

JEEM and my evolution in development

Ken Zaret

It may be hard to believe, but *The Journal of Embryology and Experimental Morphology* changed my life. As a PhD student, I was trained as a yeast geneticist and molecular biologist by Fred Sherman at the University of Rochester (NY, USA). At that time, developmental biology to me consisted of the lysis-lysogeny decision of phage lambda, sporulation in *Bacillus subtilis* and mating type switching in *Saccharomyces cerevisiae*. The real interest among my graduate colleagues was in the transcriptional regulatory mechanisms that were germane to each of these cell type decisions, and we questioned whether any other fundamentally different type of regulatory mechanisms existed. Such myopia is reminiscent of the skepticism that was met by the positive-regulation model for the arabinose operon when it was presented as an alternative to the repression model of the lactose operon in the mid-1960s. But in the early 1980s, genetics had begun to reveal that fundamental differences in mating type control existed between *Schizosaccharomyces pombe* and *Saccharomyces cerevisiae*, and as a result it came to be appreciated that cell fission in *S. pombe* was more like the biology of metazoan cells than the budding of *S. cerevisiae*. This circuitous logic led me to appreciate that, in fact, mammalian cells might have interesting regulatory mechanisms after all, and that they were most likely to be found during cell type decision making in embryogenesis.

It wasn't until after I had started my own laboratory at Brown University (RI, USA), in the mid-1980s, that I finally decided to learn something about embryology. I had already learned about mammalian hormone regulation as a postdoc with Keith Yamamoto at UC San Francisco (CA, USA) and then had started my laboratory with a new project: to determine how liver-specific gene transcription was controlled. The liver is the biggest organ in the mouse and is relatively homogeneous in cell type. In addition, at the time, the liver gene regulation field seemed wide open. But within 2 years of starting my laboratory, Ueli Schibler, James Darnell, Moshe Yaniv, Shirley Tilghman, Riccardo Cortese and other well-established investigators published groundbreaking research on liver gene regulation in some of the top journals. This intense competition clarified my thoughts: the other groups would focus primarily on adult liver gene expression, but to access the basis of cell type control, I would investigate the earliest stages of hepatogenesis. All I had to do was to get a hold of some mouse embryos and then figure out what I could do with them.

This period coincided with my having to write a competing renewal of my first NIH grant, and I spent several weeks living in the Brown University Science Library. It's a tall modern building,

but with the requisite musty smell in the book stacks. Fired by my new interest in embryology as a basis for my grant renewal, I pored over old texts and articles, catching up on what I would have learnt if I had taken a proper developmental biology course in college. And there I came upon a strange journal bound in hardcover: *The Journal of Embryology and Experimental Morphology* (also known as *JEEM*). Although, at first, the authoritative feel of *JEEM* came from its cover, heavy paper stock and glossy images, as I read more in the field of early mouse embryology, all the references seemed to point to articles in *JEEM* as providing the most definitive statements in the field.

My early readings of *JEEM* led me to papers by Patrick Tam and Michael Snow on their remarkable ability to culture primitive streak mouse embryos *in vitro* (Tam and Snow, 1980); by Snow on the clonality and autonomous development of early mouse embryo segments (Snow, 1981); by Richard Gardner on the origin of the endoderm (Gardner, 1985); by Elizabeth Houssaint and Sumiko Fukuda-Taira on the ability of cardiac mesoderm to induce liver cells within the endoderm (Houssaint, 1976; Fukuda-Taira, 1981), following on the original discovery by Nicole LeDouarin (see LeDouarin, 1975); by Glenn Rosenquist on fate mapping of hepatogenic cells (Rosenquist, 1971); by G. R. Johnson and R. O. Jones on the reconstitution of embryonic liver differentiation *in vitro* (Johnson and Jones, 1973); and by Nobuyoshi Shiojiri on the transition of hepatoblasts to hepatocytes and biliary cells (Shiojiri 1981; Shiojiri, 1984).

These papers convinced me that mouse embryos and tissue fragments could be fate mapped, isolated and cultivated like the tissues of frog embryos, and that I could gain experimental purchase on the embryology of the mouse using molecular biological approaches. (At the time, genetic approaches to studying individual cell and tissue types still seemed far off.) In the end (or rather at the beginning of my life in developmental biology), *JEEM* was instrumental in my personal evolution because it provided me, and others in the field, with a high-quality venue in which sometimes baroque, but thoughtful and fascinating, developmental biology on mouse embryos was being published. I was hooked.

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