6th Talk at Dachboden, 25hours Hotel

PhD Student Representatives

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Discussion on zeitgeist/spirit of the times, accomplishments worthy of preservation and innovative new ideas, scientific excellence and a fabulous future

Considering the path that took you to CeMM: Was it a logical and methodical process? A crazy path of chance events? A miracle? A mistake?

Genger: I thought about where I wanted to do my PhD for a long time and looked at a number of institutes all over Europe. I kept contact with alumni from my bachelor's and master's courses to keep track of where they were going. It was actually just a random chat with a friend that brought me to CeMM, because he said, "Ah, you know, a friend of mine is going to CeMM" which I had actually never heard of, but I checked it out. It was a bit like love at first sight ... maybe that sounds a bit too romantic, but I liked CeMM because it looked much different to other institutes. So, I gave it a try. It was more of a random process.

Schüller: Well, my story may not appear logical in terms of the way it began, as I actually started out studying biotechnology. A third of my studies was dedicated to process engineering, which I later completely abandoned. I do not work with reactors or anything similar now, but it was during my studies that I realized I wanted to go more in the direction of molecular biology. While I was doing my master's thesis, I think it just became kind of logical that I would go to CeMM. I did my master's just across the street at the St. Anna (Children's Hospital), and yeah, so I got to know about CeMM, and I checked it out on the homepage, just like Jakob, and the homepage is just super cool.

Vulliard: In my case, it was a structured but lucky decision, linked to science as much as the people making it. I had the chance to work with Jacques Colinge, who was in charge of bio-informatics at CeMM before becoming a professor at the University of Montpellier, and he still had a vivid and very positive opinion of the science going on here. What I found

particularly convincing as well were the selection interviews, during which I met my current PI Jörg Menche and his team. I felt we had a lot in common, scientifically and in general. In my personal story, the human factor played a major role, and this makes me realize that the best we can do outside of CeMM is probably to be kind and constructive in order to make the best impression possible and to convince even more amazing people to join us.

Traxler: I would say, for me, it was, in a sense, a logical one. It was a continuation of trying to do good research in the genetics and molecular medical fields. And I realized that I wanted to go on and work on diseases that affect humans. So CeMM was the logical continuation of the process of always striving for an excellent place, interesting scientific topics, and a great community that is also very welcoming to aspiring PhD students. So really, when I got there for the selection, it clicked for me, and it was a clear-cut decision.

Caldera: I would say for me it was quite the opposite. It was more on the luck side. So, while I was doing my master's thesis in Chemical Biology in Zurich, I wasn't really sure like ... what to do ... and what field to obtain a PhD in, or whether I wanted one. I did a check on many institutes and universities, and then, by pure chance, I was reading the newspaper while I was supposed to be working and found an article that mentioned CeMM. I looked up the website and it immediately felt like the right institution to apply to. And I did so to a group that didn't exist at the time of the PhD hearing. But, nevertheless, I found the perfect fit and the whole environment and atmosphere there during the selection was wonderful. And that's why I stayed, and I'm happy.

If you were to compare CeMM to a novel, a painting, a movie or a rock song, what would come to mind and why?

Caldera: I think that is a very easy question. And the obvious answer for me is Rick Astley's "Never Gonna Give You Up". Because it summarizes so clearly and directly the nature of CeMM, like with our collaborative spirit, that we're never gonna give up on our collaborators, we're never gonna give up on our PhD students, we help each other, and I think we're also never gonna give up on great science. So, I would say this is just perfect. I don't know what the others say, but I would say that's the correct answer here.

Genger: It's a love story.

Caldera: And it's a love story, exactly.

Genger: How can you argue with that? I was thinking of "High Hopes" by Panic! at the disco, because CeMM definitely supports you in developing your own ideas and to follow your path. I would say that is what the song is about. Otherwise, sometimes, maybe in general, a PhD can feel like in *The Old Man and the Sea*. It depends on what your PhD is like, but I doubt that this is the case at CeMM. There is too much support to let it get like that.

Traxler: I don't really have a novel or rock song or anything that comes directly to mind, but yesterday, on my way home, I listened to Run DMC featuring Aerosmith's "Walk This Way". Someone told me once that this was one of the first collaborations between rap and rock music and created an instantaneous hit, almost. I think that's why it reminds me of CeMM, because we also strive for this collaborative spirit through which two individuals who are great can make something outstanding together that otherwise would not exist. This is also what CeMM strives for.

Schüller: All this circles right back to "Never Gonna Give You Up", because we try new collaborations, and we're not gonna give that up. We have high hopes, and we won't give them up. I was thinking of *The Avengers*. On the one hand, because, as you all know, the first year PhD students always organize the Halloween party. In our year, we chose the superhero motto, and we also dressed up as superheroes with our little capes in CeMM blue. Thinking about the question, I pictured us in those superhero outfits and thought of *The Avengers*. And it also comes back to collaboration, because *The Avengers* are just a group of people that do similar things. So, they are all superheroes, but they all have different powers, and together they manage something that seems impossible. That's also

sort of CeMM's motto: Team up! Use all of the team's strength to manage great things.

Vulliard: I'd say "Even Us" by Snarky Puppy. First, the band: it brings a fresh take on jazz, just like we try to do with science. It's a collaborative effort of skilled people, striving to bring new ideas and to reach a broad audience without compromises on quality. Then the song itself mixes international influences and alternates between unisons, overlapping solos and call-and-response structures. They've been awarded 4 Grammys so far, let's see if we can get as many Nobel prizes.

If you were to build a second, better CeMM in a city of your choice: what would you keep, what would you discard, and what would you improve?

Traxler: I think CeMM already has a lot of great features. Keep those. I wouldn't necessarily discard anything at CeMM. The location directly at the General Hospital is also great. If I were to put CeMM in a different city, I would definitely keep this medical connection, but try to get a biotechnological connection as well, have some other university departments and maybe also biotech start-ups close by. That is something I would try to improve. And otherwise, it would just be minor things: maybe a bicycle rack where you can store your bikes, a bigger kitchen. We have an awesome cafeteria staff who can do magical things, but sadly they are a bit limited by space. So, it's more these minor things on the side that I would try to improve. I can't think of anything that needs to be discarded.

Genger: What we should definitely keep is CeMM's connection to art. It was actually kind of a plus for me during the selection – I mean there are a lot of research institutions that don't care so much about what they look like or don't have any connection to art. For me, it shows that we at CeMM look a bit further and engage with other communities. The art community is somewhat similar to the scientific community when it comes to the creative process. It is about inspiring each other and also about coming up with an interpretation of reality, which science does, and art does, too. It is also very helpful. I recall, for example, when Yigong Shi came to visit CeMM last year. We went to the Brain Lounge for the *Meet the Speaker Session*. He was super surprised and a bit confused, but he really loved it. The Brain Lounge kind of perturbed the usual hierarchy between students and professor. He came much more down to our level and we had much better access to him. So art is important and should be kept, no matter how we would recreate CeMM.

Caldera: Yeah, tough ... I can only fully agree with the ideas mentioned by Pete and Jakob about keeping most of CeMM the way it is, also keeping the location, close to a General Hospital, and I would like more biotech facilities. I think the art part is also very important. If these things were already there, then, in my dream universe, I would put CeMM next to a beach, maybe with a slide somewhere.

Genger laughing: Productivity would decline, I guess.

Caldera: No, no, no! That is what you think. People would just never leave the place and be there like 24 hours ... like the *Google* kind of concept.

Vulliard: We'll talk a bit later about which rooms we could add to CeMM.

Schüller: What is left to say? So, if I transferred CeMM, I would probably locate it in a campus with more different PhD programs so that they can also benefit from each other. But that's the only thing that comes to my mind right now. And, like the others, I would keep nearly all of the rest.

Genger: I think the social component should also be kept. It's a good thing that CeMM is not too big, because that way, basically everyone knows each other. As we said before, this is also a basis for collaboration. It's not just strangers that you are collaborating with but people that you know from the CeMM Happy Hours or from the CeMM Outing. It's a much closer connection that you have at CeMM. Which may cause a bit of a problem then. Because when asked what we would improve, I would say CeMM definitely needs more space. But if it grows, the probability of everyone knowing each other would decrease. And so, it's a bit of a critical intermediate state, where the optimum is probably hard to find.

Vulliard: I would opt for a warmer coastal place as well, and agree that the spirit, the small-world aspect and the fast scientific turnover should be kept. And a few more floors could come in handy as well.

Traxler: I think the coffee machines are an interesting point. Basically, every scientist drinks coffee, right?

Genger: Almost everyone does.

Schüller: Sorry, I don't.

Traxler: No? Sometimes it's annoying: you want to get your coffee fix, you go there, it's blocked by a meeting and you realize: "OK, now I have to walk through the institute to find another coffee machine." Luckily, they are

plentiful. Forced to go to other floors, you meet other people on the way and end up kind of accidentally bumping into someone. I think this also fosters a natural collaborative environment where you just talk to people that you constantly meet during the day. You have opportunities to engage with other people and you are not completely isolated in your own lab. So, this is one of the occasions where you could say: "It's not a bug, it's a feature".

Schüller: And one thing that we didn't mention yet, that I would definitely keep, is the PhD program. I'm really satisfied so far, especially with the introductory program, which also goes in line with what was said before, as it brought us closer in my year. We all started together, were like a class of 13 people and spent the whole first month together. I consider all of those people my friends now. If I need something, I can easily go and talk to them if they have some cell line or whatever ... and I think this also makes it easier to collaborate.

Genger: We also help each other to move to other places and with everything else. It's cool to have that.

Regarding research at CeMM, do you think you are living in "normal" years of routine progress or do you think this is a historical moment that will find special mention in history?

Schüller: In general, I think there is no such thing as routine in science, you always kind of make history by doing research, because you always find new things, and this will become history. But the pace has definitely increased in our times because we have all those technologies at hand and all those facilities. I think research is just making history in general. Sometimes there are more findings, sometimes less, but it is hard to pin it down to this period.

Caldera: That's a very fair point. I also agree that if you looked back in history and asked people like ... I don't know ... Newton or Maxwell: "What do you think about your time? Is it a very special time?" Well, Maxwell would have argued: "Yes, never before have we had as many discoveries as right now at the end of the 19th century, and this is truly an immersive time." And we are feeling the same right now. Every time seems to be special and the pace is always increasing. Nonetheless, I think it is quite a special time in biomedical sciences, as we have seen a huge increase in computational power in the last 50 years. There was already a lot of theoretical knowledge before that, which people could not apply because the computational power was not available. Now, for the first time, we actually have this interplay between computational power, informatics and bio-medical knowledge which makes our time quite
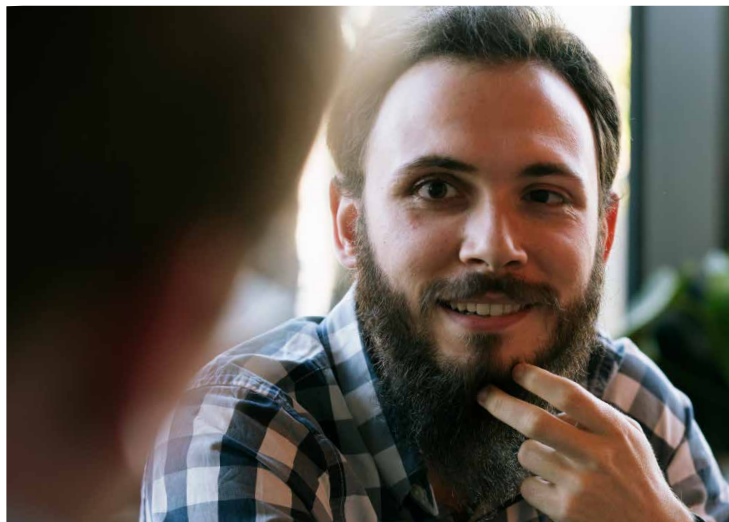
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special. This is also why we are seeing a lot of discoveries in this direction. We are right at the beginning of this interplay between informatics and biology.

Vulliard: I agree that scientists now have more tools at their disposal than ever before. Both the invention of the first programmable computers and the determination of the structure of DNA were achieved 70 years ago. Things are moving at an insane pace, and it requires a lot of adaptation skills to not only be up to date in our research but also to push the boundaries even further and to be innovative.

Genger: Wet lab-wise there have also been huge jumps, right? CRISPR is making genetic screens so super easy that basically everyone can do them now. Also, other technologies that we have at CeMM are improving. Metabolomics is getting better and allows us to focus more on metabolism and its different aspects in disease and for example in DNA repair. This is quite interesting: Metabolism is such a fundamental feature of life, but nobody thought much about it in the past 70 years. We are just now revisiting this and seeing how important it actually is in several clinical manifestations or diseases.

Schüller: But one kind of approach also requires the other: Now that we can produce more data in the wet lab, we need the computational power again.

Traxler: It's tough to add anything … it's always hard to predict, especially a true paradigm shift in the way we view the world. On the one hand, technologies like CRISPR [gene editing] allow us to modify our own genome, not only "a genome" for research but the specific genome of a patient to cure that patient from a disease. On the other hand, this will lead to a change in our perspective on what it means to … well, have a "trait" run in your family versus a "disease" that is caused by a mutation because you can potentially "treat" that now. And then we would have to have a whole societal talk, or rather discussion, about what that means. What are your genes and what are "you" in that sense? Based on that, are you allowed to modify yourself? Can you maybe … like are you confined to what you were born with? So, if you are not able, for example, to drink milk, because you are lactose-intolerant, could you at some point say: "Well, I'm tired of not being able to drink milk. I want to drink milk! So, I'm gonna go to the clinic and get treatment."

Schüller: Well … well, this is enhancement, OK.

Traxler: Sure, but I think now is the first time that molecular biology in that sense is not only able to treat diseases – which is great – but also to redefine a bit what it means to be born as a human. Which is great but also has some drawbacks. These also need to be discussed and balanced out. I think in that sense we are truly not living in normal times.

Vulliard: It's interesting that you are mentioning progress in different areas and different fields, but don't you think as well that interdisciplinarity is gaining some importance these days and that it might be important? At CeMM, we are starting to have people with really different backgrounds.

Caldera: Yes, indeed! The symbiosis between informatics and biology is obviously promising. But I think the reason why interdisciplinarity in biology is becoming more and more of a thing is because we are slowly getting stripped of this reductionist thinking that one gene or one thing causes something and are slowly shifting to a more systematic approach. And there, you need to apply methods and tools from the diverse fields.

What is the single most impressive scientific achievement that CeMM has produced in the last five years?

Schüller: That's a tough one.

Genger: No single publication can cover all the diverse groups, because we are all working on such different aspects … and it's hard to find one publication and say this is … this is the star of our institution. It would pretty much need to include all of us.

Schüller: Two things come to my mind. One is pharmacoscopy, a new tool that enables us to answer many questions in immunology. It shows the interplay between different immune cells and does not focus on only one cell type. It has also resulted in the spinning out of a company and setting up this technology was quite an achievement. Still, all the other publications were as important. Another pretty cool tool developed at CeMM is the CLOUD (CeMM Library of Unique Drugs) by Stefan Kubicek's group, but I don't know whether it falls into the 5-year range. The Kubicek Lab condensed the number of FDA-approved drugs to one compound library that spans the whole set. It is widely used at CeMM and beyond.

Caldera: I also find this very hard to pinpoint. I think there were many great papers in different groups, and I guess each group might have a certain preference of their own. What was definitely quite an important CeMM paper was Gene essentiality and synthetic lethality in haploid human cells in Science in 2015. There are many others aside from that, like pharmacoscopy, which is a great tool. I also use the CLOUD, so obviously it's cool.

Vulliard: To stay data-driven, the publications on the recent study linking LZTR1 and RAS got the most likes on Twitter and Facebook. It's always really hard to evaluate science, and I guess we will need more years to see what really has the biggest impact.

Caldera: The best is yet to come!

If you were able to magically add a good-sized room to the CeMM building, what would that room be and why?

Vulliard: We already mentioned a bike storage room, and of course a nap corner would be great. Maybe a GPU cluster for deep learning, for geeks like us.

Traxler: For me this would be kind of a library type of room. While I like these chance occurrences of bumping into people when you go to your coffee oasis, on the other hand, a big part of what we do, and of what we are supposed to be doing, is think about the big questions. First, what big questions we should be working on, and then, of course, how to answer them. This also requires us to think deeply about problems and to come up with solutions, aside from what we already do very well, which is talking to each other, and of course, discussing them. Again, we need time to explore them and also to write, for example, fellowships or grant proposals. This requires more focus than I can usually muster in a lab environment.

Genger: I also think that CeMM could maybe use a library. But not because it is a quiet place or a book repository. A library basically stores the intellectual work of previous generations and when you see that CeMM already appreciates art so much and is so open-minded, why don't we have a place where we appreciate the intellectual work done before by previous generations – previous CeMMies.

Traxler: Kind of a CeMM science exhibition showing us all the great successes.

Genger: ... and previous PhD theses, I mean a library also keeps these things. Very few people use actual libraries for their everyday work, right? With the internet, you can look up publications within seconds, but a library is more a place to keep things.

Schüller: Actually, I was also thinking of something like that because sometimes I go to the Time Capsule, which I really enjoy ... it's super quiet in there, but it's a room that only has space for two people and others might also want to use it. So, it doesn't have the availability that a library could provide.

Vulliard: A room for you, Michael?

Caldera: Yes, a bigger room for myself with a big desk. I mean, I would also think that having a room to meet people would be wonderful. What would be cool is a type of data exploration artsy room, so a room dedicated to you, where you can be creative in actually showing what you did in virtual reality. A room, where you can use a 3D printer or draw something, create something. While the Brain Lounge and the Time Capsule are very cool art projects, they were created by professional artists. It would be cool to have a big room created in an artistic way by PhDs or by employees of CeMM, with stuff and results that are also created here at CeMM: a 3D sculpture of a certain protein complex, your PhD drawn on two pages, some virtual reality where you can dig into your data. Like: "You wanna know about my project? Here, touch it".

Traxler: Generating 3D prints, microfluidic chips or other useful parts for your research would help as well.

Genger: Or virtual reality, but this is probably just coming. When you have access, you can play around a bit without the pressure of actually producing something.

Traxler: Some companies have this 10% downtime where you can work on an unrelated project. Then a lot of the projects actually get realized and really create new departments. And they stem from these 10% where creative people start to say "OK, now I won't do anything that immediately helps the project that I need to finish", but kind of let go instead and work on whatever comes to mind. Just a little bit of fun.

Caldera: And then you are double as motivated to go back to your original project.

Traxler: Afterwards the results could be awe-inspiring for the next generation. So, if you're starting your project and you enter such a room, you would see the amazing projects done previously by the scientists there – a change of environment to get new ideas. To provide this within the institute would be great.

Vulliard: Now we have the ideas, we just need the space.

What do you think CeMM should do to be at the forefront of research leading to medical innovation in 10 years from now and to become yet more attractive to PhD students?

Genger: I think, what I observe for the training part, is that there is a bit of a gap between bio-informaticians and pure wet lab scientists. And when we look at the big publications from recent years, they usually have a wet lab part and a bioinformatics part. Because, today, huge amounts of data are generated and you have to navigate through them, you have to analyze them accordingly. So, I think CeMM would probably be even more attractive to PhD students. Or, generally, it would be good to have bioinformatics training, maybe for postdocs or PhD students who haven't had so much contact with that before. This is something we are actually starting to provide with the Hackathon. I think that is something CeMM should definitely support and follow up on later because it will become even more important in the years ahead. And in ten years, this will probably be basic education for anyone who works in biomedicine – learning how to do basic bioinformatics and how to navigate through huge data sets.

Caldera: I agree, this is one of the skills: how to combine both questions in one thing, how to further increase scientific output and quality as well. That is something CeMM has also started slowly in recent years, and which is basically bringing CeMM's super-collaborative environment to a version 2.0 that includes other institutes and universities as well. By collaboration with the IST and by including physicists and informaticians or chemists, we can first of all attract more PhD students. They can learn more skills through exchange projects. Also, the science at CeMM would improve greatly, right? Because if you have these experts from universities, instead of being completely on your own, you can team up, and it would add a lot of value. CeMM is on the right track, and it should just continue moving in this direction.

Schüller: I think one major point of being at the forefront of medical innovation is to continue with and maybe even foster strong collaboration with the Medical University and AKH. We have taken a first step in this direction with the new Adjunct PIs, two of which are medical doctors. The location at AKH Campus and also the medical environment can give us a lot of perspective and provide open questions on which we can then do research to develop new strategies, to find new therapies, addressing unmet needs in medicine.

Vulliard: I would love CeMM to continue pursuing several ongoing points, such as registering its own PhD thematic program with the Medical University so that the teaching matches what we need and what we do at CeMM even more closely, keeping in touch with alumni to create a strong researcher network, or more broadly, to believe in new ideas and follow up on what the students are excited about.

Traxler: Sorry to be so biased, but tools like CRISPR/Cas9 and for example CAR T-cell engineering, allow us to have an even more direct approach in terms of influencing therapeutic decisions. For example, not only by creating small molecules to treat something and by having an impact on diagnostics, which is of course hugely important, but by truly working on this more personalized front, where you say: OK, we have a patient. We know this patient has a certain disease because we can profile it on a molecular level, and then for example, we take T-cells from that patient, modify them and return them to the patient. This is an area we can also invest in a bit more in the future and we are starting to do so already. I see a lot of potential in those two types of approaches. This is truly where molecular biology and molecular medicine shine, and this is, of course, CeMM's focus.

Vulliard: Any final statements?

Genger: Research-wise, I have the feeling that there is currently a lot going on at the interface of in vitro and in vivo, with in vitro culture systems, 3D organoids and in vivo microscopy. This might be interesting for questions that are in between in vivo and in vitro, where in vitro systems are too basic and too limited and in vivo systems too complex, where you cannot really look at specific aspects or at what is happening during the process.

Caldera: That would be a cool thing.

Genger: Modeling tissue development in vitro could be interesting for CeMM to build a bridge from in vitro to in vivo.

Caldera: One could even use the art room with the 3D printers.

Genger: We could have a connective research group, just to be doing this on the side.

Traxler: In terms of transplantation technologies, this would also help create an ex vivo type of tissue that you can then transplant back into the patient. And we are perfectly located close to the General Hospital to actually work on such projects.

Vulliard: And what about training PhD students? Should we then print PhD students as well?

Schüller: I think we have enough people ...

Caldera: ... it would be too expensive. Hiring normal ones is cheaper, I guess.

Schüller: Besides, they would be so rigid...