Kathryn V. Anderson (1952–2020)

The developmental biology community was deeply saddened to learn of the untimely death of Kathryn Anderson on November 30th. Kathryn's career embraced two distinct parts, both firmly rooted in her love of genetics. Her accomplishments have been recognised by a long list of awards. Her early contributions were to the field of *Drosophila* embryonic patterning. After a highly successful postdoc with Janni Nusslein-Volhard in Germany, Kathryn returned to start her own laboratory at University of California, Berkeley in 1985. Her focus continued on from her seminal identification of *Toll* as a key maternal gene that instructs the cylindrical fly egg to develop into a larva with a clear dorsal–ventral axis. Her rigorous and elegant genetic, biochemical and transplantation experiments conducted over the next decade revealed how components of the intracellular Toll signalling network become activated via the activities of a cascade of extracellular proteases, ultimately leading to the gradient that patterns the embryo. Kathryn's insights into Toll also laid the foundation for our understanding of its role in innate immunity, sepsis, and inflammation in vertebrates.

Not content with having almost single-handedly solved the problem of dorsal–ventral patterning in the fly, Kathryn next turned her attention to the mouse embryo. In 1993, she started a sabbatical in Rosa Beddington's laboratory at National Institute for Medical Research (NIMR), Mill Hill, London. At the time Valerie Wilson, Steve Harrison and Sally Dunwoodie were postdocs together with Ruth Arkell, a graduate student. All, including Rosa, were a little bemused that Kathryn, a highly credentialed *Drosophila* geneticist, seemed to think that six months would be sufficient to 'learn the mouse'! In the early 90's many labs were identifying genes required for vertebrate development by isolating homologues of *Drosophila* genes. Rosa, a mouse purist, stated that "the mouse is not a fly" and that "we" would approach this differently. Her lab made cDNA libraries from gastrulating mouse embryos to identify genes enriched in each germ layer. These were then mutated in vivo via gene targeting to investigate function. Kathryn wanted to assess whether *Spätzle*, one of the *Drosophila* dorsal–ventral patterning genes identified by her lab, was used during mouse development and convinced Sally to screen the mouse libraries for homologues.

Kathryn on the lawn at the Cold Spring Harbor Symposium on Embryonic Patterning. Photo courtesy of Cold Spring Harbor Laboratory Archives.

After several fruitless months the search was abandoned, and some time later it became evident that *Spätzle* is an arthropod-specific gene. Indeed, as Rosa had asserted and Kathryn now concurred, the mouse is not a fly.

Being thoroughly disavowed of the notion that the fundamental patterning mechanisms used by flies are conserved in vertebrates strengthened Kathryn's resolve that to capitalise on her foray into mouse development; a random mutagenesis screen would be the way forward. Whilst spending hours learning to dissect vanishingly small mouse gastrulae and trying to catch and handle tail-less *Brachyury* mice, Kathryn began to calculate the number of mice required for a random mutagenesis screen. Other mouse geneticists were making similar calculations, but, based on her deep knowledge of *Drosophila* screens, Kathryn embarked on a somewhat different and daring approach. On returning to Berkeley, Kathryn, together with her graduate student Andrew Kasarkis, established a genome-wide *N*-ethyl-*N*-nitrosourea (ENU)-mutagenesis screen for recessive mutations that affected embryonic development. Given that the mouse genome was not yet sequenced, many believed it would prove impossible to identify and validate the causative mutations. But Kathryn forged on, recognising that finding the phenotypes was of utmost importance and that genomics would rapidly bring the advances required for gene identification.

By 1996 Kathryn joined the Molecular Biology program of the Sloan Kettering Institute (SKI) in New York. The cross-country lab move was facilitated by her lab manager Ed Espinoza, who relocated with her and remains to the present. SKI provided the perfect environment where Kathryn could pursue her vision in the mouse model. The early days brought its distinct challenges, not the least of which was the first step, injecting feisty male mice with a potent mutagen. This was something she viewed with caution and sought advice from Liz Robertson on how she might do this unscathed. Liz's solution proved an easy one: deployment of a clear conical plastic bag device (cheerfully marketed as a "decapi-cone") which served the dual purpose of immobilising the mouse while allowing easy access to the appropriate body part requiring injection. At SKI, Kathryn's lab carried out a total of eight ENU screens. Such an immense undertaking would not have been possible were it not for Kathryn's meticulous planning and seamless coordination with her longtime research assistant Heather Alcorn, as well as her early collaboration with colleague Lee Niswander. Working as a team, they would identify mutants with interesting defects based on embryo morphology, perform preliminary mapping of candidate genes, and then hand them off to trainees to build their research projects on. One of their most paradigm-shifting discoveries was a series of mutants that linked a then obscure organelle, the cilium, to the well-studied Hedgehog signalling pathway. Kathryn's insights yielded a solution to a decade's long enigma.

Motivated by the resounding success of her approach, Kathryn continually refined the design of her screens, incorporating new ways to visualise tissues of interest. For example, in 2003 with postdoc Diana Laird she screened for mutants that affected primordial germ cell (PGC) specification and migration, wherein samples were painstakingly stained for PGC markers. By 2006, returning to *Brachyury*, she used a *Brachyury–T-GFP* transcriptional reporter generated by Kat Hadjantonakis to uncover mutants that affected gastrulation. While very few transcription factors emerged,

this approach revealed many previously unappreciated regulators that guide morphogenesis. Kathryn's most recent screen, carried out with postdocs Ben Cyge and Yinwen Liang, employed dual Arl13b-mCherry–Centrin-GFP protein fusion reporters to reveal cilia phenotypes, with Arl13b having itself been identified in a previous screen by her former postdoc Tamara Caspary. The final chapter of her career upheld Kathryn's conviction that forward genetic screens would uncover specifics of mammalian biology that were distinct from invertebrates.

In 2002, a dedicated Developmental Biology program was established at SKI, with Kathryn at the helm. Her founding faculty (Mary Baylies, Peter Besmer, Liz Lacy, Lee Niswander and Lorenz Studer) represented a diversity of interests, expertise and experimental models. Kathryn spearheaded the expansion of her program through recruitment of junior faculty. In 2004, Kat Hadjantonakis was the first to join, followed by Jen Zallen, Eric Lai and Songhai Shi. By 2007, Alex Joyner, who had pioneered the role of *Gli* genes in patterning of the mouse central nervous system, joined the group as a senior member, followed by Zhirong Bao, Julia Kaltschmidt and Mary Goll, while Danwei Huangfu, Kathryn's former graduate student, who was involved in making the connection between cilia and Hedgehog signalling, was recruited back. Maria Jasin, who had done pioneering work on DNA recombination also joined Kathryn's program. Tommy Vierbuchen was her final recruit. In building her program, Kathryn established a model for diversity in academia. She cared deeply about her colleagues and was committed to their success, and while she was not being one to impose her opinion, what she didn't say was as profound as what she did.

Kathryn was soft spoken but resolute, and possessed a quiet magnetism that drew people to her. She was extraordinarily modest and incredibly focused, often with few words to say to colleagues on topics not related to science, but always happy to join in, whether it be at the Mill Hill bar with a pint in her hand, by the dance floor at conferences, or chatting on the lawn of Cold Spring Harbor at the meetings and symposia she loved to attend. She is survived by Tim Bestor, her husband and a molecular biologist at Columbia University, and by trainees and colleagues who learned from her the secrets and rewards of doing the best experiments possible. Kathryn had a profound influence on both her fields of study. She was one of a kind; a principled colleague and simply wonderful friend. We will miss her terribly. ❐

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