Q&A: Joan Brugge on Empowering Post-docs

Challenging young researchers to think independently and follow up on unexpected findings helps ready them to launch their own labs

As a post-doctoral fellow, Joan Brugge, PhD, spent 2 years trying to identify the cellular Src protein from the Src gene of the Rous sarcoma virus. She nearly gave up before she and her colleagues finally detected it on a gel. That discovery offered clues about how normal cells turn cancerous. It also proved to be a formative experience for Brugge, now a professor and chair of the Department of Cell Biology at Harvard Medical School (Boston, MA), where she probes the cellular processes that give rise to cancer through a diverse portfolio of research projects related to breast and ovarian cancer. She spoke with Cancer Discovery’s Suzanne Rose about mentoring today’s post-docs and how post-docs contribute to the diversity of scientific inquiry in her lab.

What qualities make a young researcher successful?
I look for people who have a gut love of science, people who just can’t get enough of it. Research poses so many challenges that it takes a gut love of science to get through periods of frustration. I also look for people who enjoy interacting with others, because I want to create an environment where people collaborate and share their expertise.

The most successful people who have left my lab have been trained to be independent thinkers. They trust their instincts and try not to get discouraged by a lack of success.

How do you mentor your post-docs?
I try to provide guidance while promoting self-reliance. I meet with them monthly. We go over their data and discuss any challenges. Sometimes, I function as a devil’s advocate to ensure that we are ruling out alternative hypotheses to any challenges. Sometimes, I function as a devil’s advocate to ensure that we are ruling out alternative hypotheses to any challenges. I raise questions that will stimulate their thinking. I encourage them to come up with their own hypotheses and find solutions. I raise questions that will stimulate their thinking. I encourage them to come up with their own hypotheses and find solutions.

Has this approach helped to boost the diversity of projects in your lab?
I am interested in understanding the processes that regulate the initiation and progression of breast and ovarian cancers, so when a post-doc joins the lab, I challenge them to address important unanswered questions in that realm, but to pick questions that are of particular interest to them. We try to customize the project so that it’s something they are genuinely excited about. This explains to some extent why we have a number of different projects going on.

So post-docs play a major role in determining the direction of your research?
It’s a combination of me saying, ”These are the open questions in the lab,” and then encouraging them to come up with their own ideas, too. Of course, serendipitous, unexpected findings may emerge that add to the diversity of research.

Such as?
When we were studying the YAP oncogene, we noted that down-regulation of YAP caused an exceptionally dramatic phenotype during cytokinesis. That was difficult to ignore, so we initiated a project to understand how YAP controls cytokinesis to provide insight into its function.

In another case, we observed that when cells were detached from their extracellular matrix, one cell would literally invade another. Pathologists had observed cells within other cells for decades, but no one had attempted to elucidate the mechanism whereby that could happen. We wanted to understand the process.

Was your discovery that ovarian cancer cells muscle through the mesothelium also serendipitous?
An external stimulus and the ingenuity of a post-doctoral fellow in my lab led to that work.

The external stimulus was funding from a foundation, which contacted me about being part of an ovarian cancer research team because of my expertise in 3-dimensional cell-culture models. Then a fellow in my lab was interested in ovarian cancer invasion. I discouraged him because I thought that none of the available cell-culture models recapitulated the tumor environment well enough for us to get meaningful new information. He was challenged by this and found some papers in which researchers had incubated ovarian tumor cells with mesothelial monolayers in these co-cultures. He felt that this type of culture system would more accurately recapitulate the relevant environment for the metastasis of ovarian tumors to the mesothelium. He came up with the idea to label the tumor cells with red dye and the mesothelial cells with green dye and use time-lapse video microscopy to follow the precise temporal and spatial aspects of the process.

What are you and your team studying now?
We’re looking at tumor metabolism to identify metabolic sensitivities of tumor cells. We’re very interested in the conversion from noninvasive to invasive cancer and mechanisms associated with metastatic outgrowth. We’re studying tumor heterogeneity as it relates to drug sensitivity and drug resistance, as well as tumor initiation and metastasis. We’re also following up on studies showing that matrix-attached cells can upregulate a survival program that confers drug resistance in ovarian and breast cancer cells. We’re pursuing these findings to see whether they can be directly translated to cancer patients, and doing preclinical work to determine whether there’s sufficient evidence to launch a trial of drug combinations we’ve studied in our lab.
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