# THE MESSENGER

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NCCR
**RNA & Disease**

National Center of Competence in Research
**The role of RNA in disease mechanisms**

## *Dear colleagues*

For most of us, being a scientist is more than a job, it's part of our identity. In this edition of the Messenger, three NCCR RNA & Disease Professors share personal insights into their academic journey and the challenges and opportunities that shaped their careers. My take-home message from these inspiring accounts is that "where there is a will, there is a way" and that there are different ways to succeed as a scientist in academia. Retaining and fostering this diversity is central to the Equal Opportunities strategy of the NCCR in RNA & Disease. However, we still fall short on the number of women in academic leadership roles in the NCCR. In an article of this Newsletter, I describe how unconscious or implicit bias are one of many factors contributing to the lack of gender diversity in leading academic positions, and what we can do to minimize the impact of biased decisions on gender diversity. As a relatively small organization, we have the privilege to implement innovative measures. With the aim of minimizing the penalty of maternity on female trainees' career, we recently implemented the pregnancy and maternity leave compensation scheme. We report on the short-term impact and experiences of this scheme for the first cohort of grantees. Finally, we share some of the insights we gained at an international meeting on Equality in Amsterdam. We will continue to develop the NCCR RNA & Disease Equal Opportunities strategy during Phase 2 and hope that the novel and existing measures will contribute to an increase in diversity at all career stages and will facilitate the journeys of NCCR scientists.

***Ana Claudia Marques***
*Equal Opportunities Delegate and Principal Investigator NCCR RNA & Disease*

**Success stories of three NCCR RNA & Disease professors**

# Passion and diligence: A silver bullet to reach the top?

*Interview: Larissa Grolimund and Ana Claudia Marques*

**Three NCCR RNA & Disease professors at different career stages give deep and personal insights into their career paths by talking about opportunities, difficulties and obstacles they encountered along the way. Stefanie Jonas, Magdalini Polymenidou and Frédéric Allain share with us their view on mentoring, gendered science programs and how to juggle a career in science with having a family. Their experiences and pieces of advice are diverse and tailored for the individual situations they encountered as young researchers embarking on a career in science. But a common theme of the stories of Stefanie Jonas, Magdalini Polymenidou and Frédéric Allain is also that there is not one single road to success, although passion for and dedication to science in combination with appropriate training and support remain the critical ingredients that lead you to the top.**

**Stefanie Jonas** is an Assistant Professor at the Institute of Molecular Biology and Biophysics at ETH Zürich, Switzerland, since 2017.

*What is the main research question in your lab?*
We study mechanisms of RNA processing and RNP assembly in human cells and work towards a better understanding on how errors in these processes can lead to diseases.

*When and why did you choose to become a scientist?*
Looking back, it was not a decision that I could pinpoint, but rather a slowly growing determination. My fascination with natural sciences started early in childhood, I always wanted to understand on a fundamental level, how the world around us works. In high school, I carried out my first smaller research projects. That was the point at which I decided to study chemistry, because I was curious and wanted to learn more about the molecular principles that govern nature. My inclination towards practical research deepened during my undergraduate and graduate studies and from my Master's thesis on, I poured all my energy into basic research.

*How did you get to the position you are in today? Can you give us a short description of your career?*
Biomolecular chemistry became my focus towards the end of studying classical chemistry in Göttingen. Because there were not many opportunities to go deeper into biochemistry in my department, I went abroad for the research project of my Master's thesis. With a Studienstiftung scholarship, I joined Jennifer Doudna's lab at UC Berkeley. This was my first in-depth contact with molecular biology and RNA research. About one year later, after completion of my thesis, I moved on for a PhD

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in Florian Hollfelder's group at the University of Cambridge. There I studied how enzymes can efficiently catalyze chemically diverse reactions and how this feature is exploited by nature during evolution of new enzyme functions. For my postdoc, I went back into the RNA world. In Elisa Izaurralde's lab at the Max-Planck Institute in Tübingen, I studied nonsense-mediated mRNA decay and general mRNA degradation complexes. Before starting my own group, I joined Ulrike Kutay's lab at ETH Zurich to start working on RNP assembly during a second, short post-doctoral research period.

*Did you ever consider leaving academia and if so what made you stay?*
Leaving academia has so far not appealed to me as a goal, I have always been looking for options to keep on doing basic, academic research.

*Did you/do you have mentors during your career? How crucial do you think is mentorship for the professional development in academia? Do you think mentorship for female scientists should differ from that for male scientists?*
So far, I have not seen substantial differences in mentorship for female or male scientists. However, what is also significant is the effect of role models. They are very important, because they provide a backdrop of normalcy and templates for how "someone-more-like-me" can succeed in this job. By chance, four of the five supervisors and PIs that I have worked with were women, every one of them successfully mastering the challenges of a scientific career in their own way.

I am grateful to all my previous PIs for having granted me the freedom to drive projects into the directions that I wanted to pursue. Furthermore, they have supported me in the next steps with advice, encouragement, practical help and with recommendations, whenever I applied for fellowships or subsequent positions. This type of support network, I would argue, is essential for everyone who wants to build a career in academia.

*"This type of support network, I would argue, is essential for everyone who wants to build a career in academia."*

*What programs or events to which you have participated do you think have been most useful for your career progression?*
During my post-doc at ETH, I became a member of a peer-mentoring group. It was actually initiated by two post-docs as part of the NCCR's [NCCR Structural Biology, editor's note] equal opportunities program. It is still running and consists of an informal group of female PhD students, post-docs and senior scientists that meet monthly for discussions over lunch. We provide support and advice for each other in terms of career and scientific progress. The meetings had a very encouraging effect on me, and the group was one of the factors that contributed towards me taking the next steps and applying for group leader positions. One great thing about such an informal group is that it could be founded by any student or researcher anywhere. Time commitment is minimal, but nonetheless in our group the effects of this peer-mentoring have been beneficial for all its members.

*In your opinion do women in science need gender-specific events/awards? Why?*
In some areas that might be approached differently by women and men, I have made good experiences with gender-specific workshops that addressed e.g. negotiation tools, communication, or how to use one's voice efficiently.

*"Flexibility from all persons and institutions involved has also been key. "*

*What is your experience of balancing career and family and what are the challenges and benefits of "having it all"?*
My experience in this is only one year old. So far I can say that it is crucial to bring in all the support that one can get to organize childcare: from one's spouse, family, daycare institutions, or hired help. For us, the Kitas at ETH have proven to be very valuable and flexible programs such as "Kita Flex" have made it possible to return quickly to a sustainable working mode and to adapt to changes in professional schedules. My husband and my brother are also of great help, each contributing one day of child-care a week, which allows me to work full time. Flexibility from all persons and institutions involved has also been key. Thankfully, my team (and also our baby) are understanding of the slightly unusual circumstances and are very supportive. In summary, for both my husband and I, having a family and a challenging profession have proven a great joy, and we are immensely grateful.

*How do you handle the high demand for mobility in your career with having a family?*
In the past, my husband and I both pursued our education and specialization at the institutions that promised the best progress for our vocation. This also meant that we spent a number of years apart, living in different countries, including the U.K. and the U.S. Currently, we live together as a family in Zurich.

*Based on your professional experience so far and if you had one advise you could give your younger self what would this be?*
Take heart, there is good reason to maintain hope and keep working towards your goals. Do not let go of your dreams.

**Magdalini Polymenidou** is an SNSF Assistant Professor since 2013 with a double appointment between the Faculty of Science and the Medical Faculty of the University of Zurich, Switzerland.

*What is the main research question in your lab?*
We investigate the molecular pathways that lead to the neurodegenerative diseases amyotrophic lateral sclerosis and frontotemporal dementia. Key players in the pathogenesis of these diseases are the RNA-binding proteins TDP-43 and FUS, so our research intersects with basic RNA and phase separation biology, which are particularly exciting and active research fields. Specifically, our lab aims to 1) understand the toxic mechanisms and the basis of disease heterogeneity, 2) devise faithful cellular and animal models of disease and 3) eventually identify new molecular targets for mechanism-based therapies for these diseases, which today are incurable and fatal.

*When and why did you choose to become a scientist?*
I took the decision very early on, I guess in my childhood, even if I didn't exactly know what it meant then. As a child I was influenced by my father, who was a medical doctor and my uncle, who was an engineer and

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an academic scientist. Both had successful careers and were passionate about science and they have passed this passion on to me from a very young age. I remember stating that I will do a PhD before I could write, which made my grandparents laugh. Already then I was convinced that research was the most exciting "job" one could do. And now, a few decades later, I am happy to say that this conviction hasn't changed!

*"Already then I was convinced that research was the most exciting 'job' one could do."*

*How did you get to the position you are in today? Can you give us a short description of your career?*
Many turning points in my career path have been serendipitous and I think that this is probably true for most people. At the last years of high school in Greece – which would be the equivalent of the Gymnasium in Switzerland – I had decided that I wanted to do research on disease mechanisms. For this reason, I was intending to study medicine, which I thought would give me the best basis for this. However, in the Greek educational system, entering Medical School – or any other University level or professional school – depends on a single nation-wide exam that ranks students based on their performance and then distributes them to Schools, according to their own preference list. To cut a long story short, I did not get my first preference, but my second one, which was Pharmacy, so you can say that my career started with a failure. Studying Pharmacy at the Aristotle University of Thessaloniki, however, turned out to be just as good a starting point, if not better. During the last two years of my studies, I joined the lab of Theodoros Sklaviadis, who was our Pharmacology Professor and who had just returned to Greece from Yale Medical School to set up a research lab to study prion diseases. This at the time was a very active research topic due to the mad cow disease epidemic in Europe, so many excellent laboratories throughout Europe were focusing on it, often collaborating via European funding. Prof. Sklaviadis was my first scientific mentor and has been extremely supportive to me and to all the students that have passed by his lab over the years. He has instilled the belief that mobility is essential for evolving as a scientist and has encouraged me to search for a PhD position in a leading academic institution. This has brought me to the University of Zurich and the laboratory of Adriano Aguzzi, where I studied prion biology and disease mechanisms. Coming from Greece, where funding and infrastructure was minimal, research in the Aguzzi lab was full of possibilities. This time has shaped me as a scientist and taught me to combine focus with creativity in my research. This was a particularly productive period that set up the foundation for an academic career. In fact, I enjoyed working there so much that it was hard to leave. After I defended my thesis in early 2006, I stayed in the lab as a postdoctoral fellow for almost two years. During this time, I have worked for six months with a Novartis team in California on a prion diagnosis project. This gave me a unique perspective and appreciation of the industry world that most academic scientists don't experience. After that, in early 2008, I moved on to my postdoctoral studies to the lab of Don Cleveland at the University of California in San Diego. I chose this lab because I wanted to work on a different field of neurodegeneration and to focus on a fundamental, mechanistic question and to expand my scientific horizons. I was extremely lucky to enter the field of amyotrophic lateral sclerosis (ALS) at a particularly exciting time, when a number of breakthrough discoveries pointed to alterations of RNA-processing as a (then) novel mechanism for ALS pathogenesis. Indeed, identification of ALS-causing mutations in two new genes encoding for RNA-binding proteins – namely TDP-43 and FUS/TLS – were reported by several groups worldwide, soon before and during my postdoctoral studies at UCSD. These developments provided a unique opportunity for my postdoctoral work, which allowed me to become an "incidental" RNA biologist, as I chose to investigate how alterations in these two proteins may affect RNA processing and thereby trigger neurodegeneration. This time also prepared me well for academic independence and my next career step, which was the setup of my own research group as an Assistant Professor at the University of Zurich in September 2013.

*"I was shocked when he asked me why bother, since I will soon have a family anyway."*

*Have you actually ever thought about yourself as a "woman in science" as compared to "just" a scientist? If so, was this the case right from the start of your scientific career or did it come up later?*
Not in my early years. As a child and teenager, I never thought of this. My family's "normal" was a working mother who, although she chose a less demanding career than that of my father, never questioned gender equality in terms of career ambitions. My mother herself studied gender bias as a part of her master's degree and I remember conversations at the family table on this topic since I was a child. Both my parents have raised my older brother and myself without any such biases, at least when it comes to our professional development. The aim was the same for us both: "find something you love and do it as best as you can". I also had very dedicated and knowledgeable teachers in high school who instilled the importance of gender equality. Surprisingly, the first time I realized that other people might see things differently was in Switzerland, when after I defended my thesis I was discussing with a more senior male lab member about postdoctoral opportunities abroad. I was shocked when he asked me why bother, since I will soon have a family anyway. The most shocking part of his reaction for me was that it was honest – he didn't mean to offend me, he was genuinely perplexed – and that it came from a person that I respected as a colleague and a scientist.

*"It takes a lot of persistence and focus and it is not always easy, but it is definitely worth it!"*

*Did you ever consider leaving academia and if so what made you stay?*
I have had some disheartening moments in my career and on these moments I wondered if life would be easier had I chosen a different path. These were short-lived, however, and I soon saw that difficulties and failures are part of any career – not just in academia. It is this realization that made me stay the course and I sometimes tell my students that the most difficult part in scientific research is to deal with frustration. It takes a lot of persistence and focus and it is not always easy, but it is definitely worth it!

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*Did you/do you have mentors during your career? How crucial do you think is mentorship for the professional development in academia? Do you think mentorship for female scientists should differ from that for male scientists?*
I have had wonderful and influential mentors in my career and I consider myself very lucky for this. I think good mentorship is absolutely crucial for a successful scientific career. I think that mentorship needs to be adjusted to the personality and peculiarities of each individual and career path. Gender is a factor of this, but certainly not the only one and I don't think that there is a single recipe that works for everyone in this case. It certainly helps to talk with someone that understands the specific demands and dilemmas of your own life and that can give you some real-life examples of how to deal with them. For me a very important aspect was that my mentors, who I deeply admire for their scientific achievements and vision, believed in my own abilities and potential as a scientist. This has boosted my confidence and helped me overcome my own "impostor syndrome" that I think is characteristic for many women scientists.

*Do you think that specific programs or events that you have participated in have been particularly useful for your career progression?*
Especially in the beginning of my career, attending international scientific meetings has played a very important role, because they were the inspiration that made me appreciate the life of a researcher. I remember how fascinated I was, when, as an undergraduate student, I attended such a meeting on prion diseases in Germany. At the time it felt like an entire new world was appearing in front of me, one with likeminded people that were curious and passionate about making scientific discoveries. Later, during my PhD and postdoc years, I have attended a number of courses and workshops, organized by EMBO, CSHL or other organizations, which were intense and short – ranging from a few days to a few weeks depending on the topic – and focusing on a specific technique or scientific topic. These were fantastic for immersing the participants into a new topic and to introduce them to other scientists with similar interests from all over the world. A special course in such a setting was the EMBO Lab management course, which I took as an early postdoc and which helped me think about important aspects for taking the steps towards an independent scientific career.

*"While we are far from an ideal gender-balanced scientific world, I think that we do need to highlight, support and celebrate women scientists."*

*In your opinion do women in science need gender-specific events/awards? Why?*
This is a difficult question and I can think of good reasons both for and against the idea. On the one hand, if gender equality is the goal – which in my opinion it is – then we shouldn't need any gender-specific measures at all. In reality, however, while we are far from an ideal gender-balanced scientific world, I think that we do need to highlight, support and celebrate women scientists. This is important in order to boost the careers of talented women, but also to inspire girls and young women that are inclined towards a scientific career, but may hesitate due to societal stereotypes that are unfortunately very persistent. In my opinion, one of the biggest obstacles for the younger generations is that examples of successful women scientists are much fewer than that of men, especially in Europe and even more so in Switzerland. Putting women scientists to the spotlight in a positive manner is one way to counteract this trend.

*What is your experience of balancing career and family and what are the challenges and benefits of "having it all"?*
I think that it is hard to balance family and career for everybody, both women and men. My younger self was often annoyed by the fact that the "having it all question" is only – or mostly – asked to women. Men have always been "having it all" and no-one seems to question their abilities in this respect. However, since I have my own family, I have come to realize that it is important to recognize the fact that having children takes a much bigger toll on a woman's life, particularly during pregnancy and nursing, and that fact is independent from societal stereotypes. During this period, no matter how involved a father may choose to be in family life, women face a decrease in productivity, almost invariably. This can be a short period, however, and soon after, family-career balance is a matter that should concern both genders equally. I am lucky that this is the case in my own family. My husband, who is also a scientist, understands the demands of this career and equally shares childcare and family time with me.

For me, I guess the biggest challenge is time. Sometimes, it feels like there are not enough hours in a day and it is this feeling of "inadequacy" that I find the hardest. I think it is great that organizations like EMBO, ERC, SNF, HFSP, NIH and several others appreciate this natural "imbalance" and apply measures to counteract it. I find this particularly motivating and I think that everybody benefits from making it equally possible for women to successfully combine family and career. For me personally this combination means happiness! I could not imagine my life without the satisfaction from my research and from working with many talented students, postdocs and collaborators. But I also cannot imagine a life without my children and the joy from seeing them grow and discover the world. Ideally, nobody should feel like they have to choose between these two. And we should strive to make this possible.

*"Sometimes, it feels like there are not enough hours in a day and it is this feeling of 'inadequacy' that I find the hardest."*

*How do you handle the high demand for mobility in your career with having a family?*
This is an important point that seems to discourage many young scientists from pursuing a scientific career. For me, having to move for my PhD (from Greece to Switzerland) and postdoc (from Switzerland to the USA) were both exciting prospects that I took as life adventures rather than burdens. The fact that my husband is also a scientist helped, since moving was eventually advantageous for both careers, as is often the case for scientist couples. Once we had children, however, creating a stable environment for them became a priority. Our next move (from the United States to Switzerland) was when my first son was one year old and even though we were returning to a more familiar environment, moving was much harder than before. I think that mobility is rightfully valued in an academic CV since it offers so much in terms of training, experience and way of thinking. In my opinion, however, it is important to view

each case individually and not make mobility a hard requirement or eligibility criterion, since this disproportionally drives women away from academia.

*Based on your professional experience so far and if you had one advice you could give your younger self what would this be?*
Worry less, trust yourself more and don't forget to celebrate each step and to enjoy the journey!

**Frédéric Allain** is Full Professor at the Institute of Molecular Biology and Biophysics at ETH Zürich, Switzerland since 2010 and Co-director of the NCCR RNA & Disease since 2014.

*What is the main research question in your lab?*
In my lab, we are interested in how RNA binding proteins (RBPs) regulate gene expression post-transcriptionally. We take a structural biology approach to understand this. We solve structures of protein-RNA complexes to understand the role and mechanism of action of RBPs in regulating splicing, RNA editing, miRNA processing and translation.

*When and why did you choose to become a scientist?*
This was quite late in my studies. I always liked science but not more than politics, anthropology, history and psychology. My grandfather, who was an archeologist (pre-history and gallo-roman period), was certainly an inspiration to become a researcher; I did learn a lot from him. The excitement for biology came from studying biology at high school and then in "classe préparatoire" where I had a really fascinating Biology teacher (Mr. Darchy). He was clearly doing more than the usual classes, organizing field trips etc. and was very encouraging to me. He really transmitted a passion for biology and made us realize that there is a lot to discover in this field. This mentality motivated me to study hard and it certainly was an asset in my later succeeding in entering the prestigious "Ecole Normale Supérieure" in Paris (ENS). In that school, the goal is primarily to train teachers and researchers; so the goal was set, but the path needed to be created.

*How did you get to the position you are in today? Can you give us a short description of your career?*
This was realized step by step and not with this objective as a long-term goal. In research, I do not think that you can plan a career. I remember this discussion with an American PhD student during my PhD studies, who told me that his plan was to become a professor in one of the top five US University within 10 years. He then enquired about my plans, and I remember telling him that I had none beside graduating and publishing at least one paper. This was true, but he did not believe me! This was in 1993 and I was appointed as an assistant professor at ETH in 2001. So, to some extent, I achieved without planning it what this American student was dreaming of. His own PhD was not as successful as he was hoping for, and he never fulfilled the goal he had set out for himself.

So, to come back to the question, after studying chemistry at the ENS and doing a master in bioinorganic chemistry, I got the opportunity to visit the MRC-LMB in Cambridge (UK) during a visit to my father in Cambridge. My father, who is a professor in Hematology, had arranged for me to meet the Director of Studies of the LMB. At the time I had no idea about this lab, but after visiting it and meeting with two PIs, I was fascinated. I discovered a world-class lab and was very keen to join it! My luck was two-fold; financial support from the ENS for two years on the one hand, and on the other hand, the need for military reason to be studying abroad for 16 months under the condition that the lab would pay my salary. During the interview, I met my future PhD adviser, Dr. Gabriele Varani, who impressed me greatly with his enthusiasm. Although I had no guarantee that they would pay the 16 months, I still decided to join MRC-LMB in the Varani lab for my PhD. At that time, I also made the hard personal decision of going to the UK despite the fact that my girlfriend was staying in France to pursue her PhD. This was a very difficult decision to make, and the relationship did not survive past the first year of my PhD studies. Despite the fact that I really enjoyed my PhD at the LMB and published nine papers, which gave me a great start in the academic world, I did feel guilty about this personal decision. To the point that, three years later, I asked my "ex-girlfriend" if she would join me for a postdoc in the US. We then searched together and the choice of joining the lab of Prof. Juli Feigon at UCLA was partly motivated by the fact that Juli helped my "ex-girlfriend" find a postdoc in a neighboring lab. I do mention these personal issues to emphasize the difficulty of mixing the academic track with personal relationships. I should say that in the end, it did not work out better, as we never got back together as before, and we broke up a second time 7 months after starting our postdocs. Now, there were some advantages in what happened to me with these two "breakups", as they resulted, in both cases, with me working twice as much. Being single and living in a foreign country allowed me to focus and concentrate fully on my work. It was also a great motivation to succeed in science, as I was quite unfortunate with my personal life. In the end, the postdoc was also successful and I therefore quite naturally applied to faculty jobs in the US and in Europe. It did not work out the first year, and this is the reason why I decided to go for a second postdoc in the lab of Prof. Doug Black. There, I wanted to learn something different, i.e. alternative splicing in neurons, as my PhD and postdoc labs were both in the field of NMR of nucleic acids. Faculty job searches worked out better in the second year of applying, and I got several offers (two were tenured positions and one tenure-track from ETH). I went for the more risky one and joined the ETH Zurich as an assistant professor in 2001. I got tenured in 2007 and have been a full professor since 2010. I met my wife in 2001, in the first months of my arrival in Switzerland, and we have been living together since 2002. We have a daughter who was born in 2010, when I was 40 years old.

*"I must say that I was not very keen to have a female PI as PhD advisor. This shows that back in 1993 I had a 'stupid' prejudice against women in science."*

*Have you actually ever thought about yourself as a "man in science" as compared to "just" a scientist? If so, was it like this from the start of your scientific career, or did it come up later?*
Yes, of course. From the very beginning. I remember that when I heard I would meet with Gabriele Varani (Gab), I thought Gabriele was

a female PI, since "Gabrielle" in French is a female first name. I must say that I was not very keen to have a female PI as PhD advisor. This shows that back in 1993 I had a "stupid" prejudice against women in science. The lab I was working in at the time in Paris during my master in bioinorganic chemistry was dominated by male professors and had very few female scientists in the lead. Yet, all the PhD students were female. Anyway, I did accept the interview and found out that Gabriele was a man. However, when looking for a postdoc, I did not hesitate to apply to Juli Feigon, a female professor at UCLA. I must admit that the fact she was a female scientist was an element of my decision, along with the attraction of working in a great scientific environment. I was certainly keen to find out if there would be a difference in management compared to what I experienced during my PhD and Master. This was indeed a very different management. I think that, at times, I was emotionally closer to Juli than to Gab, but I was scientifically and intellectually closer to Gab. My lab management overall is inspired by both, as I try to be emotionally close to my coworkers while at the same time guiding them scientifically to the best of my ability. I think that working with PIs from both genders has been a plus.

*Did you ever consider leaving academia and if so what made you stay?*
I never considered this very seriously. Sometimes at home we joke about me doing another job, as mine is very absorbing, stressful, not always family-friendly and hard to share with family members. Nonetheless, this job offers the possibility to explore the unknown, it is full of surprises and we have a lot of freedom. I also greatly enjoy contributing to the development of my co-workers. I do not have much of an entrepreneurship drive and I am not after money, so the academic path suits me well.

> *"I do think that mentorship is crucial, as scientific mentors show you the path."*

*Did you/do you have mentors during your career? How crucial do you think is mentorship for the professional development in academia? Do you think mentorship for female scientists should differ from that for male scientists?*
I do think that mentorship is crucial, as scientific mentors show you the path. Of course, sometimes this is very stimulating and positive (my grandfather, Darchy or Gab), while others might show you a path that you should not follow (Juli at times). Feeling that your mentor "believes" in you is very important, but you will not go very far if in the first place you do not believe in yourself. It is interesting to see that in fact both aspects are rarely present simultaneously, me believing in them and them in themselves as well.

*What programs or events to which you have participated do you think have been most useful for your career progression?*
There are several. The first thing is meeting the right people, as discussed above. Attending meetings where you can orally present when you are a PhD student or a postdoc has been really important to me, as these meetings were a great motivation to work hard and collect enough material to compete with others and be selected for an oral presentation. In that context, the RNA society

> *"Sensitizing men to this effort is absolutely crucial."*

or the CSHL meetings are exemplary. As a PI, attending a course on lab management was very informative, not so much on the content of the course, but rather because it made me realize that when you start your lab, as much as you try to avoid conflicts, there will be problems with the lab members at one point or another.

*In your opinion do women in science need gender-specific events/awards? Why?*
It is a reality that an academic career in science is harder today for women than for men. This is just unacceptable and we should make sure to help women so that their chances are at least equal. The first thing is certainly to make women aware of the situation very early on (possibly already at high school level) and organizing events on this topic is essential. But men need to be educated, too, and they should help. Sensitizing men to this effort is absolutely crucial. My eight-year-old daughter told me recently that she did not want to be a boy because they are clearly less smart than the girls in her class. Clearly, both genders have the same intellectual capacity and it is a real tragedy that our system creates extra barriers for women. We need to remedy to this actively.

*What is your experience of balancing career and family and what are the challenges and benefits of "having it all"?*
I think this is a key question and this aspect is not so simple. As mentioned above, my rather unsuccessful personal life at the beginning of my scientific career turned up to be rather positive. My research project was the only positive aspect of my life at that time and this was almost a question of survival. Science is a creative process and suffering certainly favors creativity. Research in science is fascinating but is not made for people aiming at comfort. This is part of the dilemma we are facing between career and family. We seek comfort and stability to raise our children, but our work requires creativity that can often only be triggered by stress and instability. In conclusion, it is hard to "have it all".

*How do you handle the high demand for mobility in your career with having a family?*
Again, I come back to my story during the PhD and the postdoc. I already moved during my PhD studies and the consequence was an impaired relationship and a certain distance between me and my family in France. Yet, looking back, this move to the UK was certainly the most beneficial decision for my scientific career. I did sometimes regret it in the past and felt guilt, but for sure, I do not regret it today. I grew so much, scientifically and personally, by going to the UK, the US and now Switzerland, that I wish I could go somewhere again! I think the mobility should not be felt as a "must" but as an opportunity. Very few professions facilitate going abroad like ours does, so if you are moving, make the most of it! Of course, people with family restrictions should not be forced to move. The Americans or the British for example, do not go abroad as much, and yet there are still very good scientists around. In the end, what matters most is the quality of the scientific production, not where it was produced.

*Based on your professional experience so far and if you had one advice you could give your younger self what would this be?*
It is a really difficult question, because I am the sum of my experiences and I would be a different person if I had not lived through all these experiences. I realized that several of my career decisions were based on non-professional reasons and maybe this was not always reasonable. But from this I also learned a lot about myself and this was equally important. So in retrospect, I do not regret any period of my professional experience so far. One piece of advice I got from my stepmother Helen during my postdoc was "When life gives you lemons, make lemonade". This is key to progress.

**Is unconscious bias piercing the pipe?**

# How does implicit bias hinder career progression?

*Ana Claudia Marques*

**Why are women underrepresented in academic leadership roles (Figure 1)? And is there something we can do about it? A career in academia is an obstacle race and it's receivable that not everyone wishes work to spill over most aspects of their life, from how much time they have to accommodate family life or for their hobbies. But why are women more likely than men to change career after completing a PhD and spending a few years as a post-doc? Research done to address this question suggests women have a few more hurdles than men to remain competitive in the academic career race.**

One of the most obvious hindrances to women's career progression is the "baby penalty". While men are increasingly implicated in childcare, the decision to start a family still has a larger impact in women's careers, because of the time spent away from the lab in late pregnancy and after giving birth. In another article in this newsletter we discuss the aims and initial results of a measure the NCCR implemented to minimize the impact of pregnancy and maternity on female trainees' career progression. While we believe this measure will alleviate part of the strain on women, we are convinced that by itself this measure will not be sufficient to repair the leaks in the pipe.

Why do we think that? A number of other measures to minimize the baby penalty, for example extended eligibility criteria or reentry fellowships for women, have been in place for a few years now and their impact on women career progression in academia has is so far limited (Figure 1). So what else drives women's decision to leave academia? A recent survey carried out by Nature may provide some clues (Nature 562, 611-614 (2018)). When questioned about different aspects of their job, women consistently reported being less satisfied (on average 5%) than men. A fifth of the individuals responding to this survey claimed having experienced some kind of discrimination, the most prevalent type being gender discrimination (40%), which seemed to affect more generally women than men (91% of respondents). While other types of discrimination (age or race, for example), which are unfortunately present in academic research as well, can also slow down an individual's career progression and the overall diversity of research teams and leadership, the focus of this article is gender bias. Why? Gender bias is the most prevalent type of bias and is among the easiest to quantify. Importantly, the general mechanisms underlying gender biases and how to minimize their impact are generally applicable to all types of discrimination, making it a good test case.

It is hard to understand why women feel discriminated in a society where they can virtually access all jobs. This is even more puzzling in an academic environment where the criteria for career progression are said to be clear. But the survey in Nature (Nature 562, 611–614 (2018)) and other surveys indicate they do. Why? One possible explanation comes from a body of research on gender and career. Most of these studies suggest women may have to jump some extra hurdles to succeed, which probably contributes to fatigue and an increased rate of abandon.

These extra hurdles are there from the start of the race. For example, in life sciences a white male candidate is 9% more likely to receive a response to his spontaneous application than a female candidate (J. of Applied Psychology 100(6), 1678–1712 (2015)). And US elite biology male faculty members hire 11% fewer female graduates students and 22% fewer female postdocs (PNAS, 111(28), 10107–10112 (2014)). This may in part be due to the moderately lower competency rating a female is likely to get compared to a male with an identical CV (PNAS 109(41), 16474–16479 (2012)). Perhaps surprisingly, women are as likely as men to take gender-biased decisions (PNAS 109(41), 16474–16479 (2012)).

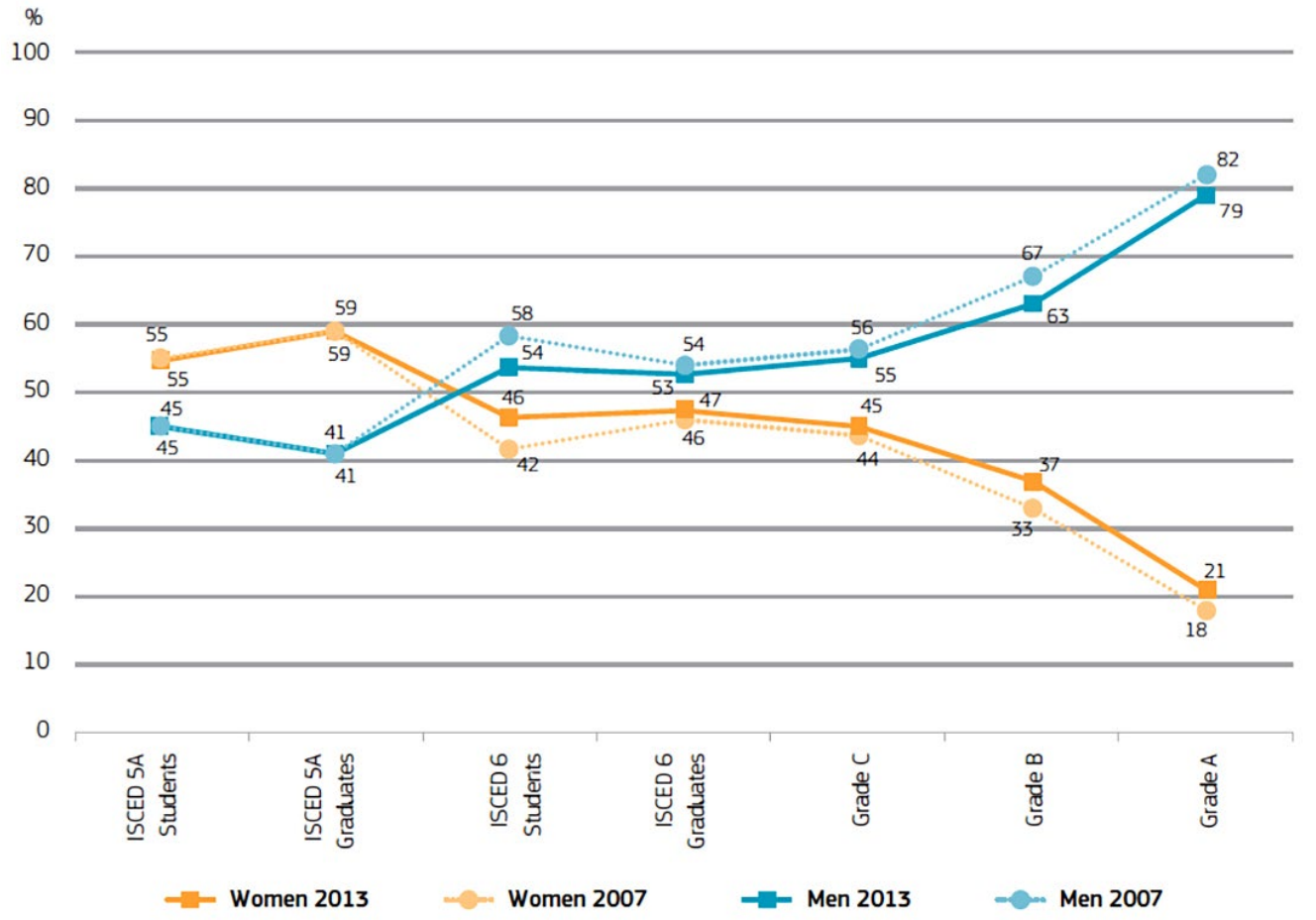
A stellar publication track record will take you a long way into landing that faculty job. But authors are not equal in the eye of co-authors, reviewers and editors, which likely contributes to the relatively fewer than expected women with first author papers in top journals. For example while 40% of postdocs in neurosciences are women, only 25% of papers in top journals in this field have female first authors (bioRxiv, doi: https://doi.org/10.1101/275362). Is it that women work less hard? An analysis of papers where the first authorship was shared between a man and a woman uncovered that males were 6% more likely to be listed first. This indicates that women get less credit for their contributions on publications (bioRxiv, doi: https://doi.org/10.1101/241554), something that has been suggested by other studies. The likelihood of getting a paper accepted if the first or last author is a male or a female is also not equal. In the fields of Evolutionary Biology and Ecology, introduction of double blind peer review led to an over 7% increase in acceptance rates of female first author papers (Trends Ecol. Evol. 23(1), 4–6 (2008)). A recent study analyzing review reports from eLife indicates that if the last author of the paper is a woman, there is a 3% lower chance of the manuscript being accepted for publication (bioRxiv, doi: https://doi.org/10.1101/400515).

When applying for funding, women also appear to be penalized. After accounting for h-index, funding history and other confounders, Tamblyn and colleagues (CAMJ, 190(16), E489–E499 (2018)) found that women received lower grant scores than men. The authors of this study suggest that the lower scores may be linked to women generally being perceived as less competent, having weaker leadership skills, and that evaluation criteria may favor male stereotypes.

The effect size of this bias, as that of all the others, is low. However, based on simulations a 4% bias in grant assessment leads to 20% lower grant success (Research Policy, 44(6), 1266–1270 (2015)), which will ultimately have a strong impact on the research led by women.

Given that careers in science are built on track record, even if these different biases have relatively moderate effect sizes, they seriously contribute to our inability to retain women in academia. Biases on the perceived contribution of women to projects, fewer opportunities to engage collaborators/mentors/sponsors, lower publication acceptance rates and fewer grants all contribute to decreased job satisfaction of women that eventually leads, in some cases, to a decision to change career path. Given the recognized contribution of diversity to increased performance on a variety of tasks/challenges, the leaks in the pipe not only impact the lives of women but also the potential of future scientific developments.

**Is unconscious bias piercing the pipe?**




Notes: Reference years Eurostat data: 2007–2012; Reference years for Women in Science (WIS) data: 2007–2013; Exceptions to the reference years (WIS): AT: 2007–2011; BE (FR), LV, RO: 2010–2013; CY, PT: 2007–2012; DK, LU (Grade A and B, C not available): 2009–2013; ES, IE: 2008–2012; BE (FL), NL, FI: 2011–2013; PL, SK: 2012–2013; FR: 2012; HR: 2014; MT: 2015; EE: 2004 (She Figures 2012); LT: 2007 (She Figures 2012); UK: 2006 (She Figures 2012); Data unavailable for: (Eurostat) ISCED 5A Students: LU (2007); ISCED 5A Graduates: FR (2012), LU (2007); ISCED 6 Students: DE (2007), LU (2007); ISCED 6 Graduates: FR (2012), LU (2007).

**Source: Women in Science database, DG Research and Innovation and Eurostat – Education Statistics (online data code: educ_grad5)**

*Figure 1: Proportion of women and men in a typical academic career (http://ec.europa.eu/research/swafs/pdf/pub_gender_equality/she_figures_2015-final.pdf)*

In the vast majority of cases, the biases described here do not reflect conscious decisions to hinder the career of women. Instead, many of these extra hurdles are a consequence of unconscious biases. As scientists, we rely daily on our logic and rational thinking to solve complex problems, and it is thus reasonable to believe such irrational behavior would not affect our daily professional interactions. However, most of the studies described here analyzed the behavior of individuals that like us work in life science research. Furthermore, a number of legal complaints of gender discrimination deposited by women at top institutions (for example at the Salk Institute) suggest that unconscious biases are prevalent in academic research.

So how can we address these biases and fix the pipe? Probably the simplest and most important step is to become aware of our biases and how they impact our professional interactions. Test your implicit biases (https://implicit.harvard.edu/implicit/) and talk openly about the topic with colleagues. Another factor that will reduce such biases is critical mass. When diversity is the norm, such biases are diluted. Increased diversity at higher ranks in academia ultimately relies on unbiased recruiting procedures. Besides specific training of search committee members on implicit bias, discussing the job profile early, deciding what are the hiring criteria and defining the questions that allow to asses these criteria in a concrete manner, minimizes the impact of bias in hiring and leads to more diverse appointments (BioScience, 65(11), 1084–1087 (2015)).

Because we recognize the impact of unconscious bias on diversity, we have made this topic a central point of the NCCR RNA & Disease Equal Opportunities strategy for phase 2. We have already started to engage in training opportunities (refer to our meeting report) and we will organize training events tailored for NCCR trainees and PIs during phase 2.

We believe that addressing the impact of implicit bias on women's job satisfaction and career progression is as important as tackling other perhaps more tangible hurdles, such as the baby penalty. We expect that this multifactorial equal opportunities strategy will contribute to increased overall job satisfaction across the network and at our scale help fix some of the leaks in the pipe.

**Lessons learned from the pioneers of the "Pregnancy and Maternity leave compensation" scheme**

# Bridging parental leave in an academic environment

*Larissa Grolimund, Frédéric Allain and Ana Claudia Marques*

**A successful career in academia is an obstacle marathon. Becoming a parent impacts everyone's performance but particularly for women, who need to be away from the lab to take care of a new child, the impact on career progression is more substantial. Taking a baby break during a PhD or postdoc feels like stepping out of the track while already seeing the finishing line and when everyone else is still running. After a maternity leave, new mothers need to quickly regain speed and catch up with their competitors in order to stay in the race.**

Most funding agencies and institutions recognize the negative impact of maternity in women's career progression and most funding schemes now extend eligibility to account for career breaks. What most schemes fail to address, though, is the appreciable setback of the progression of the research project due to health and safety issues during pregnancy, as well as the frequently complete discontinuation of the project when the scientist is on maternity leave. In a research environment, where competition is fierce and speed is critical, the delays caused by maternity represent a serious burden to women's career development. To minimize the negative impact of pregnancy and maternity leave on project progression, the NCCR RNA & Disease offers a Pregnancy and Maternity Leave Compensation support for PhD students and postdocs (PMLC). This scheme allows grantees (with the support of their host PI) to request funding to cover the salary of one research assistant during the last 3 months of pregnancy. During this period mum-to-be and research assistant will overlap, which should ensure appropriate training of the research assistant who will then continue the project of the expectant researcher during the duration of her maternity leave. The support scheme helps managing the research project during maternity leave, prevents its complete interruption and promotes a smooth re-entry after the baby break (Figure 2). These factors are also all highly beneficial for the supervisor of the expectant researcher whose interests lie in supporting the careers of his/her young academics and generating continuous scientific output on a competitive level. This scheme also offers the expectant an opportunity to build her personnel and project management skills, which will be useful for those aiming a career in academia. The PMLC fills a gap for which no other support scheme exists so far. Moreover, it is an ideal extension of the Flexibility Grant offered by the SNSF (Swiss National Science Foundation), which is currently only available to postdoctoral fellows with respect to the employment of a support person.

Since its implementation in June 2016, the NCCR RNA & Disease has issued three PMLC grants to scientists of the network. The

*"This has kept the project advancing during several months when the work would otherwise have been stopped."*

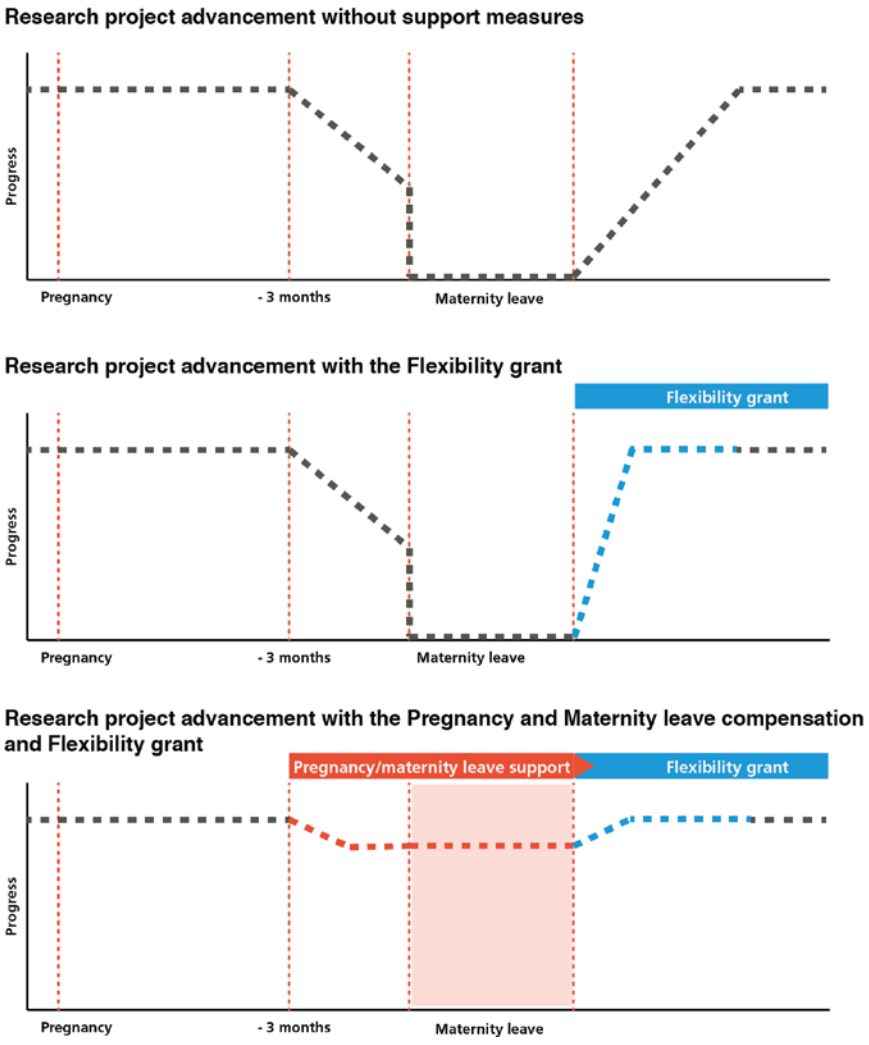



*Figure 2: Pregnancy and maternity impact career progression.*

**Lessons learned from the pioneers of the "Pregnancy and Maternity leave compensation" scheme**

*"Thanks to the NCCR and my supervisor with his modern attitude I was not obliged to interrupt or abort my PhD."*

first three grantees have highly appreciated the unique benefits associated with this support scheme. The temporal overlap between the grantee and the research assistant towards the final phase of the pregnancy has been judged as extremely valuable for training and knowledge transfer. In most cases, the set goals for the duration of the grant were met and, most importantly, all projects progressed during the maternity leave, thus fulfilling the main aim of this scheme. The grantees underlined the importance of support by their supervisor and a good information exchange during maternity leave. The commitment of the supervisor is crucial in order to be eligible for the PMLC, as the freed funds released through the maternity allowance will be invested to cover the salary costs of the support person during the grantee's maternity leave. Identifying a suitable support person for such a short-term position has been described as the most challenging aspect related to the grant. The fact that the first three recipients of the PMLC grants were all PhD students at the time of application, indicates the need for such support measures at all levels of an academic career. Therefore, we have voiced our interests towards the SNSF Directorate for making the Flexibility Grant fully accessible also to PhD students.

*"I consider myself very privileged that I could benefit, because such resources are still not a normal standard in Switzerland and the NCCR sets a great example."*

The possibility of employing a support person continuously from the pregnancy, throughout the maternity leave, and upon return, will not only allow projects to advance despite motherhood, but also improve work-life balance and, in addition, render the position more attractive for the research assistant.

Notably, one of the grantees has meanwhile crossed the marathons finishing line and successfully defended her PhD thesis, for which we congratulate her. We will continue to evaluate the impact of the PMLC grant by monitoring the career path of all past and future grantees.

*"The overlapping time in the end of the pregnancy is really important to explain the project in detail and to teach the most used methods in the lab."*

Maximum benefit at no additional expenses: This support can come at no additional financial costs for the recipient's supervisor. The NCCR RNA & Disease covers the salary of a support person during the last three months of a grantee's pregnancy up to a 100% of work-time percentage (max. CHF 20'000.–) while the supervisor commits

*"It kept the project moving forward without interruptions. It is a great scheme which helps both the student and the supervisor"*

to use the freed funds released through the maternity allowance to employ the support person on the recipient's project during her maternity leave. The supervisor may use additional funds to increase the work-time percentage of the support person during maternity leave in case the freed funds do not cover the salary of a full-time employment.

You can find more information on the Pregnancy and Maternity Leave Compensation and the Flexibility Grant on our Equal Opportunities website.

*"I think this is real support for women and definitely helps my professional career and future."*

**STEMM Equality Congress 2018**

# International exchange of strategies – Lessons learned

*Larissa Grolimund and Frédéric Allain*

**The underrepresentation of women in leading science positions has been recognized decades ago and is a globally discussed issue. Organizations, institutions and commissions have implemented numerous measures targeting the gender gap. Nevertheless, the progress in reaching a gender balance at the top level has been very slow and the issue seems persistent. At this year's STEMM Equality Congress hosted by Science Impact Ltd in Amsterdam, Netherlands, on October 11th–12th, the NCCR RNA & Disease presented its equal opportunities action plan and exchanged strategies with researchers, policy makers, NGOs, academic staff and government representatives from all over the world.**

This annually held meeting focuses on the discussion of equality, diversity and inclusion strategies in the fields of **S**cience, **T**echnology, **E**ngineering, **M**athematics and **M**edicine (STEMM). Although this year's topic was dedicated to intersectionality, the predominant and recurring theme throughout the presentations and discussions remained gender inequality in STEMM. The two-day meeting, to which over 280 participants from 28 countries attended, consisted of keynote speeches, panel sessions, workshops and poster presentations (View our Poster). The speakers presented examples and best practice of equality and diversity policy implementation with regard to leadership, as well as how to integrate equality in an organization and promote a change of culture. Some of the presented studies provided rather sobering facts and data on inequality such as, for example, how prejudices negatively affect recruitment and peer-review processes (PNAS 109, 16474-9 (2012), Nature 387, 341-3 (1997)) or nominations for prizes. Others delivered evidence-based suggestions on how to promote a change. These include the need for scientific research on existing measures (such as for example on the controversially discussed affirmative action, Science 335, 579-82 (2012)) and to act accordingly. A series of talks broached the importance of engaging male leaders as advocates for gender equality. As men fill most leading positions, they have the best prerequisites to impact cultural and structural changes. After all, the disadvantages related to women's underrepresentation and the associated loss of diversity affects all genders. Promoting inclusion and diversity by structural and organizational changes was discussed in various contexts. A very radical but effective example for a promoter to a systemic change was given by linking governmental research funding in the United Kingdom to the institution's commitment to equality recognized through an award (Athena SWAN awards).

The lessons learned from our experience at the STEMM Equality Congress include the importance of carefully studying the impact of equality initiatives in order to effectively apply them, the engagement of power players, and importantly men, in promoting a systemic change of culture, as well as the benefits of exchanging best practice and experiences with other organizations, which ultimately face similar challenges with regards to closing the gender gap.

**Role models and mentoring**

# Inspiration by role models

In the context of the NCCR seminar series, we regularly organize female scientist lunches with women speakers to provide junior women scientists the opportunities to meet outstanding and inspiring female researchers. Attendees evaluate this initiative very positively. The latest female scientists lunches took place in Bern and Zurich on December 3rd and 4th with Prof Dr. Marina Rodnina (Max Planck Institute for Biophysical Chemistry, Göttingen, Germany).

Visit our Webpage to find out more about the NCCR RNA & Disease seminar series. If you are interested in attending a lunch with a speaker, please contact the NCCR office (office@nccr-rna-and-disease.ch) at the latest one week before the seminar.

*Attendees of the lunch for female scientists with Marina Rodnina (5th from left) in Bern on December 3rd.*

# Research highlights from NCCR laboratories

Roland Fischer

## Too much Stress and Pressure

**Some people with amyotrophic lateral sclerosis or frontotemporal dementia accumulate deposits of the nuclear protein FUS in the cytoplasm. What drives this relocation? Researchers led by Magdalini Polymenidou at the University of Zurich blame osmotic pressure.**

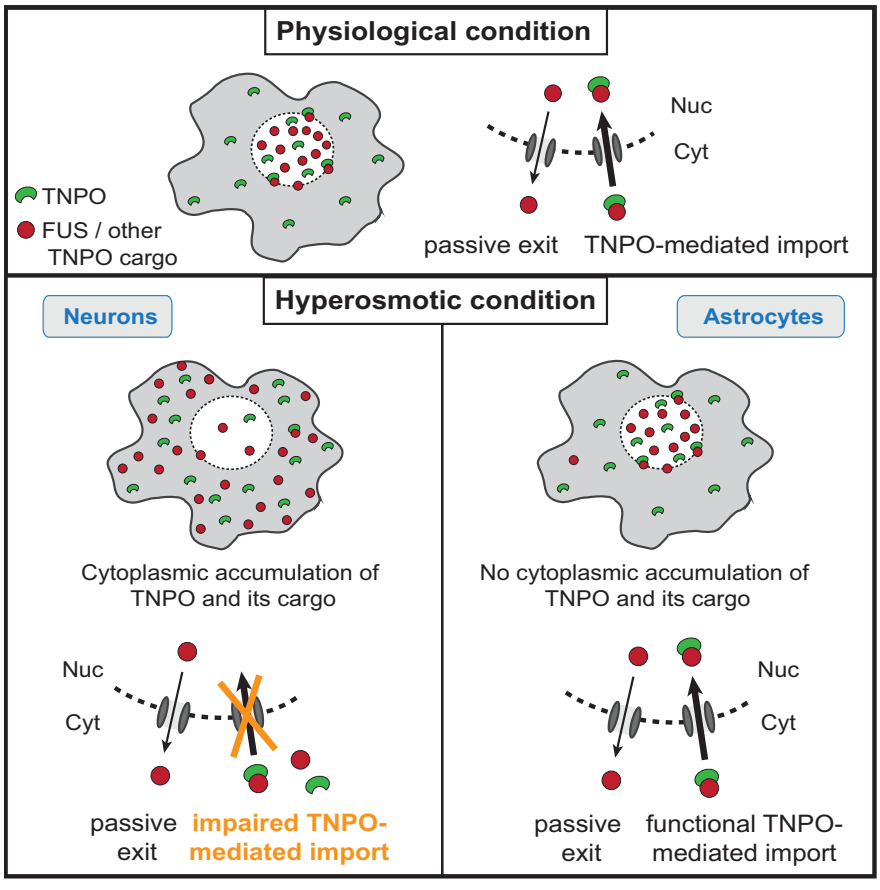
UniProt is a bit vague when it comes to the RNA-binding protein FUS: "May play a role in maintenance of genomic integrity." What is certain: In healthy cells, FUS is transported to the nucleus and binds to both DNA and RNA, mediating the synthesis of a whole range of proteins. But in ALS and frontotemporal dementia – a common dementia – the entry of FUS into the nucleus of nerve cells is compromised. Aggregates of FUS and RNA transform into so-called stress granules. The role of these granules in the pathological process is still unclear.

Frontotemporal dementia is the second most common type of dementia after Alzheimer's disease and typically affects individuals under 65 years of age. In a subset of these patients, affected neurons present a characteristic pathology with cytoplasmic mislocalization and aggregation of the RNA-binding protein FUS, which normally resides in the nucleus. Since no mutations in FUS or any other proteins have been described in these cases, the trigger of FUS mislocalization that likely initiates the cascade of events leading to neuronal dysfunction and death remains enigmatic.

The new study by the Polymenidou group, published in Cell Reports, shows that hypertonic stress leads to cytoplasmic translocation and loss-of-function of neuronal FUS. Surprisingly, and opposite to current thinking, the osmosis-triggered cytoplasmic shift of FUS is independent of stress granule formation or the molecular pathways induced by hyperosmolarity in cells.

FUS mislocalization could be the first step toward disease, Polymenidou suggested. She believes osmotic stress acts as the trigger that sends FUS to the wrong place, where a second stressor could then cause it to aggregate. An important implication of the work for public health is the fact that hyperosmolar therapy, which is the method of choice for release of inter-cranial pressure after brain trauma, may trigger the initial events that lead to FTD. Indeed, a strong association between brain trauma and FTD has been described in the past years by several groups, but no mechanism that could explain this association has been described to date. It is also known that hyperosmolarity can trigger the release of proinflammatory cytokines. Inflammation is a known risk factor for many neurodegenerative diseases.

Hock et al., (2018) Cell Reports 24, 987–1000



Research highlights

## Ribosomal proteins taking over

**In a recently published Science paper, David J. F. Ramrath and Moritz Niemann from the Ban and Schneider groups shed light on the evolutionary shift toward protein-based architecture in trypanosomal mitochondrial ribosomes.**

Mitochondrial ribosomes (mitoribosomes) are more closely related to bacterial ribosomes than to eukaryotic cytosolic ribosomes. However, they have undergone extensive structural and compositional change throughout evolutionary time. Most notably, mitoribosomes have acquired a large number of mitochondrial-specific ribosomal proteins, and the mitoribosomal RNA has been shortened in many organisms, including mammals, but most extensively in *Trypanosoma brucei*, the parasite that causes sleeping sickness.

Because mitoribosomes are conserved to a high degree, the observed variability is of particular interest, especially in extreme cases as *T. brucei*. In these mitoribosomes featuring the smallest known rRNAs, the severe rRNA reduction is accompanied by the recruitment of many additional proteins. Trypanosomal mitoribosomes therefore represent an excellent system to reveal the minimal set of rRNA and protein elements essential for ribosomal function and to investigate how ribosomal proteins compensated for the missing rRNA.

To address these questions, the Ban and Schneider groups determined the atomic structure of the mitoribosome from T. brucei using cryo–electron microscopy. The structure shows how the proteins have taken over the role of architectural scaffold from the rRNA: They form anautonomous outer shell that surrounds the entire particle and stabilizes the functionally important regions of the rRNA. The paper reveals the "minimal" set of conserved rRNA and protein components shared by all ribosomes, which will help define the most essential functional elements.

The trypanosomal translational machinery adopted unusual solutions to accomplish some basic protein synthesis mechanisms. Notably, the structure unveils two intriguing functional details: Their nascent polypeptide exit tunnel branches into two exits – it is conceivable that nascent proteins with different characteristics take different paths. Furthermore, in a subpopulation of isolated small-subunit particles, mitochondrial initiation factor 3 was observed interacting with the decoding center via its unique C-terminal extension. This might compensate for the essential function of initiation factor 1 that is absent in all mitochondria.

Ramrath and Niemann et.al., (2018) Science 362, eaau7735

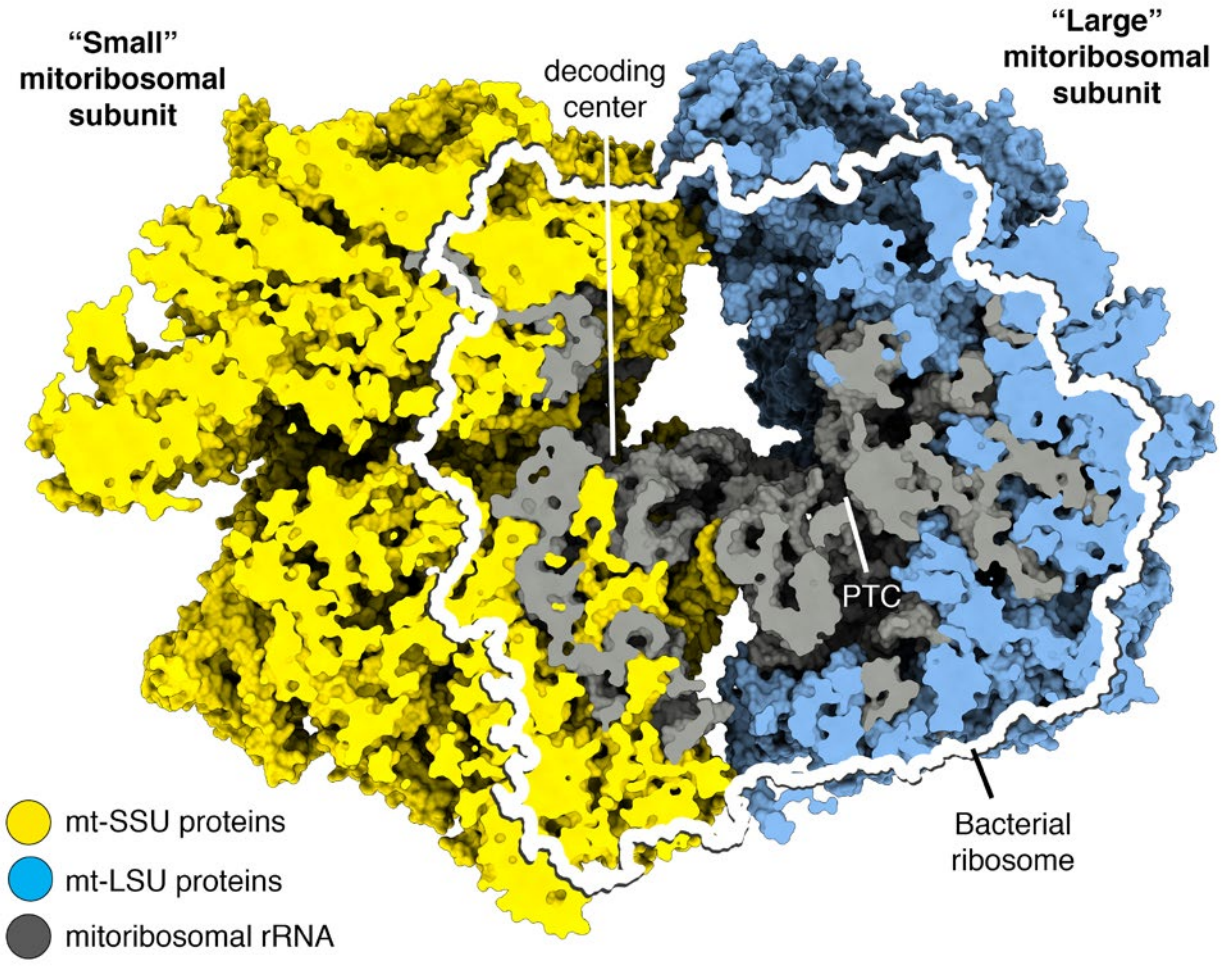



*Image kindly provided by David Ramrath*

**Research highlights**

## If it's complex, it's possibly quadruplex

'If G-quadruplexes form so readily in vitro, Nature will have found a way of using them in vivo', said Nobel prize winner Aaron Klug already some decades ago. The Hall group from the Institute of Pharmaceutical Sciences at ETH Zurich has now clarified one of these functions: the control of the polyamine biosynthesis pathway by G2-quadruplexes.

G-quadruplexes are naturally-occurring structures found in RNAs and DNAs. Over the past two decades biologists and bioinformaticians have unearthed substantial evidence for G-quadruplexes as important mediators of biological processes. This includes telomere damage signaling, transcriptional activity, and splicing. Although their structures are difficult to characterize in vivo, G-quadruplexes are recognized as important elements regulating gene expression, and they are increasingly linked to diseases. As in DNA, regular RNA G-quadruplexes have shown to be highly stable due to stacked planar arrangements connected by short loops. More interestingly still, reports of irregular quadruplex structures are increasing and recent genome-wide studies suggest that they influence gene expression. Thousands of such motifs have been identified, the majority of which comprised canonical short-looped G3-tracts (G3-quadruplexes). Stable G3-quadruplexes (i.e. strong enough to stall reverse transcriptase) in eukaryotic cells have been shown to be frequently unwound; so the physiological relevance of quadruplex structures should not be automatically inferred from their stability. Consistent with this, several hundred putative metastable RNA G2-quadruplexes have also been predicted throughout the transcriptome. So far, few G2-quadruplexes have been studied in detail biophysically, structurally and functionally.

As reported in the open-access journal eLife, the Hall group has investigated a grouping of G2-motifs in the untranslated regions (UTRs) of eight genes involved in polyamine biosynthesis, and concluded that several likely form novel metastable RNA G-quadruplexes. They performed biophysical characterizations of their properties, comparing them to a reference G-quadruplex and discovered how some of these motifs are able to regulate and sense polyamine levels, creating feedback loops during polyamine biosynthesis. With the key help from the Allain group, the team demonstrated using NMR spectroscopy that one particular long-looped quadruplex in the AZIN1 mRNA co-exists in salt-dependent equilibria with a hairpin structure.

The group identified 35 putative G2-tract quadruplex structures in the 5' and 3' UTRs of genes in the polyamine (PA) biosynthesis pathway. Using cellular reporter assays they could identify twelve of these covering eight PA synthesis proteins that altered reporter activity in comparison to mutants. Strikingly, most of these structures had the effect to reduce PA levels. This suggested they might act in unison as regulatory elements to control PA homoeostasis.

The study thus expands the repertoire of regulatory G-quadruplexes and demonstrates how they act in unison to control metabolite homeostasis. More specifically, the group's findings reveal a previously unrecognized mechanism of PA self-regulation. They expect that such mechanisms through G-quadruplexes may be a common feature in other metabolic pathways.

Lightfoot et al., (2018) eLife 7:e36362.

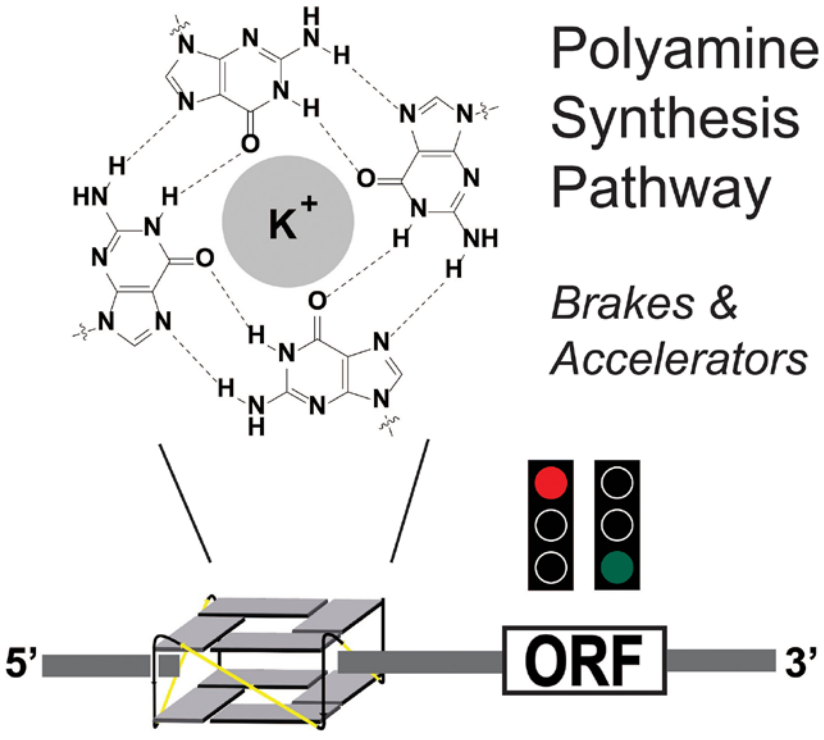



*Image kindly provided by Timo Hagen*

**Announcements**

## People

We congratulate Michael Hall on receiving the 2019 Charles Rodolphe Brupbacher Award for Cancer Research.

Congratulations to Martin Jinek and Lukas Jeker for being awarded an ERC Consolidator Grants.

We would like to welcome Francesco Bertoni, who is a group leader at the Institute of Oncology Research (IOR), Bellinzona as a new associate member of the NCCR RNA & Disease. His group researches the genomics of lymphomas.

## Support Grants

Please visit our webpage for more information on the Lab exchange program, the Doctoral mobility grant and measures in equal opportunities.

## Swiss RNA Workshop

The 20th edition of the Swiss RNA Workshop will take place on January 25, 2019, in Bern. Keynotes will be given by Eric Miska (Gurdon Institute, University of Cambridge, United Kingdom) and Alena Shkumatava (Curie Institute, Paris, France). Registration and abstract submission is closed.

Visit the workshop's website for more information.

## Upcoming events organized or supported by the NCCR RNA & Disease

> NCCR Seminar Series:
**Jennifer Doudna** (University of California, Berkeley, USA) March 3, University of Bern & March 4, 2019, ETH Zurich
**Alexander Mankin** (University of Illinois, Chicago, USA) March 18, University of Bern & March 19, 2019, ETH Zurich
**Reinhard Lührmann** (Max Planck Institute for Biophysical Chemistry, Göttingen, Germany) April 1, University of Bern & April 2, 2019, ETH Zurich
**Michaela Frye** (University of Cambridge, Cambridge, UK) May 13, University of Bern & May 14, 2019, ETH Zurich

**3rd NCCR RNA & Disease summer school** "RNA Regulation in Health and Disease: Genome architecture and gene expression – RNA turnover – Epitranscriptomics – Phase separation", August 26 – 30, 2019, Saas-Fee (Registration opens soon)

**Special NCCR TransCure and RNA & Disease Seminar**
**Gail Robertson** (Dept. of Neuroscience, University of Wisconsin, USA) January 14, 2019 University of Bern, EG 16, 16.30–17.30

## NCCR RNA & Disease Internal Events

> Joint retreat with the with the Vienna RNA research community, January 30 – February 3, 2019, Fuschlsee, Austria
> NCCR RNA & Disease "Séance de Réflexion", March 15, 2019, Haus der Universität, Bern

## Jobs

**PhD program in RNA Biology**
The next application deadline is July 1, 2019.
Find out more on the PhD program website

Update links

Postdoctoral Position – circadian clocks & RNA biology – Gatfield lab University of Lausanne

PhD and Postdoc Positions – Gene Regulation by RNA modifications – Pillai Lab, University of Geneva

Check the jobs's section of the NCCR RNA & Disease webpage for other openings.

**IMPRINT**

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