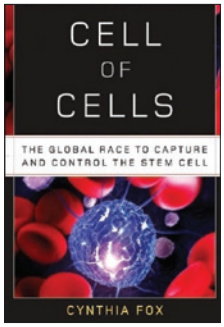
The stem cell parade



Cell of Cells

Cynthia Fox

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Reviewed by Margaret A Goodell

The stem cell field has exploded over the past ten years, from a few curious and dedicated investigators to a virtual Mardi Gras parade of scientists, with young investigators joining in droves and senior investigators donning stem cell cloaks to jump on a passing float. Cynthia Fox takes a historian's perspective to explore the key transforming events in this field, such as the first isolation of human embryonic stem (ES) cells and the *in vitro* fertilization–based origins of therapeutic cloning. Fox presents a lively and readable story, getting most of her facts right, although the history will undoubtedly be refined with time as we gain greater perspective on the relative importance of various events.

For Fox, her research seems to have been a religious experience, as she makes religious allusions throughout, titling one chapter "In the Beginning" and another "Scientific Pilgrimages." While visiting human ES cell labs in Israel, she is told that the Old City of Jerusalem is dangerous to visit but feels compelled to go (without incident) to soak in the atmosphere, as if stem cells were somehow prophesied in the ancient stones. She also describes some clinicians as "saviors" and talks about "miracle cures," emphasizing a sense of worship toward the exalted stem cells. A no-nonsense scientist may find the reverence excessive.

Still, I enjoyed Fox's exploration of the "ancient" history of the field, some of which was new to me. She describes events in animal cloning research surrounding the report of Dolly, the first cloned sheep, including interest in regenerating the mammoth for a Pleistocene park in Siberia and the desire by Chinese agricultural experts to expedite introduction of hyper-lactating American cows into their herds via *in vitro* fertilization. Fox also gives due credit to Leroy Stevens, who first worked with teratomas, recognizing that they harbor cells with extraordinary developmental potential; Stevens' work is now considered to have driven the isolation of ES cells. Fox even manages to cite Virchow, the mid–nineteenth-century German pathologist who first posited the existence of stem cells. But how did she miss recognizing Till and McCullough, the 2005 Lasker Award winners who were the first to publish definitive evidence that adult stem cells truly exist?

Also enjoyable is her portrayal of the unique personalities of the field as real people. She managed to capture the elfin nature of Ron McKay, the joyous pontificating of Irv Weissman and the intellectualism of David Anderson, who is described as reading a textbook while attending a baseball game with his colleagues. These characters, and the stories Fox uses to illustrate her history, bring the science to life. Nonscientist readers may eventually appreciate that not all scientists are humorless nerds, but lively and varied people who are driven by their love for their work and yet sometimes go on vacations (when inevitably something interesting happens in the lab).

Praiseworthy, too, is Fox's unusually global depiction of the development of the field, which is refreshing in our typically US-centric (and even California-centric) view. She starts out with camels in Egypt, describing a tentative collaboration between Egyptian and Israeli stem cell scientists, and devotes an entire chapter to "Stem Cells in the Sahara." She travels to Jordan, Australia, Singapore, China, Korea, Japan and, of course, all over the US (she seems to have bypassed Europe and the UK). Whereas most US scientists have a more myopic view, the very dynamic picture that Fox draws is rich and fascinating.

Although the book is entertaining, there are some shortcomings that are probably inevitable when one is trying to write a history of a field that is still developing. First, Fox sometimes seems unable to distinguish between the truly significant events (and people) in the history and those with transient importance. There are events, as well as clinical vignettes, that Fox devotes a great deal of attention to that will probably fade in importance with time. Fox also misses the induced pluripotential stem (iPS) cell revolution, and, although this is in part a misfortune of publication timing, she seems not even to have seen it coming. Despite her focus on the developments of therapeutic cloning, she does not explain that their goal was to turn everyday cells into pluripotential stem cells that could do anything. Many in the field felt that nuclear transfer was important to prove that reprogramming could be done, but that it was unlikely to be practical on a large scale. Hence many labs worked to identify pluripotency factors that could reprogram a differentiated cell. Shinya Yamanaka's first paper describing mouse skin cells reprogrammed into ES cells was published in 2006, before the book went to press; he also presented the work at major meetings that year. Eighteen months later (after the book was published), multiple labs. reported the generation of human iPS cells Although the speed of this human translation was unexpected, the importance of the 2006 Yamanaka paper was widely appreciated in the field. The scientific and ethical impact of iPS cells is enormous and alters the importance of some of the issues Fox considers, such as problems with egg procurement and immune rejection. The iPS race, too, is filled with colorful personalities who will undoubtedly comprise a fabulous addendum.

Fox apparently had no fact-checker, and thus some errors are introduced, probably owing to mistranscription from taped interviews (in her words, sperm are "boiled" at 19 degrees Celsius). However, the index is terrific—I could easily find plenty of pithy quotes from my inimitable colleagues, although the number of their citations sometimes has less to do with their contributions to the field than with their oratorical style!

The book is written for an educated lay audience, but could also be enjoyed by interested scientists within or outside the stem cell field. Even though it is not yet the definitive history of the field, Fox has beautifully described a broad swath of this exciting parade.

Cynthia Fox's response to this review

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