

Dr. Daniel Graf is a professor at the Department of Dentistry and Dental Hygiene at the University of Alberta and violinist for the Concordia Symphony Orchestra.

Thank you Daniel for being our feature researcher for this issue! Could you tell us about yourself, what your role is at the University of Alberta, and what kind of research you do?

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I am a biologist and biochemist with degrees from the Swiss Federal Institute of Technology in Switzerland. I didn't follow the most linear academic path, I went to do a PhD in biological sciences and I was initially working in immunology. I then did a Postdoc in London, England, followed by another Postdoc at Greece, which were both research institutes and not Universities. I then moved back to Switzerland to the University of Zurich, where I started working on craniofacial research. Thus, I moved from immunology to the development of the immune system, inflammation and tissue repair, to developmental biology. In Zurich I was with the Centre for Dental Medicine from

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where I was recruited in 2014 to the University of Alberta. At the school of dentistry, I am one of the faculty members in foundational sciences. My role is to be engaged in undergraduate and graduate dentistry student training and teaching, the concepts they need to know in terms of foundational biology, genetics, some immunology and so on. And then of course I have quite a bit of protected time for research, which I predominantly dedicate to craniofacial development.

What do you think about the path you took to academia?

Actually my path wasn't the shortest way to academia. I was much more open and I was looking for opportunities. If I see opportunities I like, I take them. This probably wasn't the best choice in terms of a linear career, because you need extra years to do one or the other, but all of this is a journey, you don't actually waste time, you learn throughout. Yes, it is important to look at where you want to go in your career, but your career is not yet all defined

and you should also have a life at the same time. You should be happy with what you're doing, you should be happy where you are, and there should also be time where you can explore a couple of things. I feel nowadays students are more focused but that might just be my perception - I feel like the environment here is tremendously competitive. Students are very anxious and feel they have to get everything right. Yes, you want to have an idea of what you want to do, but whatever you do, you should do with dedication, rather than just for collecting points!

You mentioned that you went from immunology and into craniofacial research. What was the driver for this? Was it your curiosity of the specific fields or just having an opportunity to branch out?

It's a little bit of both! If you study biology, you don't study a priori something specific. I had an interest for immunology and started shifting into the immune development just out of curiosity. Moving from one centre to another, you start interacting with new environments. In London, I found myself surrounded by cell and developmental biologists! You may expand your interests, and I am open minded too, so I started doing different things, and in the end, the shift to what I am doing now was actually very simple. This shows how you cannot really plan your life, or the more you plan your life, the harder the coincidence will hit you. In my case, I was really interested in the types of molecules I was working with, they were important for development, important for immune regulations, chronic inflammation, tissue repair. I had this idea to try to understand what happens in the context of chronic inflammation, and I realized that I was looking into a black box. I had no idea where to start. Over 20 years ago, the research tools and the amount of information we had was exponentially less. This was when the human genome wasn't fully sequenced. I had to first

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ask the question, “What are the molecules actually doing?” That’s when developmental biology came into play. This was really my push into developmental biology. In developmental biology, you can study any tissue or organ. And it just so happened that we got some nice data related to craniofacial development, and there was a new opportunity that presented itself. And the more I looked at craniofacial development, the more fascinated I got by it. My first interest was immunology. It was something that I thought I really wanted to do. During my PhD, I was very successful in immunology, I had a lot of publications and I

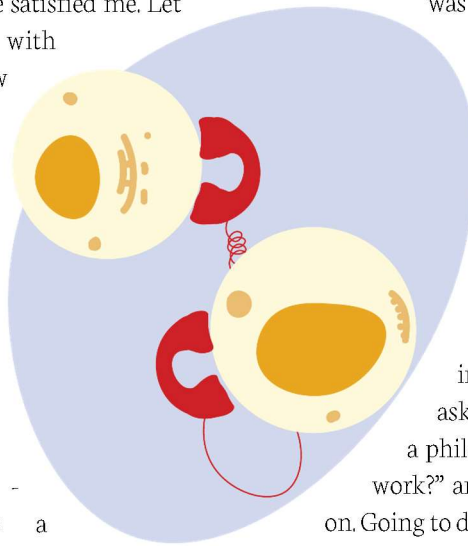
“I kind of always wanted to understand the social aspect of biology - communication.”

just could have said I’m going down this immunology route for the rest of my life. Probably most of the young scientists would have done this. I just didn’t care! I just did what I wanted to do, not what I was expected to do. I did not continue with immunology and I am happy with it. I have great immunology colleagues, I can talk with them and can still understand most of the current concepts. But I realized when I moved into other fields that immunology was a type of research that never quite satisfied me. Let me tell you why - when I started with immunology, I wanted to know how cells communicate with each other, communication and decision making by cells has always interested me. In immunology, cytokines and cell surface receptors were the really interesting parts for me. I was less interested to understand how signals then are processed within cells. I kind of always wanted to understand the social aspect of biology - communication. Immunology as a discipline had developed this technique called flow cytometry, where cells can be phenotyped with very high resolution based on antibody staining. However, this necessitated to isolate single cells in order to run them through the flow cytometer. While you get a lot of information about each cell, you completely lose the information of where the cells were located within the tissue. It turned out that this bothered me, because if I

wanted to know how the cells communicate, I need to know where they are. Most cells are not going to shout over the mountain - they’re going to talk to their neighbours close by. I guess this is one of the reasons why in the end I was happy to let go of immunology. Something was missing for me. So, I think what is really important is to be open minded about what you are interested in and also to accept that your flavour develops. Maybe similar to as you get older, you don’t like sweets, you develop a taste for pickled stuff or for the bitter - it’s also the case in science, you will develop different tastes.

You also did mention that being exposed to different environments and labs internationally drove those changes in you as well. Did you have certain people that were driving forces to what you did as a young researcher?

Absolutely! I was fortunate to get to know quite a few people with different backgrounds. Some of them really became mentors, and not only mentors where we had very organized discussions, but people you just talk to, have discussions with, and get advice from. An important part of my training during my postdoc in the UK was how science was done differently in England. It was quite different than how it is done in North America. First of all, there is the concept of mentoring. I never worked once in a lab which was cutthroat, and I’ve heard of stories where two students were working in a lab where they were competing with each other and things like this. I don’t believe in this. I think research should all be a collaborative effort. The training in the UK taught me to look at the fundamental questions and I am really trying to do this. I was fortunate to work with some individuals who were successful with asking very simple questions, almost from a philosophical point of view, “How do things work?” and “How can this happen?” - I took this on. Going to different places is also very important, and going into different research systems is even greater. The way science is done in Europe is quite different than how it is done in North America, and the main difference is that in Europe, most funding agencies are much more interested in ideas and what you want to do, while in North America, they want to see that you have basically done the work before they give you the money. It is quite different, and I am still struggling with this because I am a person that



believes that research comes from ideas. Yes, you need to be able to do the experiments with what you have, but if you don't have the ideas, you only get incremental knowledge gain because you're not making the big steps. If you really want to do something very different, they will tell you that it's too much or too risky - but only if you're risky, do you get new things, otherwise you just get predictable results.

Right, and I think it's often the case now-a-days in publishing where results are predictable probably because of the pressure from the whole publish and perish mentality.

Yes, it is freaky, the publish and perish mentality in the academic world. Yes, publications are very important because in the North American system, if you don't have publications, you don't get scholarships. It really is a cutthroat situation right now, which might be necessary to some degree, but I also greatly lament it. I don't think you can distinguish the best students or researchers by the number of publications. I am not sure what is a good system or what is a better system. For graduate students, publications are important because this is a way for them

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to show that they can close off and finish a research project, although research projects are never truly finished, but you know, this is the point when - I write it all up, document it, and I am happy that I have done this instead of being in this limbo all the time, having all this data, and not getting it together. It is this important last step where you write up the collected data, and I think that is an important part of the training. I would expect every student to publish simply for this experience. For me it is less important, whether you have a nature communication paper or you have a paper in a smaller journal. What really counts is the way you have done your work. Whether it's careful work, original work, the way you think about and present it. You might be working on a research topic that is less fashionable, so it will be much more difficult to get this work into a high impact journal. While it is important to publish, it is more important to publish good work. Publications are your business cards. Through your

publications or conference presentations and so on, you build your reputation. Whatever goes out there, I think that's an important point to mention, stays out there. Don't just to go to a conference with poor or wrong data, because it will stay forever. Be careful with how you present yourself. If you have publications that are good quality and you're happy with them, I think that's the most important part. And you should be able to get them into decent journals. I am more into quality than quantity. Aim for good quality publications that make you feel proud rather than splitting a project into two just to have two papers in your CV.

Do you have any advice on how students can face challenges in pursuing research?

I have observed this in some of my students in Edmonton and when I was working in Greece. I worked for quite a few years in Greece, and one of the experiences I have with the Greek students is that they often didn't really believe in themselves. One reason may be because they were trained in a very small and almost isolated environment, I mean, it's a smaller country and has less research exposure. They don't necessarily have the confidence thinking they can join a big lab and can do cutting-edge research, and I was really trying to argue and talk to students to go out and do this. I sometimes feel this from students at the U of A as well. U of A is a nice university, but it is still not really a big global player because we are quite isolated from other places. Sometimes this gets to the students, and it can be hard to build that sort of self-confidence, that you can do this. It is important to realize that people who are trained at Harvard University also only cook with water - they do the same. Sure, if you have more money, you can do more things, buy more antibodies or kits, but it's not necessarily the finances that makes your project successful, it's the way you're trained to use your brain. The biggest part for your research is using your brain to come up with the best approach. If you don't come up with a good experimental strategy, or a good strategy of how to approach your investigations or do your study, you can waste a lot of time. That's one of the things I tell students, going out to other places and systems really helps you to broaden your horizon. I think this is very important. I learned a lot having been in different places, having seen how different systems work - for me it has been fantastic. If I would give

advice to any student that would want to get into a research career – I don't believe that the academic career is the only way. There are different things you can do. Really go for what you feel you have an interest in, but make sure that in whatever you do, you keep getting challenged. Unless you do your PhD because you want to collect a title, and I am sure there are people who want to do this, you do it out of curiosity and because you want to grow on it. You have this thing inside of you, so you should be able to continue this wherever you go – I think it is very important to recognize this. There's no right or wrong way, but you need to know what to expect and why you do it, and at least if it doesn't work out, you'll be certain you have considered this.

I could certainly relate with young researchers or undergrads that might not have the confidence to move forward in sharing their research or pursuing more opportunities in this way. One of the key motivations for our team at Eureka is to provide resources and an avenue for undergrads to build that confidence in showcasing their research!

“Working hard is not a ticket
for success.”

I wanted to talk a little about work-life balance, which many people consider now-a-days as a work-life cycle that goes up and down. What has your experience been in finding this balance throughout the years as a busy professor, researcher, and violinist!

I have always been busy! I like to take on work and usually I take on too much and then I come into these crunch times when I realize I have signed up to too many things and I am not sure how to manage them. I can say I have survived so far! Finding the balance, I wouldn't call it “work-life” balance, but finding the balance that works for you is really important. There might be times when you work 70-80 hours a week, it's very busy and you want to get things done and whatever. You can do this, but you cannot sustain this for months and years. I don't believe anyone who tells me that they work 16 hours a day. There might be exceptions, but I don't believe anyone can really sustain

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this. They're not working – they're just doing things, meeting people, talking to others, but that's not necessarily time well spent. I have examples of colleagues that were working 9 to 5 because they had kids. They did everything by simply asking good questions, doing the right type of experiments and getting high impact papers. And then you have others that work 70 hours a week non-stop and they're not achieving this. Working hard is not a ticket for success. Working hard might be required to get things done the way you want them to be done, but I think much more important is that you think about what you do and why you do it. When I train my students, I am very open and ask, “What is a good experiment?” and “Why are you doing it?” I always push students to try this and do that. I will always branch out because that's how I am, and I think that it's important for the researcher to have an open mind. But at the same time, whenever you do something, you have to make sure you do it for a good reason rather than just doing it. You can waste a tremendous amount of time and resources by just doing things without really thinking about why you do it and how to do it.

However, it is important to find the balance, and the balance is different for everyone. Some people might want to have every weekend off or to be with family. I don't think there's a clear rule. For me it helps that I can go on and play music and see different people and do something completely out of it. It's important to have something on the outside. When you go through your career, you realize that you will have ups and downs. One of the things that one has to learn is to balance this out. Research can be extremely rewarding – you have a nice result, and it takes you on a high, and you think that's plain sailing, and then boom! It hits you and you're down again. So, you go up and down, you have these elevator rides. For me, it was helpful to learn how to put these things into perspective. If something is so high, yes enjoy it, but don't let it take over. Similarly, when you have disappointments, you don't want the disappointments to take over. It would be a constant emotional roller coaster and I am not sure if that's a really healthy state to be in, at least I don't enjoy it that much! But it happens, because you get excited about something and it comes down again. So, make sure you have something that balances your work life. It might be sport, music, a hobby, family – I think it is really important, to stay grounded. But I also realize that everyone has different needs!

As an academic and researcher, you have had a fair share of eureka moments! Can we have a glimpse of your experience?

I have some very specific examples! One of the things I tend to do is to tie together loose ends. I have a couple of observations and then say that these have to come together and it has to be like this - that's probably one of my strengths. One of my first big hits happened during my PhD. I was working on a gene which I had cloned, and I had no idea what it really was doing. At this time, we had to manually or physically sequence DNA. We didn't know where the gene was located on the chromosome. We had a collaborator coming to visit us who was able to do the chromosomal localization of genes. Why is this important? Well, in those days, if you had a genetic disorder, typically a geneticist would have mapped this disorder to a specific location on a chromosome without necessarily knowing what gene might be involved. Bringing these two pieces of information together allow you to do something. So, I was working with this gene which I knew was expressed on this one type of cell and likely was important for signaling to other cells. I had taken this initiative and I had asked this person to do this chromosomal localization. This person came back and told me that this gene is located at a specific location on the X chromosome. I searched the literature and found an immunodeficiency that was mapped at this location. Now, I had a molecule which I suspected to be important for cell-cell communication, and then you have a disease. Bingo. I got this information and I remember it was on an evening when I was working late in the lab. My PI gave me a lift to my place. I told him about it and said "Hey, that's it!" This is a eureka moment - eureka from Greek, "I found it", that's what it means. At this moment, I knew! It took a couple of months and then we had a Nature paper. Recognizing when you have these different pieces of information and what it could mean is important. This is something that happened to me again and again (but without Nature papers), and the important thing is that when you experience this, you have

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to have the confidence to believe in yourself. Because then you have to plan all the experiments and go for it, and you basically commit on something which might not be much

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more than a hunch. You are not 100% certain about. You look at this evidence and you say, "That's what it has to be... so let's do that," which might take you into a completely different direction than what you had planned to go with your project. This is how I get my eureka moments. I am doing all this work on craniofacial development, and now, for instance, I have branched out into knee osteoarthritis (so looking at the knee, cartilage, cartilage in the face. And of course, osteoarthritis is a much bigger health problem), for the same reason I said, "Look at this, we have a malformation in the nose... this looks like an osteoarthritic cartilage. Okay let's apply this to osteoarthritis" - and everything we have done in osteoarthritis so far turns out to be right. You need to have this confidence to say that there's something and you have to have the guts to go for it even though no one else initially believes in it. That's not easy, because guess what? You constantly have doubts! I mean, you don't know whether you are right. There is always a risk, but this is what I like about doing researching biology. In the end, think about what will make a difference. Everyone will have slightly different stories on how to approach this, but I think it's important to have this open mind and bring information together.

Are taking risks something you can foster in research?

In part I think it is personality driven. I am just a person that is quite confident with not everything being super organized and trying to bring things together. That's how I function. There are some people that have to go step by step because they get very anxious if things are not clearly organized. I am not saying this is the only way to do it because there are many other people that have been very successful using a stepwise approach. So how do you do this? I think you have to learn to foster your strengths. You have to recognize them first and then foster them. There are many ways you can do science. In whatever you do, you have to know your strengths, you foster them, and ideally you work in an environment where these strengths are being appreciated and can be further developed. Once this is not happening, then you are in the wrong place. It's very much that you need to be aware of who you are and what you want. That definitely becomes important. However, you shouldn't measure yourself constantly against your

peers since everyone is different. Some are long distance runners and some are sprinters. They're both excellent athletes but very different. I think this is true for any profession. Get to know who you are, and don't compare yourself to somebody else with a very different personality - you will only be disappointed.

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In a world of open access journals and online conferences, there are many avenues where young researchers can be engaged in science and try to explore more about themselves. Do you have any insights on this topic for our undergrads?

Try to build confidence! Almost everybody suffers from imposter syndrome, and I think it has gotten worse. There is so much information out there. Gosh, I know so little about biology, and I have been doing this for quite a few years now! You start with something, but with the amount of information out there, I think it's overwhelming, in the true sense of the word. In the North American system unfortunately, everything goes with being competitive, and I say unfortunately because I don't believe this system serves us well. But this is the system. So, let's say you want to get scholarships - well, scholarships breed scholarships. Everything is GPA oriented, and it sometimes really hurts me because students that might have a GPA of 3.0, might be one of the brightest students and do a lot of things great, they don't end up being competitive in this environment. I don't know whether I have a good piece of advice, but that is something that people should at least be aware of, and I think that the people that have had a background, either from family or somewhere else, where they know how the system works, just have this intrinsic advantage - they just know that that grades matter in North America. In Europe, nobody ever asked me about my grades - if you

pass, you pass! The other thing is, you can only get experiences by seeking out experiences and going for them. There are many things on offer, you guys are doing a great job with Eureka, and there are many other research opportunities out there. Become aware that these things exist, but also reach out. Either take your official channels or use the student group organized exchanges, or directly contact faculty members if you would like to work with them - of course in a nice way. Don't send them an e-mail in May when you want to start in June and be aware of the timelines. Seek out these opportunities, take advantage of them and reach out. Don't expect too much of yourself or don't put your expectations so high that you cannot fulfill them. Develop

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the confidence to reach out. Typically, people are not coming to you, that's one of the things I again had to learn. You have to contact them and tell them what you've done. You don't have to brag, but you can politely let them know. Sometimes I still forget about this. Reaching out can be very easy, for instance if you're doing a course and you like the topic, you can always go and ask this professor if there are any opportunities to do research. That's just a verbal interaction at the end of a lecture. Yes, I mean you have to pull yourself together, you have to walk up to this person and ask a question, but guess what? The worst-case scenario is a no, and this puts you at the exact same position as before you asked the question. So, the chances are there that you can get something from this, but you have to make the first move - there are all these helps out there, but you still have to make the first move.

