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CELL SCIENTISTS TO WATCH

Cell scientist to watch – Dana Branzei

Originally from Iaşi, Romania, Dana received her bachelor's degree in pharmaceutical sciences and a master's degree in molecular and cellular biology from Tohoku University in Sendai, Japan. For her PhD, she joined the lab of Takemi Enomoto to work on DNA replication and recombination in yeast. After a short postdoc with Kunihiro Ohta at the RIKEN laboratory in Wako, Dana took a position as a staff scientist with Marco Foiani at the Institute of Molecular Oncology Foundation (IFOM) in Milan, Italy. There, she became a junior group leader in 2008 and tenured principal investigator in 2013. Dana was elected a member of EMBO in 2016 and has been the recipient of both a European Research Council (ERC) starting grant and an ERC consolidator grant. Her lab is interested in the mechanistic interplay of DNA damage response and regulatory pathways of chromosome structure during replication.

Dana Branzei

What inspired you to become a scientist?

Nature has always been a source of inspiration to me. I was interested in finding principles that govern life and I guess I could have followed different paths in science. I loved chemistry when I was in school, and I loved thinking about how a reaction would take place. But later on, I discovered that biology was even more interesting; to me, it was chemistry at a different level and now I was interested not just in making reactions happen, but in uncovering basic mechanisms that happen inside cells. It was a very natural transition – I always just followed my heart.

For your graduate studies and PhD, you moved from Romania to Japan. How did this come about?

When I was in high school in Romania, I learned about the opportunity to study in Japan. I was reading Japanese literature at that time and I was fascinated with the Japanese approach to life; they seem to respect nature and wonder about the universe in a way that westerners really have forgotten about. Now, as a scientist, I want to know how science works, but as a human being, I'm interested in understanding the meaning of our fleeting existence in this dynamic universe. I thought that Japan was a curious mix of an ancient culture and curiosity towards innovation and technology. The Japanese attitude towards approaching life and the tasks at hand was somehow similar to my own; I thought it would be an interesting challenge for me to live in their environment and to experience Japanese standards for a while.

How were the first months as a student in Japan?

It was very frightening and challenging at the beginning and, to be honest, I really considered giving up. We had about one year to learn the language in an intensive language school, but that was not really enough to be a good student at university. The Japanese taught in class did not allow us to read the text books with reasonable speed and to really understand what was going on in class. Therefore, the first semester was daunting and I wasn't happy. With half of my heart prepared to give up, I still decided to give it a completely new, fresh try and it worked – I do not know how or why. Also, after the first 18 months, I took my first holiday to go back to my country; when I came back, everything seemed much easier. I do not really have an explanation for this; I guess there is no elevator to success, one really has to take the stairs. Maybe it was the change in my attitude that really made a huge difference – I did not care anymore about being perfect. I just tried my best and did not worry about what other people would think or if my parents would be disappointed with my decision. That really helped me a lot and things worked out very well in the end.

What motivates you now?

A passion for science, first and foremost. It is fascinating to uncover the principles that govern life. I think that the more I understand about what I'm working on, I also comprehend better our place in the universe. I feel we are all a part of something really big, and we all can give our own contribution; for me this contribution is through my science.

> "…there is no elevator to success, one really has to take the stairs."

What questions are your lab trying to answer just now?

We have a long-standing interest in DNA damage tolerance principles and mechanisms. DNA damage tolerance pathways (DDTs) are the first line of defence when replication forks encounter DNA lesions, which cannot be repaired when contained within single-stranded DNA, and thus need to be bypassed. DDTs allow this bypass to take place, but they are not canonical repair pathways. Bypassing the lesions prevents extremely deleterious replication

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fork breakage, but in doing so, mutations or genomic aberrations might be introduced. DDTs are thus very important in promoting replication completion and allowing proliferation, but at the same time they can also be extremely error-prone. Now, the timing by which these DDTs are being activated is also important in deciding whether they are error-prone or error-free, but little is known about the principles that coordinate the DDT pathway choice. We want to understand how this DDT choice takes place and at what point these pathways become aberrant. In the process, we also realised that SUMOylation is very important in response to genotoxic stress; therefore, another line of research in my lab is trying to understand more about the SUMO-orchestrated events in the replication stress response. This does not only apply to DNA damage tolerance, but also different types of replication stress or even replication initiation itself. We also pursue how chromosome structure and DNA repair defects might arise in response to replication stress.

What has been the most influential publication or work in your field recently?

There are many, but I will mention one that broadened the research directions in my lab. In 2010, a paper came out from the lab of Johan de Winter on a new human genetic disorder showing co-existence between DNA repair and chromosome cohesion defects. Of course, sister chromatid cohesion is important for homologous recombination repair and the genetic disorder class of cohesinopathies was known; but the unique phenotype of DNA repair, homologous recombination repair and cohesion defects attracted me a lot and I wanted to know more about how these processes are interrelated or co-evolving. We realised that things are not as simple as people usually think; for sister chromatid cohesion to take place, it needs a protein complex called cohesin that is essential to tether sister chromatids. There are a number of other factors associated with the replisome that are important to cohesion as well. Now, people always tried to look at how these replisome-associated factors affect the loading of cohesin or if they interact with cohesion, but actually, a few years ago in my lab, we found that cohesin and replisome-associated cohesion factors affect DNA damage tolerance in similar ways, but by profoundly different mechanisms.

What challenges did you face when starting your own lab that you didn't expect?

I did not really assume anything about what this transition would be like, so I would be ready for challenges. However, a difficult part was to keep up with the various duties I had. Another challenging, and maybe sometimes disappointing, part was the fact that I had difficulties in getting work published in high-impact journals. We had several very good papers and obviously I was the same person writing the papers as I had done as a postdoc or staff scientist, but it was much, much harder to publish as a new group leader.

How are the challenges that you're facing now different?

I have to keep up with multiple research projects that are running in the lab and I also want to broaden our expertise. This requires a lot of learning and networking as well, so perhaps this is the most difficult part apart from publishing and securing funding. Also, building a good team is always a challenge; I keep learning how to be a good mentor and leader, how to motivate people, and how to get them to be self-motivated along the way.

What is the most important advice you would give to someone about to start their own lab?

I think nothing of value can be achieved without working hard and doing your best. Our reputation precedes us; we must care about publishing good work – no matter the journal it is published in – and the published work must be correct and represent us well. As a scientist, it's key to uncover new knowledge. This novelty might be very important one day in the large scheme of things, even if we do not realise how important certain things are when we are at the beginning. I always listen to my inner voice of interest and I think this is what science is about. We are not rock stars, we do not have to be acclaimed by the whole world – we just need to be humble, to show up and do our work.

What is the best science-related advice you ever received?

To be humble is advice that I received from members of my family and from people I respect. In fact, it is something that empowers me a lot with gratitude and kindness and it allows me to see that we just need to play our part. If you want to come to the lab and discover something great, it's very likely you will fail. But if you come to do your part of the work, the best you can, and follow your curiosity with passion and leadership, you are going to end up with things that are gratifying and also allow you to simply enjoy the process.

How do you achieve a work–life balance when you're trying to establish yourself as an independent investigator?

When I started the lab, I was worried about my results getting published, so it was work and work and work. There was no balance, but this does not mean that I felt out of balance. Work can be very energising, at least for me, even if it's hard work. The problem is that if we do not care about our personal needs, we can feel imbalanced. When I feel tired, I will take time for myself – take some walks in nature, read some books; these are activities that have always been very energising for me. But, in the end, work has been the largest part of my life and I guess it will continue to be.

"We are not rock stars, we do not have to be acclaimed by the whole world – we just need to be humble, to show up and do our work."

What is your advice on establishing good collaborations?

Collaborations can take more time than you initially gauge, so it's not just about doing two or three experiments and describing the experiments to your collaborators, but thinking of the whole data and discussing the broad meaning of the results. So it's a lot of learning; it's also an opportunity for those people to get to know you better and to know that you're doing excellent work. But at the same time, one has to be very careful in choosing the people to collaborate with and choosing topics that will extend your vision, but will not compete with what you are already doing.

How do you get the most out of the meetings you attend, particularly in the early stages of your career?

I was very lucky because early on I had the opportunity to replace the director of the institute to give talks at big meetings; this helped me become visible at an early stage. Also, I was advised to be very open and present new stories at conferences, which I did. It helps, but it is very risky and I am more careful now. I'm still open to people I know about sharing ideas, but one has to be more cautious towards a very broad public. I think that giving talks is essential – but early on in my career I hadn't realised how

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‘Life Spikes’ by Dana Branzei (September, 2016)

I have quietened my heart to hear the leaves.
The rustle of the dry ones under my feet
The whisper of the green ones still hanging to the trees.
I would like to borrow their incredible faith
And also, to have more of their grace.
So pondering about life I wander through the park
Until I kick my head into a branch
It’s curved and undulating, ending with many leaves.
From the down point that my head full of thoughts met
Six branches spike up, brave and unique.
Six is my life path number, I think.
What is God telling me
In the language of trees
In the shape of branches and leaves?
The tree has remained all green,
And the sun, a bit shy, reaches for its trunk
With rays like arms, golden and big.
Three warm hands on my body I feel
Two on my belly, one on the back
I now count seven little branches
Spiking up from that branch.
My life-number six or God’s seven, I ask?
It’s seven it seems, as I count again,
But how does this matter anymore
When my life spikes up from within
And I become for a moment a rainbow of light
At God’s feet, in the park.

important it was to prepare a good talk. It takes time to organise your presentation and to have a clear message. There is a huge difference between reading a paper and listening to a talk, even if the paper and the talk will discuss the same subject. Now I take the time to prepare my talks before the conference and not after it has started; before, I would have to skip some talks to get mine ready and I think that was a little bit unfortunate because going to a good meeting is a great opportunity to learn new things – it’s a festival of science.

Could you tell us an interesting fact about yourself that people wouldn’t know by looking at your CV?

I love poetry and I write poems. Words can have a special meaning to me. Of course, I do not write poems every day, but sometimes my soul speaks in poems and I write them down. It may be something related to science, to love, to nature… I also appreciate spirituality, the Japanese approach to life, the Chinese philosophy of feng shui, the Tibetan way of looking at life cycles, the Christian approach to faith and kindness. I also like to read prayers and blessings from different languages and religions: I think they extend our view on how we have evolved but never really changed at the very bottom of our hearts.

Dana Branzei was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.