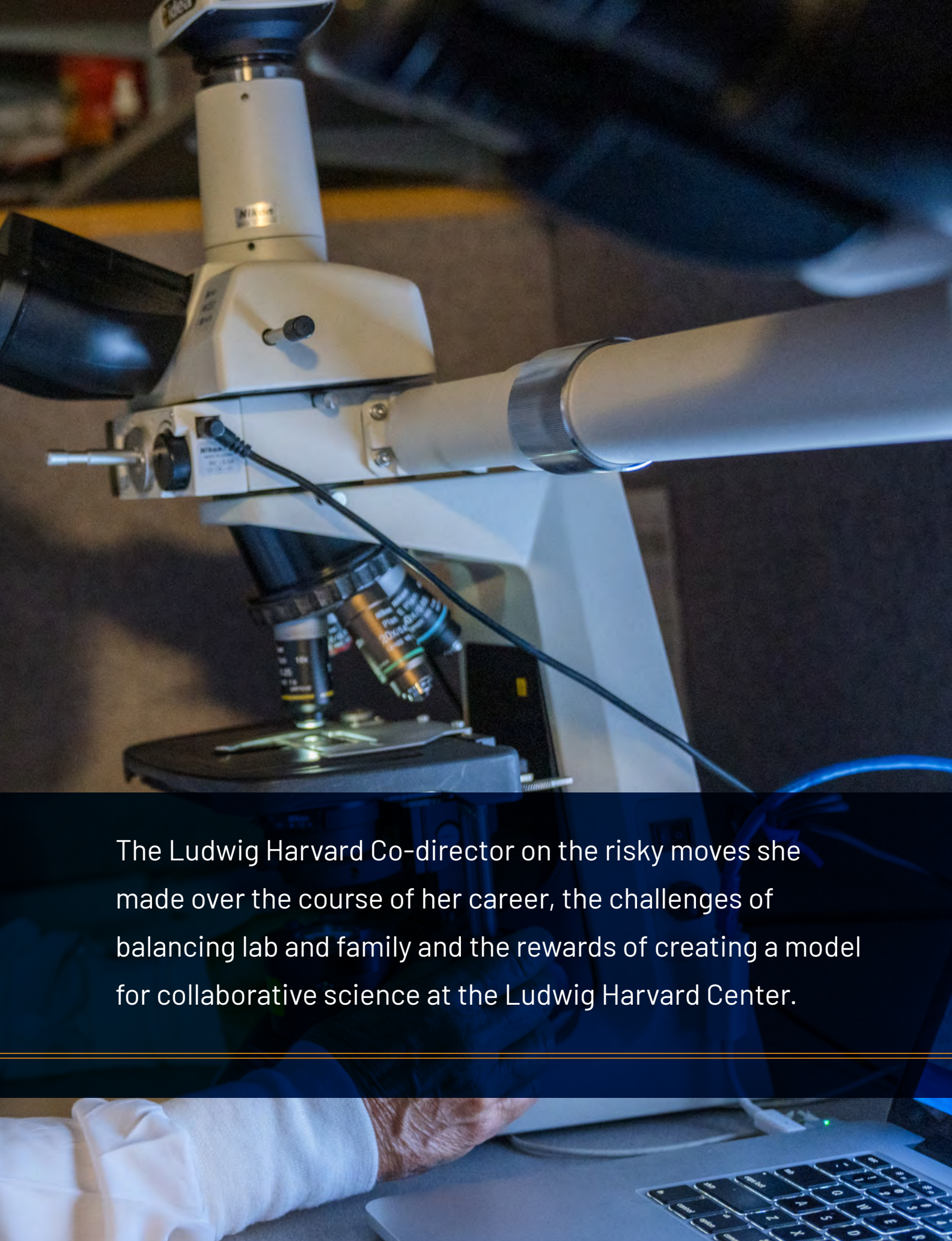


Joan
BRUGGE



The Ludwig Harvard Co-director on the risky moves she made over the course of her career, the challenges of balancing lab and family and the rewards of creating a model for collaborative science at the Ludwig Harvard Center.

Joan Brugge was 25 and finishing her PhD at Baylor College of Medicine in Texas when she began worrying that she wouldn't be able to excel as a scientist while simultaneously being a good mother and wife.

So, she decided she would complete a postdoc to hone her skills, but then seek a job as a research associate in someone else's lab instead of trying to start her own. "I was concerned that I wouldn't be able to handle the responsibilities of being a lab director and faculty member without it significantly compromising my ability to be a good mother and wife," Brugge recalls.

Aware of Brugge's concerns, her graduate advisor and role model Janet Butel pleaded with her to reconsider. As a young assistant professor who ran a rigorous lab investigating tumor viruses while raising two young kids, Butel had shown Brugge that it is possible to have a family and still be a successful scientist. Brugge just didn't think it was feasible for her. It would take several years—and a breakthrough scientific discovery made during her postdoctoral studies—to convince her otherwise.

That breakthrough was her identification of the Src protein, which is encoded by the Rous sarcoma virus and turns healthy cells cancerous. On the foundations of that discovery, Brugge went on to elucidate many basic mechanisms of cancer initiation, progression and resistance to therapy. After an interlude at a biotechnology company in the early 1990s, she returned to academia to take a new approach to studying cancer, developing three-dimensional cell culture models to better capture cellular evolution and behavior in tumors. Brugge, who is today co-director of the Ludwig Center at Harvard and professor of cell biology at Harvard Medical School, has used these sophisticated

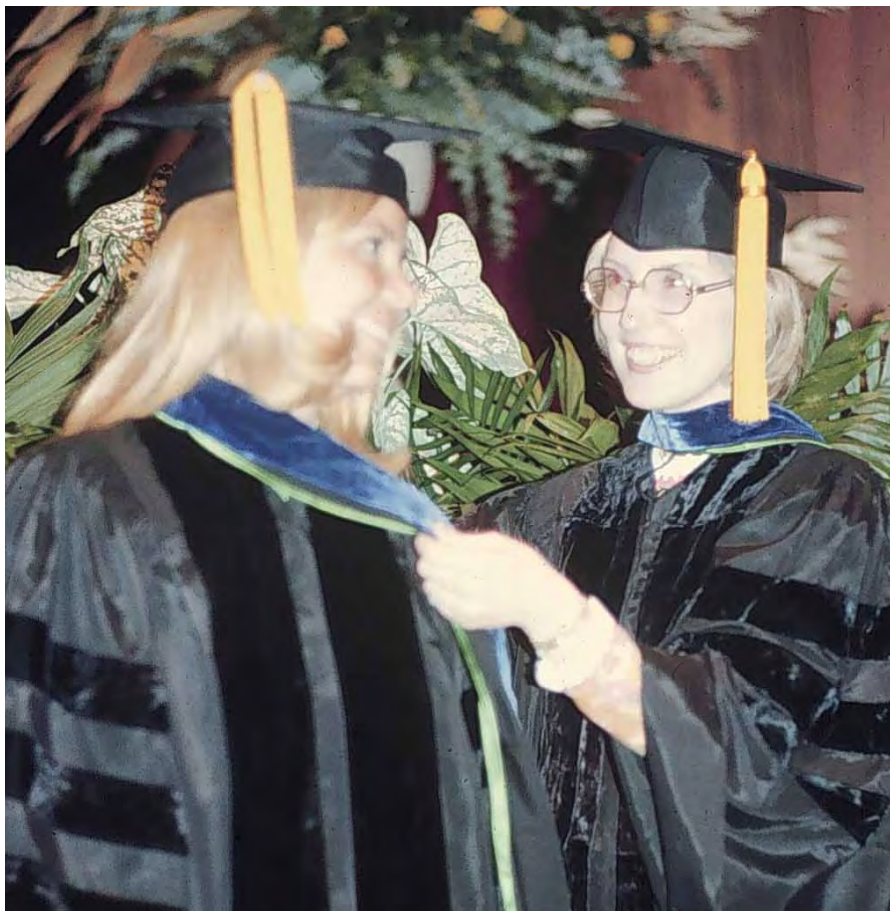
culture systems to make notable discoveries on the cellular heterogeneity of tumors and contribute to new strategies to treat the stubborn problem of drug resistance.

Her other passion is leading, in partnership with George Demetri, the Ludwig Center at Harvard, which the pair structured to encourage a highly collaborative and multidisciplinary approach to cancer research. "George and I wanted to harness the enormous expertise and brilliant minds within the Harvard community to collaborate to break through the enormous barriers to highly effective cancer therapies," says Brugge. "We built a community of investigators who are dedicated to this goal and recognize the value of collaboration. After six years, weekly interactions have led not only to many productive collaborations, but also an enormous expansion of our understanding about aspects of cancer outside our own areas of expertise."

A BEACON

The daughter of a paper salesman and a homemaker in Cincinnati, Ohio, Brugge was drawn to science and mathematics as a child. But she didn't even consider a career in either field until she got to college. "I had absolutely no role models to be inspired by," Brugge says. "At the time, the career options I was aware of were teaching or nursing. For young women in my generation, those were the opportunities."

Brugge was a sophomore at Northwestern University studying to be a high school



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Joan Brugge, left, at her PhD hooding ceremony with her mentor, Janet Butel.

math teacher when her younger sister was diagnosed with glioblastoma. She coped by reading everything she could find about cancer. “I wanted to understand how someone so young could develop cancer. Everybody I knew of who had cancer was older,” Brugge says.

Her readings focused on the accumulating evidence that viruses can cause cancer, and she was intrigued by both the hypothesis and the methods of its examination. “I was exposed for the first time to how experimental science was carried out—forming hypotheses, designing experiments, interpreting them, refining hypotheses,” Brugge recalls. “I was totally fascinated and just couldn’t get enough of it.”

Hooked, Brugge changed her major from

mathematics to biology. “My sister’s diagnosis and then death has really been the beacon for my interest in and devotion to cancer,” Brugge says. “It’s kept me on the track of doing something about it after seeing what she went through.”

A SLICE TO CELEBRATE

Brugge was well into her postdoc at the University of Colorado when she isolated the viral and cellular forms of the Src protein. The discovery marked a major advance in cancer research: it was the first retroviral oncogene product ever identified and her discovery laid the foundation for understanding how an oncogene could transform a normal cell into a tumor cell. Brugge was so excited she wanted to celebrate with champagne. But Ray Erikson, her advisor, urged caution. The



Joan Brugge with postdoctoral fellow Carman Li.

Photo by Sam Ogden

finding had to be confirmed, he said. Brugge settled for a commemorative pie.

By the time confirmation arrived, Brugge realized that aiming no higher than research associate would no longer suffice. “I wanted to have my own lab and be able to pursue this,” she says.

It also helped that her son Shawn, who was a year and a half when she was ready to start her search for an independent faculty position, was thriving in his new daycare. “We had a great situation where a family took care of Shawn because they wanted a playmate for their youngest daughter,” Brugge explains.

Even though there are more daycare options available to young researchers today, Brugge still sees members of her own lab struggling with finding childcare. “A postdoc in my lab, who’s pregnant and at the time was due in a few months, told me recently that she’s on the waiting list for five places,” Brugge says.

In this regard, societal and cultural norms tend to put more pressure on women scientists than on their male colleagues, Brugge notes. “When a child is sick, women, still more so than men, are seen as the go-to caregivers. For couples, it’s usually the woman who feels the sense of responsibility to take over under those circumstances. Part of it is society—I think it’s not as acceptable for a man to say, ‘My son’s sick,’ or, ‘My daughter’s sick. I can’t come in.’”

CHANGING COURSE

Brugge’s postdoc was followed by faculty positions at the State University of New York at Stony Brook and the University of Pennsylvania. But while Brugge found running her own lab at UPenn fulfilling, she soon felt she was being pulled in too many directions. “They hadn’t hired a senior person in 20 years, and there was a new dean, and he wanted to revitalize,” she recalls. “I was asked to get involved with

everything, and it felt like 80% of me was in 1% parcels all over the place.”

This was one factor in her decision, in 1992, to accept a position as the scientific director at ARIAD, a startup focused on structure-based drug design. Another was the opportunity to apply her skills to research that might benefit patients. After five years in industry, however, Brugge missed being more directly involved in research, so when a faculty position at Harvard Medical School became available, she accepted.

Brugge used the return to academia to shift her lab’s focus away from tumor viruses and the SRC gene. “It’s funny because people say to me, ‘Weren’t you scared to do that?’” Brugge says. “It just seemed like a really interesting thing to do. In retrospect, I see that it was risky, but I wasn’t even thinking about that.”

Brugge’s group began using a three-dimensional cell culture system that more closely resembles the structures of normal tissue and the distorted microenvironment of tumors to better study the initiation of cancer. “Up until that time, most of the studies in tumorigenesis were performed using fibroblasts cultured as a monolayer,” Brugge explains. “But most tumors are derived from epithelial cells, which were more difficult to culture. So, we decided to work on epithelial cells.”

OBITUARY EXERCISE

At Harvard, Brugge found herself struggling with balancing the demands of personal life and research. Brugge suspects this is a challenge that especially affects women.

“It is not uncommon in academics, for women especially, to be overly conscientious in contributing to the welfare of others and their institution, their department, their scientific community. I was not able to control this well and in addition, I was somewhat off-the-scale

in my scientific curiosity and tended to take on too many projects,” Brugge says.

Fortunately, a friend who witnessed Brugge struggling intervened and introduced her to a professional coach who taught her the importance of prioritizing her time and the need to say “no.”

For example, the coach had Brugge write out how she wanted her obituary to read. “It included descriptions of my contributions to cancer research, leadership and mentoring and other elements related to family. Then she says ‘If you want to accomplish these things, you have to stick to your priorities. You can’t let what you’re doing for others interfere with your ability to achieve your own goals and make a difference.’”

It’s a lesson Brugge tries to impart to others whenever she can, often using the same obituary exercise she was asked to perform. “Whenever I do a mentoring talk anywhere, especially with junior faculty, I talk about it,” Brugge says. “What I suggest to them is that they choose two important activities that they really want to do as service to their department and institution, then talk with their chair about it and use that as the reason for saying no to other things.”

It’s also important, especially for young women scientists, not to compare themselves to their senior role models, Brugge says. “I think one of the most significant factors leading to women dropping out at the postdoc stage is this. They look at more senior women and say, ‘I just can’t do that, and I don’t want to do it. I don’t want to sacrifice my family time for this.’”

Brugge advises young researchers to instead look at people who are on the next rung of the career ladder from themselves. “If you’re a postdoc, look at the junior faculty. If you’re junior faculty, look at the next rung, because you have to take baby steps. This is a job you grow into.”