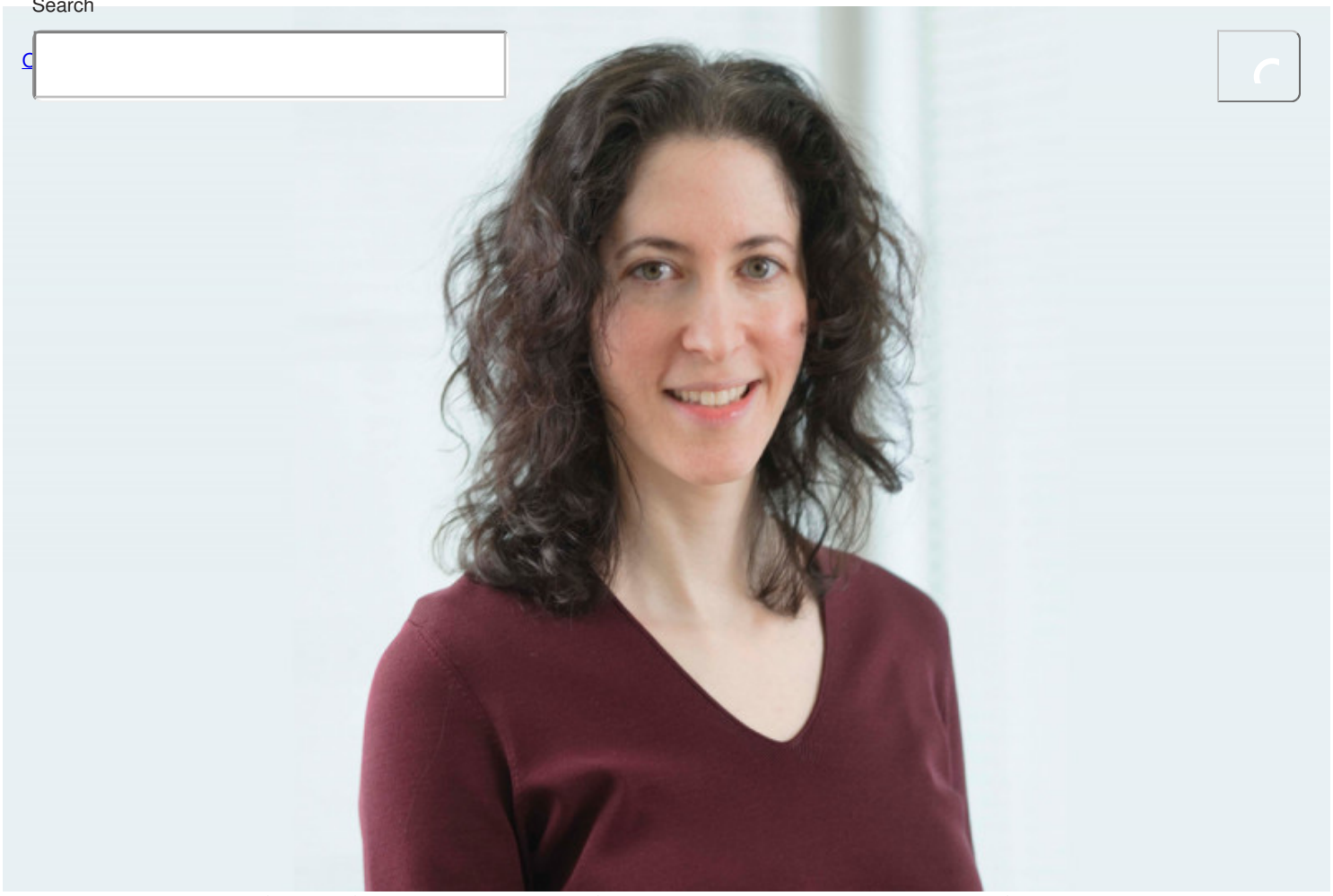
At Work: Developmental Biologist Jennifer Zallen



Developmental biologist Jennifer Zallen focuses on the generation of tissue structure through the collective action of cell populations. We spoke with her soon after she came to Memorial Sloan Kettering in late 2004.

For Jennifer Zallen, Head of the Morphogenesis and Polarity Laboratory in the Sloan Kettering Institute (SKI), science was and still is a family affair. From an early age, her mother, a biologist, and father, a physicist, showed her the wonders of science.

“I liked the idea that you can learn something about the world that wasn’t previously known,” Dr. Zallen explains. “Through my parents and their excitement for science, I learned that science gives you the opportunity to figure out how the world works.”

Her high school interest in math and science evolved, at Harvard University, into a burgeoning fascinating for biology. “It was the combination of my first molecular biology class and an opportunity to work in a lab that helped to set my direction,” she remembers.

Her undergraduate research was conducted at Harvard Medical School, where she studied the p53 gene, which is implicated in certain familial cancers. “We were looking at other families with slightly different presentations to see if they might also have mutations in p53.”

Dr. Zallen had chosen the field of human genetics for one simple reason: She wanted to know how humans work. As she quickly discovered in the course of her training, the path to understanding humans often begins with the study of simpler model organisms.

Graduate Study with C. elegans

After graduating from Harvard in 1992, she chose to do her doctoral work at the University of California, San Francisco, working in the lab of Cori Bargmann, a neuroscientist who was then in UCSF’s Department of Anatomy and of Biochemistry and Biophysics and is now a lab head at The Rockefeller University.

In her graduate work, Dr. Zallen studied the development of the nervous system, using the nematode *C. elegans* as a model system for investigating how neural circuits form. “The green fluorescent protein had just become available and I expressed it in a subset of neurons in the worm, which allowed us to observe part of one circuit,” she says.

Next, she disrupted genes at random, then looked for mutant worms where the circuits were aberrant. During this work, one of the genes Dr. Zallen cloned was the roundabout gene, which is a receptor that allows the growing axon to sense repulsive guidance cues in its environment. In an exciting turn of events that often comes about in studies on model organisms, these same repulsive cues that shape the developing nervous system have been shown to inhibit metastatic properties in human breast cancer cells.

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Convergent Extension

In 2000, Dr. Zallen started her postgraduate work at Princeton University with Eric Wieschaus, who won the Nobel Prize in 1995 for his pioneering work on the genetic control of development. Dr. Wieschaus’ research is centered on patterning and morphogenetic events in the early Drosophila embryo.

“I wanted to take these studies to the next level to ask how populations of cells work together to generate the coherent structure of a tissue or organ,” Dr. Zallen says. As a result of this desire, she chose to focus on a process called convergent extension, a dramatic example of coordinated cell movement that drives elongation of the body axis in both vertebrates and invertebrates.

“This is a situation in which communication between cells influences their decision about how to move,” Dr. Zallen says.

As she explains it, each cell only moves a very small distance — about one cell diameter from where it began — as a result the whole embryo doubles in length from head to tail. This highly efficient restructuring of the body axis arises from the coordination of cell movement across a multicellular population.

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Bipolarity and Disorder

Back in 1994, Ken Irvine in the Wieschaus Lab videotaped embryos to prove that cells actually move relative to their neighbors. Now, as Dr. Zallen explains, scientists can tag specific proteins with fluorescent markers and make high-resolution movies using lasers for illumination. “With this technique,” she says, “we can see what kind of changes are going on at the single-cell level, down to the fine details of cell morphology.” As a result, Dr. Zallen was able to identify proteins that localize to specific parts of the cell and predict which way the cell will move.

“It is valuable to have a molecular description of what is going on as the cells are moving,” she notes. “This gives us the opportunity to discover the mechanism that allows these cells to move in concert with their neighbors.” Dr. Zallen’s lab is now making use of the powerful genetic screens that are possible in the fruit fly in order to identify new genes involved in this process.

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Jennifer Zallen
Morphogenesis and Polarity Laboratory Head

Dr. Zallen has also sought input from a long-trusted source and recently published a paper with her father, a professor of Physics at Virginia Tech, describing their analysis of cell patterns in the fly embryo using approaches derived from condensed matter physics.

“We found that organized cell rearrangements that elongate the body axis are accompanied by an increase in disorder on the cellular level,” she says. “This disorder is a measurable feature of normal development that now provides us with a quantitative way to analyze a wide range of normal and abnormal scenarios.”

These are some of the areas of research that Dr. Zallen is pursuing in her new Morphogenesis and Polarity laboratory at SKI.

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Next Steps at SKI

The process known as tissue remodeling that she is currently studying is fundamental to establishing body form and generating the distinct shapes and functions of different organs. Morphogenesis relies on the integration of multiple cellular processes - such as cell polarity, motility, and adhesion - and these processes are directly modulated by communication between cells. Moreover, these processes can also be co-opted to promote the renegade cell movements that lead to tumor cell metastasis.

During convergent extension, cells have to recognize their appropriate neighbors. In metastasis, cells fail to recognize where they’re supposed to be, and this failure allows them to move to new locations in the body. She explains the implications: “By understanding how cell movements are normally regulated, we may be able to learn how to rob metastatic cells of their ability to spread.”

“I’m really excited to get my lab up and running, so we can dig into the research,” Dr. Zallen says with noticeable excitement. “Right from the start, the support at SKI has been incredible. The value of developmental biology is really appreciated here, and it’s exciting to be part of a program that is growing so rapidly.”

But of all the resources at SKI, Dr. Zallen counts her fellow scientists as the greatest asset, both within the Developmental Biology Program and in the Institute at large. “It’s been my great fortune to have worked every step of the way with inspiring scientists whom I deeply respect and admire,” says Dr. Zallen. “And I can only hope to follow their example in my own lab here at SKI.”

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