Being at the right place at the right time

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ABSTRACT I am tremendously honored to receive the 2012 Women in Cell Biology Junior Award. In this essay, I recount my career path over the past 15 years. Although many details are specific to my own experiences, I hope that some generalizations can be made to encourage more women to pursue independent scientific careers. Mine is a story of choosing a captivating question, making the most of your opportunities, and finding a balance with life outside the lab.

It is a great honor to have been awarded the 2012 Women in Cell Biology Junior Award from the ASCB. Looking back at the 15 years I have spent doing research in cell biology, my overwhelming feeling is that it has been and still is a lot of fun. I am extremely fortunate to have a job that I truly enjoy and that gives me complete intellectual freedom. My lab choices over the years were motivated by scientific curiosity and enthusiasm for new environments and topics, rather than by career building. It is thus truly amazing to be rewarded for (rather a lot of) work enjoyed.

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FOLLOWING ONE'S INTERESTS

My decision to study biology came relatively late during my school years. I had always been fascinated by how things are built, taking a brief interest in architecture, but a couple of weeks spent in labs oriented my choice to biology. At the end of my bachelor degree studies, I was extremely fortunate to be invited by Susan Gasser at the Swiss Institute for Cancer Research to join her lab for my diploma thesis after we met in her undergraduate cell cycle class. Joining her lab was the first turning point of my as-yet nonexistent career. She was extremely present in her lab and taught all of us very high standards, and her excitement was highly communicative. She also showed me, through example, that one can be both a highly successful scientist and a mother. Under her guidance, we showed an interplay between telomeres and DNA double-stranded breaks in yeast, with the DNA end-binding Ku proteins localizing at and clustering at telomeres at the nuclear periphery but relocalizing to DNA breaks upon DNA damage (Laroche *et al.*, 1998; Martin *et al.*, 1999). This study, which suggested that pools of Ku proteins at telomeres can be released to scan the genome for DNA strand breaks, raised my interest in the spatial organization of cellular functions and oriented my choice to further study this broad topic.

During my undergraduate studies, of which I spent one year at the University of Zurich, I had been captivated by courses taught by Konrad Basler and Ernst Hafen on *Drosophila* development and pattern formation, and I thought this topic would be fun to study for my PhD. Although graduate programs are now becoming more common in Europe, they did not really exist at the time, so I simply wrote to and interviewed with a number of labs whose research excited me. I decided to join the lab of Daniel St Johnston at the Gurdon Institute in Cambridge. This happened at an extremely exciting time: the lab was full of fantastic PhD students (most of whom now have their own labs), including my future husband, Richard Benton. It was also a turning point in *Drosophila* research, with the genome having been just sequenced, allowing one to clone a gene in only a few months, rather than years. A postdoc, Katia Smith-Litière, had initiated a clonal screen in the germ line for mutations affecting oocyte polarization, so together with another postdoc, Vincent Leclerc, we visually screened more than 5000 manually dissected fly ovaries (Martin *et al.*, 2003). This screen

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Abbreviation used: SNSF, Swiss National Science Foundation.

identified the *Drosophila* homologue of the conserved tumor suppressor gene LKB1, and we went on to demonstrate that LKB1 has a general role in cell polarization (Martin and St. Johnston, 2003). Because of LKB1's well-established role in tumor suppression, our work also led to the proposal—relatively novel at the time—that loss of cell polarity may contribute to the formation of tumors.

While doing my PhD work, I realized that I liked to study patterning but became aware that I was more attracted to the cellular than the organismal level. I therefore took the somewhat unusual decision to start postdoctoral work on a simpler model organism, thus dispensing with the complexities of multicellularity. During my first ASCB meeting in 2001, I had been struck by the beauty of individual microtubules probing the cellular space in fission yeast, as presented on an animated poster by Fred Chang. New York seemed like an exciting place and large enough for Richard and me to find exciting positions. I therefore joined Fred's lab at Columbia University, where I started delving into the cross-talk between microtubule and actin cytoskeletons. I discovered a physical link between proteins at the microtubule plus ends and a formin, which nucleates actin filaments, suggesting a mechanism by which microtubules may remodel actin structures (Martin *et al.*, 2005). I also studied the regulation of the formin For3, describing an unexpected dynamic retrograde behavior of For3 with actin cables (Martin and Chang, 2006) and showing, in collaboration with the group of Pilar Pérez, that For3, like other formins, is regulated by an intramolecular autoinhibitory interaction (Martin *et al.*, 2007). Fission yeast work was and remains beautiful for its apparent simplicity, although I have somewhat progressed from my enthusiastic, naïve start, realizing things are sometimes more complex than they appear.

SEIZING OPPORTUNITIES

The chance to start my own lab presented itself unexpectedly less than three years after I settled in Manhattan. The Center for Integrative Genomics at the University of Lausanne was looking for potential applicants to a Swiss National Science Foundation (SNSF) program aimed at attracting scientists with Swiss links back to Switzerland to set up their own labs. I had met one faculty member, Christian Fankhauser, who suggested I come for interview, which resulted in my applying for and obtaining the SNSF funding. In the meantime, my husband obtained a tenure-track assistant professorship position in the same department, so we moved to Switzerland in the summer of 2007 with our newborn daughter.

Anyone who has started a lab knows that the early years are both thrilling and terrifying. Luckily, having secured SNSF funding before starting, I spent very little time on grant writing. I could instead concentrate on research and spent most of my time in the lab. During my stay in Fred's lab, while working with a PhD student (Padte *et al.*, 2006), I had discovered a hint of an unexpected function of a polarity factor, the kinase Pom1, in the cell cycle. Fred gave me the freedom to pursue this in my own lab, which I turned into a project for myself and for an excellent technician, Martine Berthelot-Grosjean. It turned out to be fascinating: we discovered that the Pom1 kinase forms gradients from each end of the rod-shaped fission yeast cell that extend to the middle of the cell and negatively regulate a medially localized protein kinase, Cdr2, itself an indirect activator of Cdk1. As cells grow in length, less Pom1 reaches the middle of the cell, thus relieving the negative regulation and promoting Cdk1 activation. From this, we hypothesized a model for how fission yeast cells can perceive their own length and couple mitotic entry with attainment of a sufficient size. What a surprise—and fright—when I heard the same model presented by Jamie Moseley (then a postdoc in Paul Nurse's lab) at the first conference I was invited to as an independent group leader! Jamie and I decided to openly communicate and, when both our papers were accepted back-to-back a few months later, I realized this was possibly the best friendly competition that had ever happened to me (Martin and Berthelot-Grosjean, 2009; Moseley *et al.*, 2009).

TOWARD THE FUTURE

Since then, I have obtained a tenured position in the neighboring Microbiology Department at the University of Lausanne, and our son was born (both events occurred at nearly the same time). The lab has grown a lot, and I regret I don't get to spend much time doing experiments anymore, but I still get just as excited about new results and enjoy immensely the intellectual stimulation that I receive from my students and postdocs. We have gone on to dissect the molecular mechanisms behind the formation of Pom1 gradients (Hachet *et al.*, 2011), showing these gradients are nucleated by a local dephosphorylation event that reveals a lipid-binding domain and are shaped by autophosphorylation and lateral movements. We have also probed morphogenetic questions, showing that normal rod shapes are formed by the combined action of actin-based transport and exocyst-mediated vesicle tethering at cell poles (Bendezu and Martin, 2011), but that actin-based transport can be circumvented by rerouting vesicles along microtubules (Lo Presti and Martin, 2011). Some of our next, exciting questions are defining how these or other morphogenetic pathways are regulated when cells exit their normal rod shape and grow toward mating partners during sexual differentiation.

It is only recently, on coming back to Switzerland to start my lab, that I became acutely aware of women's issues, simply because there are very few women here. In my faculty, currently less than 10% of tenured professors are women, and this is not an exception among similar faculties in Switzerland. Let me finish with a simple message drawn from my experience and addressed especially to young women considering a research career: first, do what interests you—your enthusiasm and curiosity will take you a long way. Second, take opportunities as and when they arise. Finally, with the help of a supportive partner, career and family are not mutually exclusive, and if both require adjustments, they also complement each other by bringing (dynamic) balance to one's life!

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