LUDWIG CANCER RESEARCH

Q&A

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What are the biggest questions you aim to answer in your lab?
How do cancer cells establish a dialogue with normal cells within their microenvironments? How does that conversation change during the course of cancer progression and metastasis? How is that dialogue affected by different therapeutic interventions? We want to answer these questions in different cancers, with a recent emphasis on brain malignancies, both primary gliomas as well as brain metastases that originate from the breast, lung and other organs and disseminate to the brain. Brain metastases are very challenging targets for therapy and prevention. By developing a comprehensive understanding of the complex and interconnected microenvironmental landscape of brain malignancies, we're getting closer to understanding this very intricate communication involving many different cell types within the brain microenvironment. We can use these datasets to then identify weak points and therapeutically intervene, and either stop that communication altogether or change it such that the normal cells are re-educated to actively fight the cancer.

Did you have any early influences that put you on the path to a career in science?
My teachers and professors in high school and university were instrumental in reinforcing my innate interest in science. I remember one high school teacher in particular—Mr. Bennett—who had an

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infectious enthusiasm for chemistry, which he was able to convey to his students. His classes were key in reinforcing my own enthusiasm for science. As an undergraduate at Trinity College in Dublin, we had outstanding professors in genetics. They taught us to think about and approach fundamental questions of biology from a genetic perspective and were very adept at unlocking many of the mysteries of biology and the beauty of genetics.

When you were 14, you moved from London to the Irish countryside. Was the transition difficult?
At the beginning, yes it was quite an adjustment. At 14, I was starting to become independent and I wasn't happy to leave my friends behind. Now when I look back though and see how my life has worked out, I'm really pleased that my family made that decision, as it ultimately benefited all of us.

Did it influence your decision to pursue science?
The Irish school system allowed me to explore a wider range of subjects—history, geography, French and English in addition to the sciences—than I would have been able to in the more restricted English school system. In England, I would have had to concentrate just on the four sciences. In my opinion, 14 is far too young to specialize because at that age, you tend to change your mind pretty frequently about what you want to be when you grow up. But I'm fortunate in that I've always been drawn to science. It's what I always found most fascinating at school, and having many different perspectives when thinking about scientific problems can be influenced by input from other subjects—so that was definitely another good outcome of our move to Ireland.

How would you describe yourself as a child? Introspective or outgoing, bookish or athletic, intense or laid-back?
Probably none of those strict 'either or' adjectives actually apply. I would say that I was very curious as a child, and an avid reader. I devoured books. I was always asking a lot of questions and always wanted to discover new things and walk into the unknown.

You've been quoted as saying that you tend to approach life as a game of Snakes and Ladders. Does science ever feel like the board game?
Very much. Often, you feel as if you take two steps forward and one step back. You're advancing on a project and all of a sudden you uncover something that forces you to take a step back and reflect on what the data are telling you. But I think of science more as a journey where we encounter obstacles along the way. They can be frustrating but I see them as challenges. One of the fun parts of doing science is in fact when the outcome is not

what you expect it to be. The obstacles or roadblocks force you to think about a problem more creatively and approach it from different angles.

What has been your best or most satisfying moment in the lab?
About seven years ago, several lab members were collaborating on a project targeting macrophages in an animal model of gliomas (brain tumors). Glioblastoma is a very challenging disease to treat and they found that using an inhibitor of macrophages was essentially curing the mice. These were animals that were days away from having to be sacrificed because their tumor was growing rapidly in the brain. Yet the treatment with a specific drug completely reversed the process. The tumors regressed and the mice survived. That effect was so striking, so profound, especially when you saw the effect that it had on the animals' behavior. That was a very special moment because we not only saw its potential implications but also, in retrospect, because that particular finding set my lab on the path to where we are now, which is working on trying to understand the brain tumor microenvironment as one of our major challenges. Many people in my lab were involved in different ways on that project and we certainly benefited from working on it together as a team. Of course, everybody hopes to have one of those moments in their scientific career and I've been fortunate in having several of those, including in my research as a student and as a postdoc. But that is one that will always stay with me.

Who are the scientists, living or dead that you admire? If you could, whom would you work with?
Barbara McClintock. She was a geneticist who won the Nobel Prize in 1983 for discovering transposable elements—the ability of special DNA sequences to move around in the genome. She was inspirational in a number of ways. She made multiple landmark discoveries, some of which took decades to be recognized and appreciated. She was ignored by her peers and for years they dismissed her findings. But she never gave up and continued to work on her own. Here was a scientist who was doing creative, transformational research, being ignored, being told that she was wrong and yet she was never discouraged. She just kept going. Her research has had a fundamental influence on much of what we understand about the mechanisms underlying inheritance and her discoveries have had an effect on everything from genetic engineering to cancer research. She was also a scientist

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at a time when it wasn’t easy for a woman to pursue a career in science and yet she was so single-minded and persistent, she prevailed. She was a true innovator in her field and is an inspiration to aspiring scientists.

Working in science is wonderful and challenging but is not without drawbacks. What has been a particular challenge to you?
As you progress in your career, you have many more demands on your time—you have responsibilities to the people in your lab, you have administrative responsibilities, you have to travel a lot. And this is in addition to having a family. These are challenges every professional faces. When I say yes to something I only say yes if I’m able to do it well. And for me that means more and more having to say no. I have to ask myself where can I have the most impact, so I’m very selective about which committees I’ll sit on, which conferences I’ll attend or organize. You have to be very organized and I basically schedule down to the hour. When I’m at work I try to be as productive as possible. When you have young children, you have to leave at a certain time and that is a great external force to then be incredibly efficient with your time while at work. This is of course true for men as well as women.

Have you ever followed up on a failure?
In my lab, we aim to explore big questions and test open-ended hypotheses. That way, even if the answer ultimately is negative, it’s still as informative as if we had gotten a positive outcome. You don’t end up with failures as such because you asked a question that was worth answering to begin with. I’d almost characterize a ‘failure’ as a new challenge resulting from an unexpected finding that then needs to be explored further.

There has been a lot of discussion in the media lately about women in science. What has been your experience as a female scientist?
It’s complicated. I don’t consider myself to be a ‘woman scientist’ but a scientist who happens to be a woman. We never talk about male scientists. Never. But we talk about women scientists all the time. Bottom line, there are not enough senior scientists who are women. Young female postdocs don’t see enough women in the career stages ahead of them, and they are then led to believe it’s too challenging and not compatible with having a family or interests outside of the lab. We need to encourage more female postdocs to apply for faculty positions. This is precisely where the drop off is happening. It’s not as if there are women applying and they are not getting the positions at the same rate as men. It’s just that not as many women are applying. The University of Lausanne sees this is an issue and has set a target of having women fill 40% of new faculty posts by 2020. The universities in Switzerland and the Swiss National Science Foundation are also implementing various programs to try and change these metrics and I think they should be commended for this. Hopefully these programs will provide constructive and informative examples for initiatives that can be considered and implemented across the world.

How do you see your role in helping to mentor young scientists?
Mentoring is very important at the postdoc level and in particular during the transition to independence. Everyone needs a supportive community of people who are pleased to write letters when you're applying for grants, nominate you for awards and suggest you as a speaker at conferences. I remember how it was for me at that early stage in my career and the wonderful support that I received from a number of senior colleagues, and I'm a firm believer that it's really important to give back when you're in a position to do so.

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You are also a professor at the University of Lausanne. Can you tell us a little bit about your teaching philosophy and what brings you the most joy in interacting with students?
My teaching philosophy is to engage my students—not lecture to them. My classes are very interactive and foster a lot of discussion. I think that's more enjoyable and more informative for them and also far more rewarding for me. I don't want them to just absorb a particular topic but to critically assess what they are learning, which has far more of an impact on their understanding and retention than just the traditional, rote learning approach.

How do your teaching and research experiences intersect?
Quite a bit of the teaching that I do focuses on topics that we basically research in my lab—the processes of cancer invasion and metastasis, and the critical importance of the tumor microenvironment. When I teach, I try to use language that's accessible, simple and straightforward. I aim to do away with the jargon and distill the concepts down to the basic principles. This forces me to then reflect on some of the research that we're doing in the lab and what's happening in the field. Too often we get caught up in dogma and in the preexisting literature. When I'm teaching I can take a step back and reframe the way I think about questions in the context of how I explain concepts and theories to my students. In that way, teaching and research can actually be quite closely intertwined and definitely feed off each other.

What else do you love in life?
I love spending time with my husband and kids—outside of our lives in science, much of our time is spent outdoors, especially around Lake Geneva. Switzerland is a beautiful place to raise children, and we feel very privileged to live here.