With the help of our students, this interesting day provided interdisciplinary insights into the research performed in Vienna. We were truly impressed by the Dutch students and the vivid and eloquent discussions that evolved. We profited from this event, and hope the same for our visitors.

Four Austrian schools participated in a project called "Next Nature", a philosophical concept that was introduced by the Dutch artist, philosopher and scientist Koert van Mensvoort. The project encompasses all changes and developments of nature since the expanding influence of humanity on earth. We had the privilege of hosting the Viennese Gymnasium Maria Regina's 7th class, on May 27th, 2013. Giulio Superti-Furga and Kaan Boztug provided an overview about CeMM's research. The lively and interactive visit quickly developed into discussions about scientific education's importance as a gatekeeper from prejudices that are so often built on missing knowledge. The students then visited Kaan Boztug's lab, where our students had prepared for some hands-on experiments. The feedback of the class: The visit was the highlight of their project; the students felt well cared for and they developed a keen interest in science.

On December 19th, 2013, we celebrated our traditional Christmas Party. Our second year Ph.D. students arranged for the first time a charity-tombola in support of the "Sterntalerhof", a children's hospice where families can find peace and re-build their inner strength. The creativity and enormous efforts in organizing this (especially Katrin Hörman and Bernd Boidol) was truly amazing.

Research Report and Brain Lounge

On May 15th, 2013 we hosted and launched our annual Research Report 2012 that introduced the CeMM Brain lounge to a wider audience. This year joining us were the Austrian Academy of Science's newly appointed Vice-President Michael Alram and Georg Brasseur the President of the Mathematics and Natural Sciences division. Also, joining us from the Medical University of Vienna was Christiane Druml, Vice-Rector for Clinical Affairs and Chair of the Austrian Bioethics Commission. Other guests included Peter Pakesch, the Executive-Director of Joanneum Universal Museum, in Graz, and our befriended artists Peter Kogler, Martin Walde, Dorothee Golz, Iris Ranzinger, Karl Emilio Pircher and Fidel Peugeot.

2013 also included as a highlight two of the so-called "thinking rounds" in our Brain Lounge. Scheduled one year after the official opening of the Brain Lounge on December 16th, an inspiring evening took place on December 16th that fostered the interaction between Art, Science and Society. The quantum physicist Markus Aspelmeyer from the University of Vienna chaired one session entitled "Paradoxes of physics of atoms". The second discussion round was chaired by CeMM's Christoph Bock, and was dedicated to the important topic "the meaning of human genomes for science and society". Although some questions such as the impossibility of beer-teleportation remained unanswered, all participants felt enlightened by the newly obtained knowledge.

Excursion to Mauthausen

On October 4th, 2013, CeMM committed its yearly excursion to the 75th anniversary of the "Anschluss" to Nazi Germany in 1938. Starting at the festive hall of the Austrian Academy of Sciences, President Anton Zeilinger welcomed us and joined us for a lecture given by the journalist and historian Klaus Taschwer on the "Biologische Versuchanstalt". The "Biologische Versuchsanstalt" was a pioneering Viennese Institute of Experimental Biological Research, privately founded in 1902 by the Jewish scientists and philanthropists Hans Leo Przibram, Leopold von Portheim und Wilhelm Figdor. Hans Leo Przibram led the institute in an unprecedented, visionary manner. Their mission was to 'address global questions of biology', rather than tackling individual problems, and they did so by combining scientists from different disciplines, such as biology, botany, chemistry and physics. This was an unparalleled strategy at this time and attracted international attention. Adding to their function as role models for modern science, the researchers even embodied scientific citizenship as they opened their doors to the public and installed showrooms and a micro-cinema. In 1911 the founders donated the Biologische Versuchsanstalt to the Austrian Academy of Sciences to ensure its future. With the "Anschluss" of Austria to Nazi-Germany in March 1938, the institute was "aryanized" by the Nazis. Hans Leo Przibram had to flee the country and he died in the KZ Theresienstadt in 1944. The building was bombed in World War II and was never restored.

Our subsequent visit to the concentration camp Mauthausen sparked a new type of discussion at CeMM and reawakened our awareness about the importance of safeguarding key values that should go hand in hand with the research endeavors of an international, inclusive and democratic science community.

Research Report 2012
On May 15th, 2013, some 50 people joined the presentation of CeMM's Research Report 2012.

Visit to ISTA
On May 16th, 2013 a delegation of CeMM visited IST Austria. Giulio Superti-Furga presented President Henzinger with a print (graphical elements of the CeMM facade) by Peter Kogler.

International Interdisciplinary Exchange
In April 2013 students of pharmacy from The Netherlands visited CeMM and the Anna Spiegel Research Building.

Visit to CeMM within the "Next Nature" Project
On May 27th, 2013, 25 pupils were invited to CeMM to get some insight into molecular medical research and hopefully some inspiration for a scientific career.

Welcome to CeMM
On October 29th, 2013, CeMM was honored with a visit from President Anton Zeilinger and Vice-President Michael Alram.

Science and Diplomacy
Her Britannic Majesty's Ambassador to the Republic of Austria and the UK Permanent Representative to the United Nations in Vienna, Susan le Jeune d'Allegeershecque and her delegation visited CeMM on April 14th, 2013.

European Forum Alpbach
Giulio Superti-Furga moderated the break-out working session "Creating Knowledge: The freedom of research" at the Health Symposium of the European Forum Alpbach 2013.

Excursion to Mauthausen
The excursion to the concentration camp rose awareness about the importance of safeguarding key values and solidarity.

Thoughts on CeMM's Visit to the Mauthausen Concentration Camp by Lisa Bauer

Today, the only reminder of an outstanding biological research center from the beginning of the 20th is a street named Vivariumstraße. The reason why the "Biologische Versuchsanstalt (BVA)" no longer exists because of one of the worst incidents of mankind – the second world war, and, as a consequence thereof, the deportation of Jews and so-called "inferior human beings" like disabled people, homosexuals, Roma, Sovjets and Prisoners of War.

Klaus Taschwer, an Austrian science journalist, gave us CeMMies a talk about the BVA and anti-Semitism in science during the first half of the 20th century. In 1902 the BVA was founded by Jewish scientists. The first years of this outstanding interdisciplinary and international institute were characterized by remarkable publications. The research was focused on experimental biology.

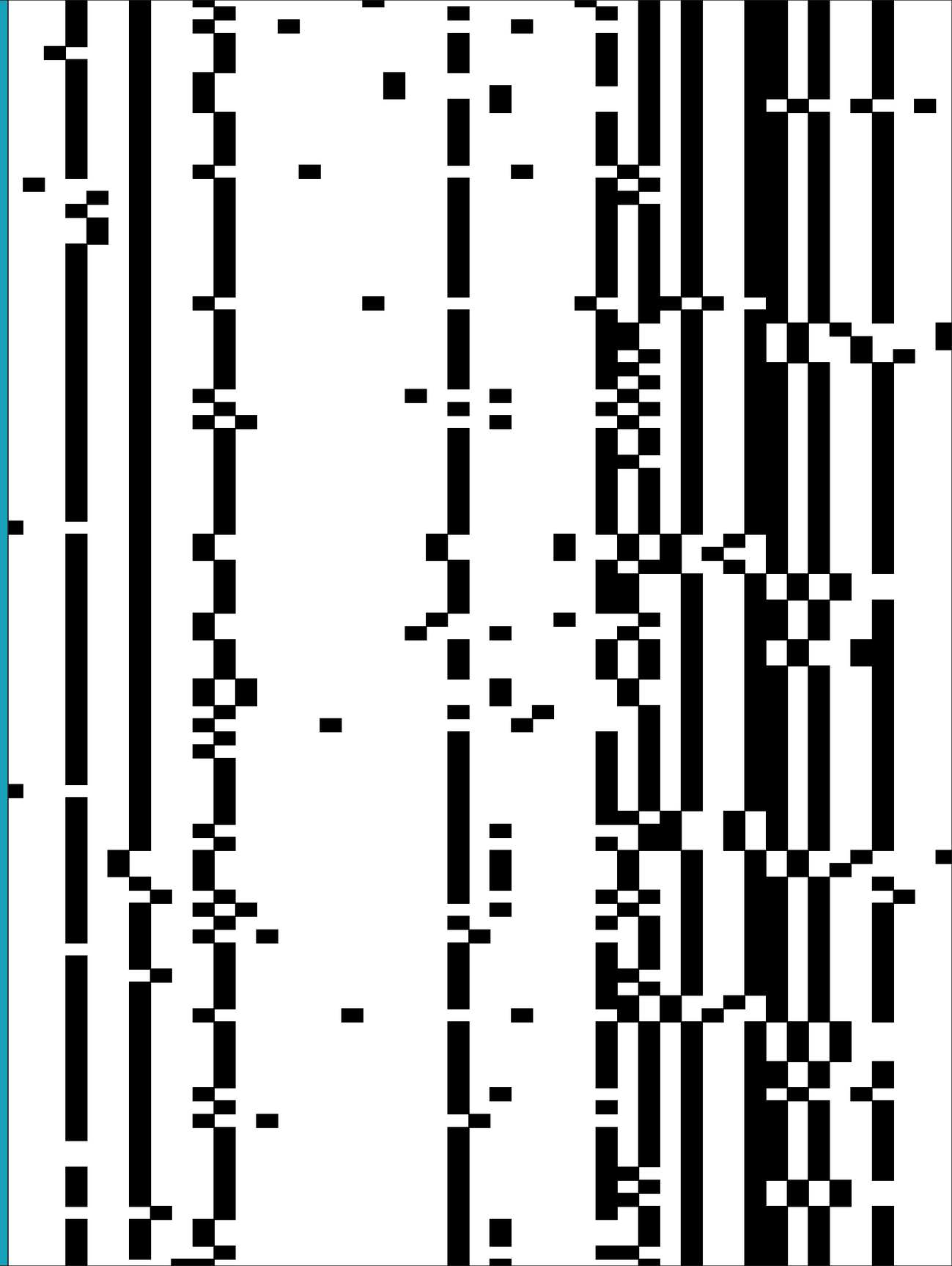
Mainly from the 1920's on, the increasing antisemitsm led to financial problems at the Jewish institute, which culminated in the prohibition of the founders to enter the research building at the time of the Anschluss. During the morally reprehensible deportation of "inferior human beings" to concentration camps, the BVA was the scientific institute with the most holocaust victims relative to the number of employees. One of the founders and his wife died in a concentration camp, and the "Biologische Versuchsanstalt" was destroyed in the last day of the Second World War and nearly forgotten.

One of these concentration camps is located in a small town called Mauthausen. Mauthausen, which we visited after the talk, is a friendly little town along the banks of the Danube. If you drive up that little hill, a building comes into sight, which looks like a prison with high stone walls. This is the place where innocent people lost their lives simply because they were accused of not being in accordance with the National Socialist German Workers Party.

For me, the most terrifying part of this day in the concentration camp was that I recognized it as my grandmother had described it to me. She survived. The room of names reminds us of friends, relatives and all the other people who were executed and died in this concentration camp.

We, all together, should be aware of the possibility that this can happen again at any time in any country of the world, and we, all together, have to form a world without racism or discrimination but with understanding and respect to prevent such terrifying, abhorrent, and contemptuous things in the future.

A contribution by Lisa Bauer, diploma student at CeMM, whose grandmother was an inmate in Mauthausen.



Science

Director's Intro
Discussion on Art and Science
Science at CeMM
Cancer
Infectious Diseases
Immune Disorders and Inflammatory Diseases
Post-Genomic Technologies
Diagnostics and Therapeutics
Principal Investigators

Life

Great Lectures
Scientific Meetings
Great Competitions
Great Celebrations
Good Scientific Citizenship

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CeMM Facts

To give you more information about CeMM we have gathered together all the practical details, i.e., the nuts and blots of the institute, which are presented here.

Here we proudly illustrate the diversity and characteristics of all the people working at CeMM, including their position, nationality, and gender. We also present an overview of CeMM publications, expenses and sources of funding in 2013. This is followed by our staff directory and a full publication list.

We will also introduce you to the Austrian Academy of Sciences and our current Scientific Advisory Board, who support us with their invaluable expertise. We also provide space to other notable people who helpfully imparted their thoughts and views on the institute in previous years in our widely anticipated Testimonials section.

CeMM and the Austrian Academy of Sciences

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

The Austrian Academy of Sciences, founded in 1847, is the major 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 1300 employees, which are located in several federal states of Austria, with the headquarters in the Old University in the center of Vienna.

At the beginning of the new millennium, the Academy gave new impetus by taking up forward-looking research areas. CeMM was founded as an interdisciplinary research institute committed to advancing the understanding of human diseases through basic and biomedical research. Located in a tailor-made building in the midst of the campus of the Medical University of Vienna and the General Hospital, CeMM is dedicated to its mission statement "from the clinic to the clinic" and fosters a highly collaborative and interactive research mindset. Scientific quality, innovation potential and sustainability are the main criteria for its research profile, and made CeMM within a few years a flagship institute of the Academy and a key player for biomedical research in the heart of Europe, focusing on cancer, inflammation and immune disorders.

The Austrian Academy of Sciences is promoting a new quality in the dialogue with society and in the awareness for the societal impact of research and technological advancements and the importance of interdisciplinary and cross-cultural approaches. In this respect CeMM is totally in line with the goals of its mother organisation by bringing together different disciplines, initiating science and arts projects, popular lectures and sociological, ethical and health-political debates, for instance on the future of genome-informed medicine. 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.

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
Chairman of the Board of the Nobel Foundation

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,
National Institute of Allergy and
Infectious Diseases, Bethesda, USA

Prof. Dr. Hidde Ploegh
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

Ph.D. Program

The CeMM Ph.D. Program trains a new generation of researchers based on a novel, post-genomic, molecular understanding of biological and pathological systems and will thereby contribute to shaping the predictive, preventive and personalized (also termed "precise") medicine of the future. To reach this goal, students are made familiar not only with biomedical technologies, but also with the basic principles of cell- and molecular biology and the application of this knowledge for a molecular understanding of diseases and targeted therapeutic concepts. The Ph.D. students also learn how to navigate the complexity of translationally-minded multi-disciplinary biomedical projects at the level of communication and management.

Access to top technology
CeMM offers a range of cutting-edge technological platforms for modern post-genomic methods – including deep sequencing, proteomics, chemical biology, a virology lab and access to imaging and sorting, biological-chip technologies and bioinformatics. CeMM's expertise and state-of-the-art instrumentation are accessible to all its employees. Emphasis is given to unusually strong support through freedom and scientific infrastructure as well as supervision and administrative services that are needed to carry out the proposed project for the entire duration of the Ph.D. Program.

Translational research
CeMM's mission is to combine insight obtained from basic and clinical research and use it to implement the development of innovative therapeutic and diagnostic strategies – from the clinic to the clinic. CeMM is positioned in medically-oriented research. In its short history it has published a growing series of "translationally" relevant publications (e.g. a Nature paper on acute macular degeneration mechanism by Weisman et al., or a NEJM paper that brings hope to many MPN patients; a newly identified mutation fills the gap in the molecular pathogenesis of MPN by Klampfl et al.).

Inter-group collaboration
With 13 successful research groups on-site, CeMM's students benefit from the experience and expertise of a diverse range of research scientists. CeMM offers a collaborative culture, according to which students, postdocs and PIs contribute their expertise generously while accessing the expertise of all others in a modular fashion to lead multi-disciplinary projects efficiently and professionally.

For further information including application deadlines please visit:
http://www.cemm.oeaw.ac.at/phd-program/

When you're trying to decide where to do your Ph.D., it helps to know what past and current students think of the CeMM Ph.D. Program experience. Here some CeMM students, past and present, share their thoughts with you to give you "the insider" perspective on some of the highlights of being a CeMM Ph.D. student.

Elisabeth Salzer
Boztug Lab: 2010 – present
"My decision to do a Ph.D. after finishing medical studies was mainly based on the fact that as a medical doctor you are often confronted with facts about disease entities, causalities or treatments you have to study, internalize and apply but you are not really supposed to challenge them. Therefore I decided to do a Ph.D. in molecular biology before starting my medical specialization to broaden my scientific horizon and to get a profound education in science. It was important for me to work in an institute, which is tightly interconnected with clinicians and focused on clinically applicable research but at the same time also known for cutting-edge technologies and great expertise in a broad scope of scientific genres. Now, after three years at CeMM I can say it is indeed a truly unique place in many ways. The atmosphere is international and very open-minded also towards non-biological topics such as music, arts and humanities."

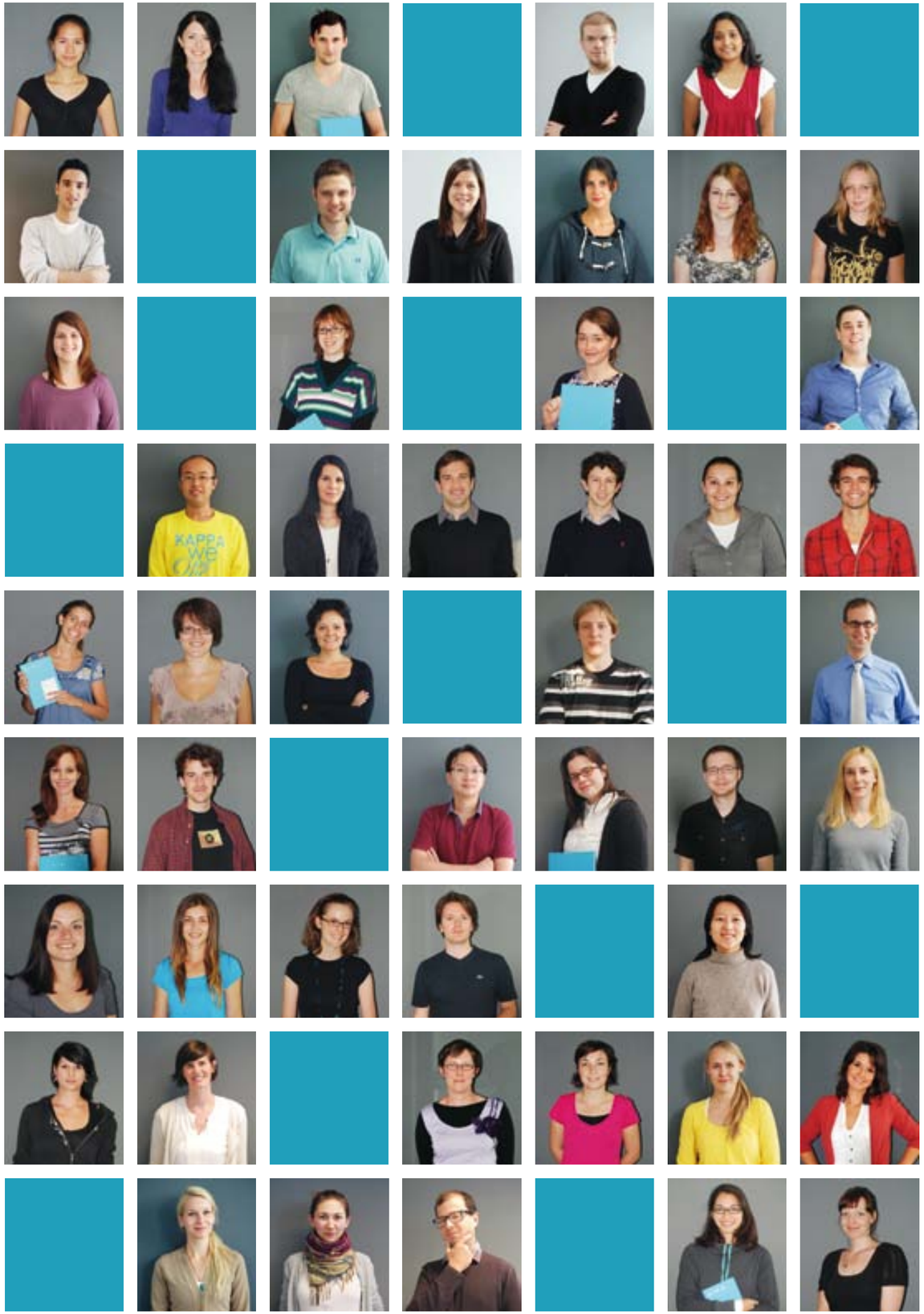
Thorsten Klampfl
Kralovics Lab: 2008 – 2013
Current Position: Postdoctoral research associate University of Cambridge, UK
"The highlight of my Ph.D. was, of course, when all of my hard work and experiments bared fruit and contributed to ground breaking findings. Making use of the possibilities at CeMM I had the privilege to identify novel mutations that contribute to specific blood cancers which we studied in Robert Kralovics' lab. In an incredible group effort, with the selfless dedication of my fantastic colleagues in the lab and with the help of collaborators within and outside CeMM, we studied these mutations for their biological and clinical implications. The findings will contribute to a better diagnosis of the disease and will lay the foundation for development of new therapies. Just recently the paper describing this research was accepted for publication in the New England Journal of Medicine and it is said to represent a landmark paper for the understanding of the blood cancers we studied."

Georg Winter
Superti-Furga Lab: 2008 – 2013
Current Position: Postdoctoral research fellow Dana Farber Cancer Institute/Harvard Medical School, USA
"Reflecting on my time as a Ph.D. student is certainly looking back with a smile and I can say that for me, CeMM was, in many different aspects, just the best spot to pursue my studies and a perfect match from the first day on. CeMM was unique in its capability of providing me access to cutting-edge technologies, a good funding situation and great expertise in a broad scope of scientific genres, all three of which are key features to succeed in science. I learned how much I can benefit from working together with talented people experienced in very specialized fields like bioinformatics, genomics or protein mass spectrometry. Given the international focus of CeMM, it was easy for me to attend scientific conferences in Europe and the USA that allowed me to further expand my professional network which, in turn, also helped me to find my current position."

Georg Winter in the Superti-Furga Lab

Employees

34 Nationalities
Austria, Algeria, Armenia, Australia, Brazil, China, Colombia, Croatia, Cyprus, Czech Republic, DR Congo, Finland, France, Germany, Greece, Hungary, India, Ireland, Italy, Lebanon, Lithuania, New Zealand, Poland, Portugal, Russia, Serbia, Singapore, Slovakia, South Korea, Spain, Switzerland, The Netherlands, United Kingdom, United States


KAPPA

Directory

Management

Giulio Superti-Furga,
Scientific Director

Gerhard Schadler*,
Managing Director

Anita Ender,
Administrative Director

Georg Casari
Intellectual Property &
Technology Transfer

Principal Investigators

Denise P. Barlow

Andreas Bergthaler

Christoph J. Binder

Christoph Bock

Kaan Boztug

Sylvia Knapp

Joanna Loizou

Robert Kralovics

Sebastian Nijman

Giulio Superti-Furga

Department Heads

Keiryn L. Bennett

Jacques Colinge

Stefan Kubicek

Adjunct Principal Investigator

Thijn Brummelkamp

PostDoctoral Fellows

Barbara Drobits

Doris Chen

Matthias Farlik

Adriana Goncalves*#

Maria Gorna
ERC AdG I-FIVE

Florian Grebien
FWF P22282

Barbara Gritti
MedUni Vienna

Leonhard Heinz
ERC PoC AIRSHIP

Barbara Herdy
ERC AdG I-FIVE

Kilian Huber
EU ASSET

Quanah Hudson
FWF P25185

Roland Jäger
FWF J3269 ESF

Kumaran Kandasamy
ERC AdG I-FIVE

Thomas Karonitsch
Interdisciplinary PostDoc,
ERC AdG I-FIVE

Freya Klepsch
JDRF Grant

Tomasz Konopka
ERC SG "Genes.Drugs.Cancer"

Peter Màjek

Markus Müllner
ERC SG "Genes.Drugs.Cancer"

Harini Nivarthi
FWF F28

Nikolina Papac-Milicevic
MedUni Vienna

Angelo Nuzzo

Florian Pauler
FWF F43

Jana Prochazkova
FWF P24766

Manuele Rebsamen
EMBO Long Term Fellowship

Roberto Sacco
FWF P24217

Erika Schirghuber
CDL "Chemical Epigenetics and Anti-Infectives"

Christopher Schliehe
DAAD Fellowship

Christian Schmidl
EU Project "BLUEPRINT"

Michael Schuster

Sara Sdelci
JDRF Grant

Omar Sharif
FWF P25801

Nathan Clark Sheffield
EU Project "BLUEPRINT"

Michal Smida

Berend Snijder
Swiss National Fund Fellowship

Alexey Stukalov

Chris Soon Heng Tan
FWF F47

Claudia Trefzer
Swiss National Fund Fellowship

Georgia Velimezi
Swiss National Fund Fellowship

Bojan Vilagos
FWF P25360

Gregory Ian Vladimer
EMBO Long Term Fellowship

Katharina Willmann
ERC SG "ImmunoCore"

Ph.D. and Diploma Students

Tim Alber

Amir Shazada
MedUni Vienna

Daniel Andergassen*

Sol A Ban*

Philipp Bammer
FWF P25185

Lisa Bauer

Anannya Bhattacharya
ÖAW Doc-Fellowship

Johannes Bigenzahn

Bernd Boidol
CDL "Chemical Epigenetics and Anti-Infectives"

Florian Breitwieser*#
FWF P24321

Laura Brückner*
EU MCCIG EPICAL

Clara Jana Busch

Elisangela Calheiro dos Santos Valente°

Adrián César Razquin

Ciara Cleary
FWF P23257

Paul Datlinger

Cecilia Dominguez Conde
FWF P24999

Christoph Dotter

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Legend of Grants

CDL "Chemical Epigenetics and Anti-Infectives"
Christian Doppler Laboratory "Chemical Epigenetics and Anti-Infectives"

DAAD Fellowship
German Academic Exchange Service (DAAD) Fellowship

EMBO Long Term Fellowship

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

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

ERC Starting Grant "Genes. Drugs.Cancer"

ERC SG "ImmunoCore"
ERC Starting Grant "ImmunoCore"

EU MCCIG EPICAL
EU Marie Curie Career Integration Grant "EPICAL- of Epigenetic Cancer Lesions by Chemical Biology and Functional Genomics"

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

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

EU Project "BLUEPRINT"

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

FWF F28
Special Research Program "Jak-Stat – Signalling from Basis to Disease"

FWF F43
Special Research Program "RNA regulation of the transcriptome"

FWF F47
Special Research Program "Myeloproliferative Neoplasms"

FWF J3269 ESF
FWF J3269 Erwin Schrödinger Fellowship

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

FWF P23257
Stand Alone Project "Heriditary Predispositions to Myeloproliferate 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 of Protein Modification Regulation"

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

FWF P24999
Stand Alone Project "Inflammatory Bowel Disease"

FWF P25185
Stand Alone Project "Long non-coding RNA"

FWF P25360
Stand Alona Proejct "Antiviral Immune Response"

FWF P25801 Stand Alone Project "The Role of TREM-2 in Pneumonia"

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

FWF W1207
Doctoral Program "Bioinformatics Integration Network III"

JDRF Grant
Juvenile Diabetes Research Foundation Canada

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

OeNB
OeNB Jubiläumsfonds "Resistenz gegen PI3K/m TOR Inhibitoren bei Brustkrebs"

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Facts & 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.

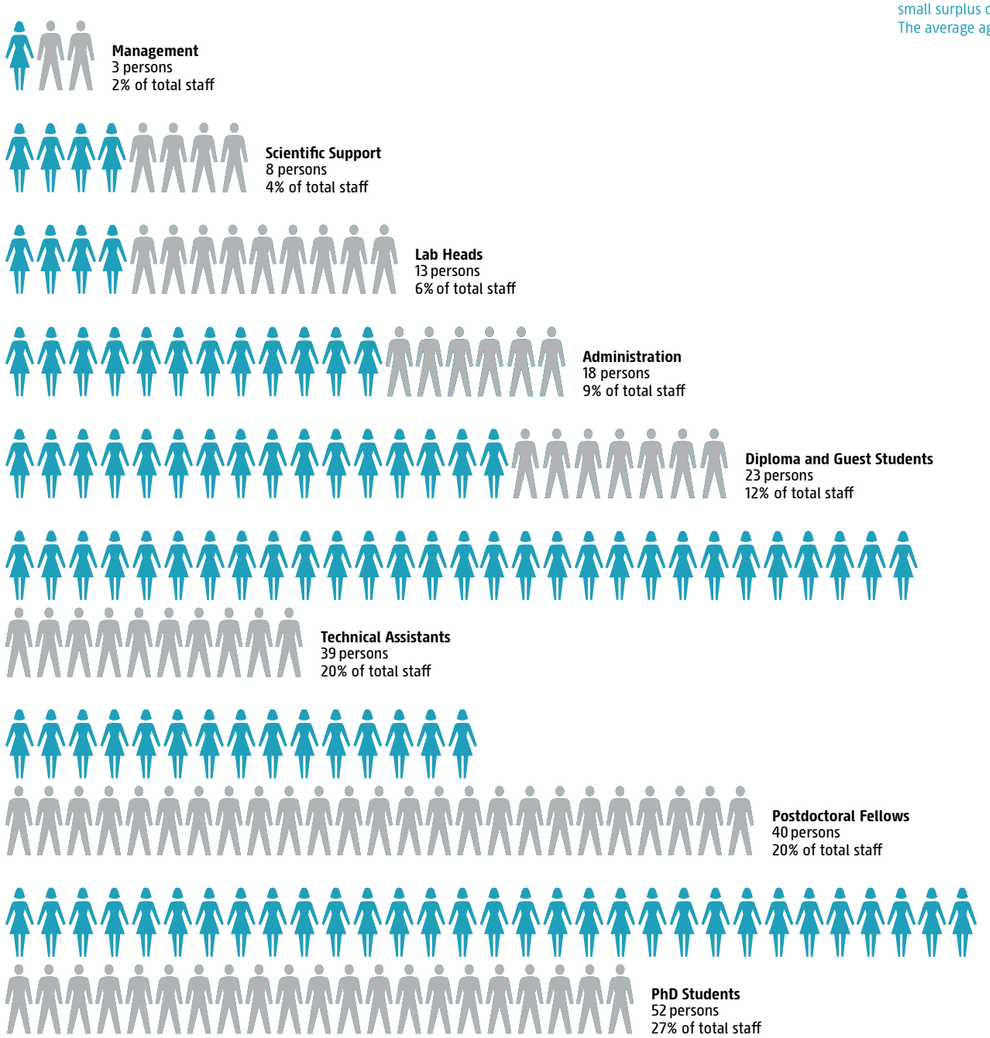
At CeMM, emphasis is given to mentoring independent young investigators and scientists early in their careers, through freedom, availability of infrastructure and a strong support system. A flat hierarchy, where the input of every single person is appreciated and required, leads to an enjoyable work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

Staff

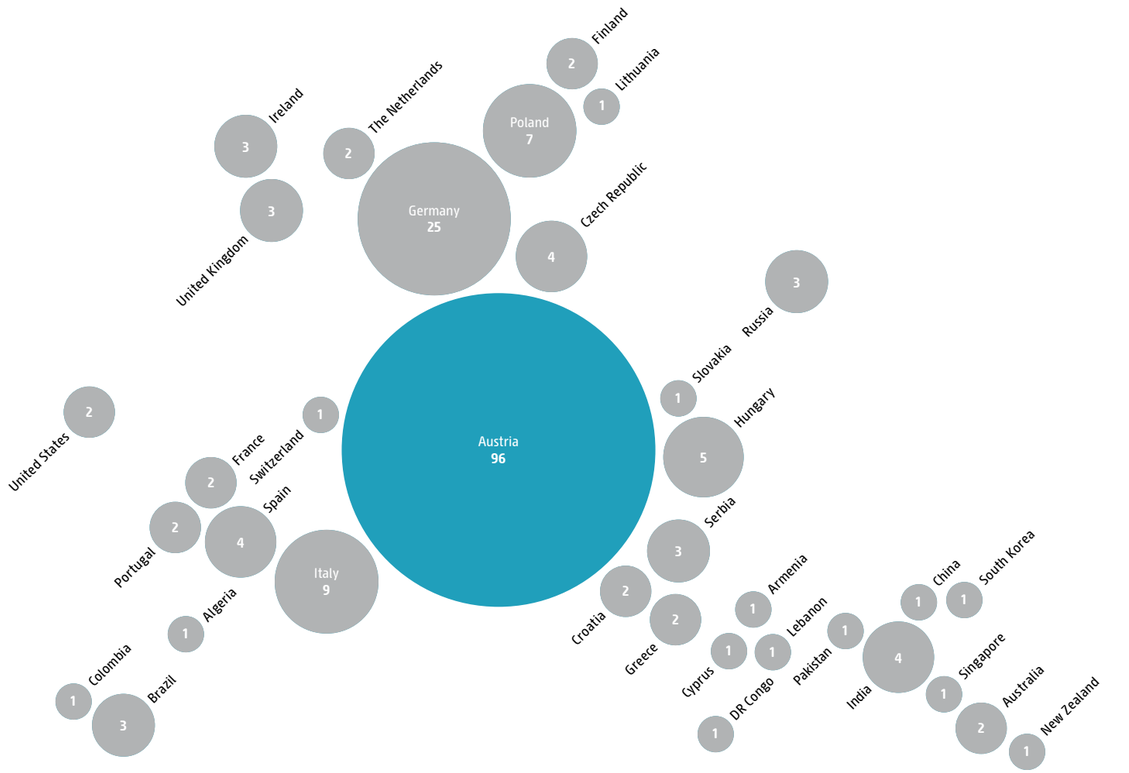
Listed by number of persons per field of work

CeMM stresses keeping the administration very lean and efficient. We have a very good gender balance, with a small surplus of women (57%). The average age is 31,76 years.



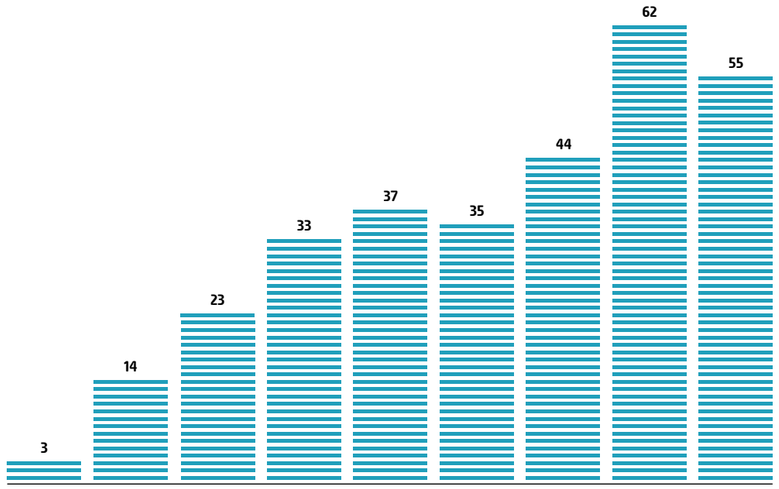
Nationalities at CeMM

34 different nationalities
are represented at CeMM.

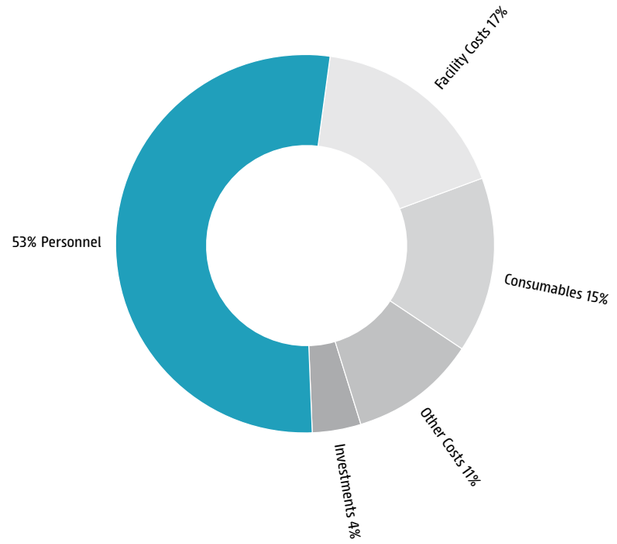


Publications

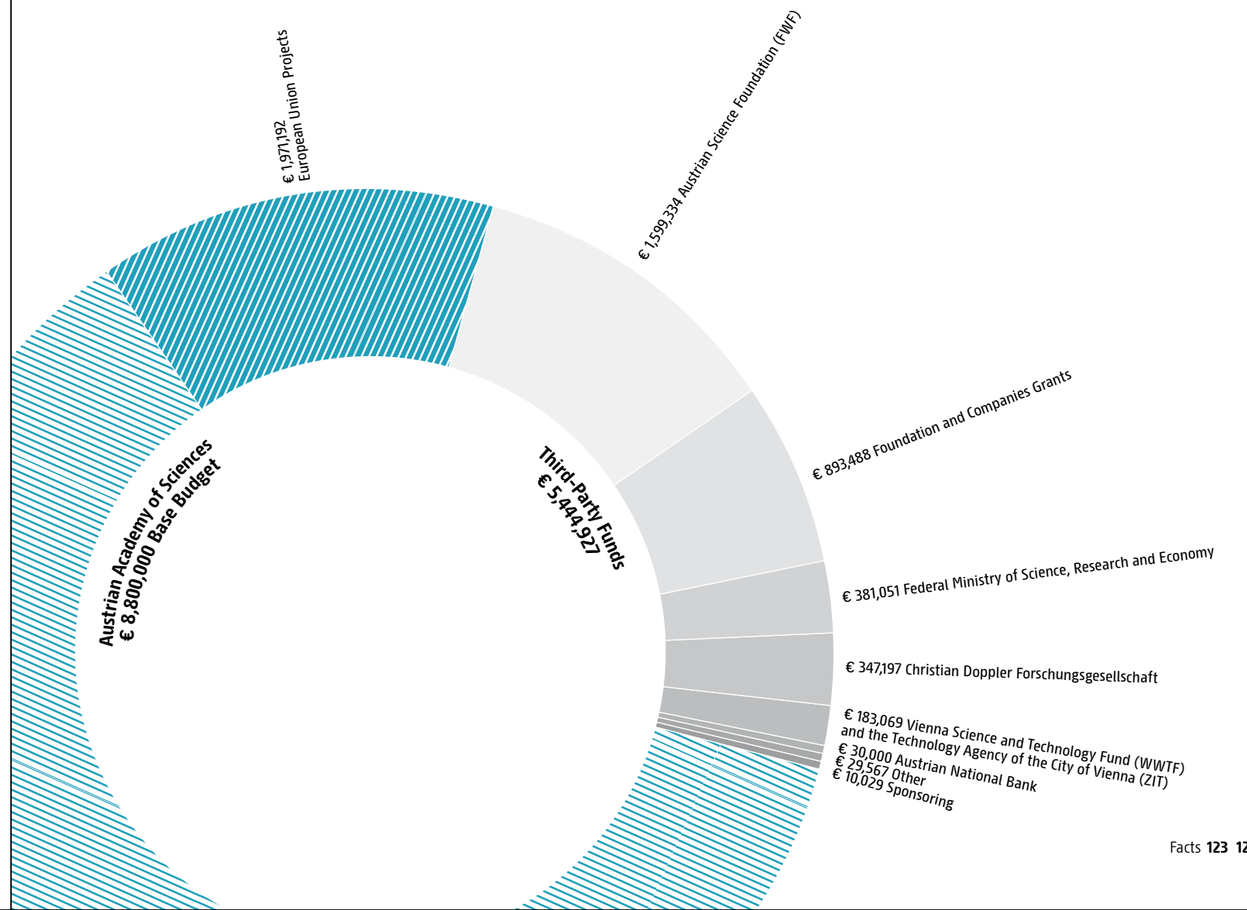
Includes all publications
by CeMM staff members
from the date of joining
the institute.



Expenses in 2013



Money Sources in 2013



Testimonials

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

The photographs of those who have imparted their testimonials in the past are presented in the following pages. This year, the new contributions can be found collected in the "life" part of the research report. We believe that we can learn from their opinions, and benefit from their approval and encouragement.

Dr. Johannes Hahn
Commissioner of the European Union

Dr. Beatrix Karl
Former Austria's Federal Minister of Science and Research

Peter Kogler
Artist

Prof. Dr. Karlheinz Töchterle
Former Austria's Federal Minister of Science and Research

Dr. Michael Häupl
Mayor of the City of Vienna

Niki Lauda
F1 World Champion and Airline Founder

Brigitte Kowanz
Artist

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

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

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

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

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

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

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

Prof. Dr. Helga Nowotny Ph.D. Founding member and former President, European Research Council

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

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

Prof. Dr. Hans Tuppy Chair of the Board of the University of Natural Resources and Applied Life Sciences Vienna

Dr. Heinz Fischer
President of the Austrian Republic

Martin Walde
Artist

Dorothee Golz
Artist

Prof. Dr. Josef Penninger Scientific Director, Institute of Molecular Biotechnology (IMBA)

Dr. Benedikt and Beatrice Spiegelfeld
Sponsors of the Constantin Spiegelfeld Lecture

Prof. Dr. Helmut Gadner Former Director, St. Anna Children's Cancer Research Institute

Esther Stocker
Artist

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

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

Eva Schlegel
Artist

ÖAW Austrian Academy of Sciences
MUV Medical University of Vienna
AKH Vienna General Hospital

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

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

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

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

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

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

Prof. Dr. Christoph Zielinski Chairman, Department of Medicine I and Cancer Center, AKH/MUV

Thomas Feuerstein
Artist

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

Prof. Dr. Christine Mannhalter Molecular Diagnostics MUV, Vice President of the Austrian Science Fund

Walking Chair
Artists

Acknowledgements

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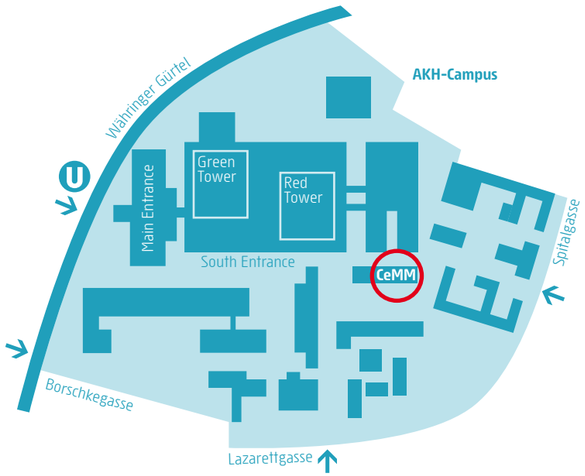

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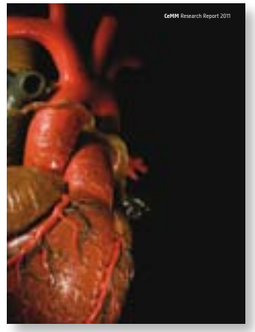

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