Johanna JOYCE

The Ludwig Lausanne Member on her good luck in teachers and mentors, the dire need for childcare and technical support programs for researchers starting families and stanching the flow of young scientists out of academia.

Photo by Hugues Siegenthaler

With a talent for deductive reasoning and inspired by a couple of gifted chemistry teachers, Ludwig Lausanne Member Johanna Joyce had little doubt which career path she wanted to pursue by her final year of high school.

Johanna Joyce in 2005

Her parents, who had moved their family from London to a farm near Dublin a few years prior, hoped she would become a physician. "But I said, 'No. I want to be in a lab, I want to discover; I want to be a scientist,'" says Joyce. That's also what she told the career guidance counselor at her high school, when she dropped by his office for a required consultation. The idea was met with skepticism. "He said, 'Do you think maybe you should reconsider that and pick something that might be easier for a girl to do?'" Joyce recalls.

"I just mentally rolled my eyes and obviously ignored him," says Joyce, who is today, in addition to her Ludwig appointment, also a professor at the University of Lausanne. "When somebody tells me I can't, or shouldn't, do something—it generally has the opposite effect!"

The effect, in this instance, propelled Joyce into the elite ranks of budding scientists at Trinity College, in Dublin, where she completed an honors program in genetics led by scientists she considers the best teachers she ever had. Fascinated by genomic imprinting, the subject of her honors undergraduate thesis at Trinity, Joyce next made her way to the University of Cambridge where she earned her PhD in Paul Schofield's laboratory exploring how the faulty regulation of imprinted genes causes a disorder that predisposes children to cancer. Eager to delve more deeply into the molecular and cellular

Joyce hiking with her children in Rochers de Naye, shortly after moving to Switzerland.

complexity of cancer, she subsequently moved to the University of California, San Francisco, for postdoctoral studies in the laboratory of Douglas Hanahan (now once again a colleague of hers at Ludwig Lausanne), exploring a family of proteins named cathepsin proteases and their involvement in the progression of pancreatic cancer.

Joyce opened her own lab at New York's Memorial Sloan Kettering Cancer Center in early 2005 and began studying tumor-associated macrophages (TAMs), immune cells that can, depending on their state, either support the growth of tumors or target their constituent cancer cells. In 2013, her laboratory made a key discovery that had

significant implications for our understanding of gliomas. She and her colleagues reported that when TAMs, which abet glioma growth in mouse models, are exposed to an inhibitor of the CSF-1 receptor (CSF-1R)—whose activity is normally essential for macrophage survival—they don't die off, but are instead "reeducated" to target the cancer cells.

Since then, Joyce's exploration of the immune cells of the tumor microenvironment (TME) has only grown in its scope and sophistication. She and her team have revealed, among many other things, how anti-CSF-1R therapy alters the gene expression and activity of TAMs and microglia (the brain's resident macrophages), shown how resistance to such therapy develops in brain metastases of breast cancer and developed therapeutic strategies to defeat those mechanisms. Her lab has uncovered how radiotherapy alters TAMs to drive therapy resistance and growth of gliomas, and interrogated the immune landscapes of primary brain tumors in patients, comparing them to those of various brain metastases. She and her colleagues have developed and freely shared powerful new methods to map the TME and, most recently, to watch its evolution in real time during glioma progression and following therapy by literally looking inside the brain. With its breakneck pace of discovery and collaborative generosity, the Joyce lab is today at the forefront of a field that has dramatically enriched our understanding of tumor biology and promises to revolutionize the treatment of some of the deadliest manifestations of cancer.

FAMILY SUPPORT AND MENTORSHIP

What, apart from a knack for scientific reasoning and creativity, accounts for all this success? Joyce credits her parents first and foremost, who shaped her, equipped her with a vital self-confidence and offered their unconditional support no matter what she chose to do, or how far her pursuits took her from home. Her husband, a neuroscientist,

Joyce in the lab with postdoc Daniela Quail, now an assistant professor at McGill University in Canada.

has been equally important. "I think having a supportive life partner, as a woman scientist and a mother, is key," she says. "It could arguably be the most important thing."

Joyce was also fortunate in her science teachers and mentors. She was, she notes, blessed with the best instructors—almost all of whom were male. "Never, not once, was there anything my mentors said or did that made me feel that I, or anybody in the lab, was any different from anyone else. It just never, ever came up," she says. Ditto for her professors. "Honestly, it was never seen as a problem, or as something we even talked about much as undergraduates, PhD students or postdocs. We were all genders, all ethnicities, all cultures just coming together in the shared pursuit of scientific discovery."

Joyce in the lab with postdocs Alberto Schuhmacher and Leila Akkari, now assistant professors in Spain and the Netherlands, respectively.

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BEING A WOMAN SCIENTIST

This is not to say, however, that Joyce believes her early experiences were necessarily typical or that sexism in science is a thing of the past. She is acutely aware that gender parity is today a prominent issue in scientific circles, especially in academia. Part of the reason for this, she ventures, is considerable disappointment with the slow pace of change. She recalls that when she was a PhD student, she was led to believe that gender discrimination in the field was a problem of the past. "Yet here we are, more than 20 years later, and we're still talking about the exact same problems," she says. "It certainly hasn't changed as much as we all expected. I think that's part of the frustration—that change happens incredibly slowly, and now as a result of the pandemic, we are regrettably seeing many of those hard-won advances for women actually slide back again. This concerns me tremendously."

Joyce also worries that while greater awareness of sexism in the field is commendable, and of course critical, one downside is that it may discourage some women from pursuing scientific careers. "I point out to the young women who worry about this that many of us senior women have advanced despite implicit, and sadly all too often explicit, sexism—and that we are trying to forge a path forward for all the women who come after us. We are really trying our utmost to make it less challenging."

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FUTURE SCIENTISTS

One way she does that is by advocating for young scientists, especially women, and recommends that they, for their own part, cultivate a network of advocates. Joyce, for example, receives many more invitations to speak at conferences and write reviews than she can accept. So, she keeps a list of people she has trained—or met and been impressed by at conferences and other venues—who she then puts forward as alternatives every time she has to turn down such invitations. “It’s very simple to do, and it can really help many young scientists who are just starting out,” says Joyce. “Organizers are delighted to have alternatives, and they frequently then do invite those people.” Similarly, she encourages young scientists to develop a network of mentors who can advise them on a range of matters beyond the nitty-gritty of their research, like writing grant proposals and hiring laboratory staff. “At the University of Lausanne, for example, we have a mentoring program that pairs female postdocs with senior faculty, which is a great way to get advice from someone other than your PI—particularly if there might be issues or concerns, so that these can be discussed in a supportive and confidential manner to identify constructive solutions.”

On a higher level, Joyce says institutions can support young researchers by providing affordable, subsidized or free childcare. By the time people begin stints as research fellows, many are at an age where they’re starting families. “Access to affordable childcare is a big challenge for many young scientists,” she says. “Some institutes do provide that support, and I see that the postdocs and students in those environments are very happy.” Joyce further cites another beneficial program in Lausanne, which gives parent scientists the opportunity to apply for technical support. “I think this is key—the scientist can train the technician before going on parental leave, and in this way experiments can still continue during those months,” she says. “For researchers working with animal models, for example, this can have a critical impact in enabling their long-term experiments.”

On a still higher level, she believes the field at large needs to pay postdocs much more than is now customary. Not doing so, she worries, could precipitate the global and growing trend of young researchers leaving academia for more remunerative careers because their salaries simply do not cover the cost of living, especially when that includes paying for childcare. This is likely to significantly affect the future of biomedical research, not to mention the prospects of young PIs starting up laboratories that depend on recruiting qualified research fellows. As an example, Switzerland, says Joyce, has set pay standards for PhDs and postdocs relatively high and, consequently, she has not seen a similar drop-off in postdocs applying to her lab.

“As institutes, and as individual group leaders, we must respect our lab members, treat them fairly and equitably, and value them as highly-qualified young scientists,” says Joyce.

And those suggestions apply, of course, whatever the scientist’s gender happens to be.