STEM CELLS

Single-cell breast implants

Two groups have independently isolated mouse mammary stem cells, definitively demonstrating their pluripotency by showing that a single cell can reconstitute an entire mammary gland *in vivo*.

The best known adult stem cells, hematopoietic stem cells, can generate the entire set of cells that make up blood. The existence of equivalent stem cells for epithelial tissues has been suspected for a long time, but proof that this regenerative capacity comes from a single cell was missing.

Now two groups, led by Jane Visvader and Geoffrey Lindeman at the Walter and Eliza Hall Institute in Melbourne, and Connie Eaves at the British Columbia Cancer Agency in Vancouver, have identified surface markers that can be used to isolate stem cells from the mouse mammary gland. In recent *Nature* articles, they describe how they isolated cell populations with these markers and diluted the populations down to single cells that demonstrated regenerative capabilities in a transplant model (Shackleton *et al.*, 2006; Stingl *et al.*, 2006; **Fig. 1**).

Their techniques were largely similar to those used to identify hematopoietic stem cells. "Experimental hematologists have provided the gold standard here," explains Visvader, "because they performed experiments at limiting dilution using a stringent *in vivo* assay." Unlike blood cells, however, epithelial cells are not normally found in suspension, and both groups acknowledge that the preparation of initial suspensions of viable cells by fine-tuned enzymatic digestion was no small feat. But it was worth it because the optimized preparations were fast, allowing the use of fresh cells—a key to success.

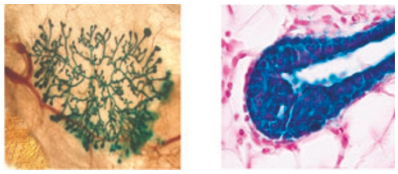

Figure 1 | Epithelial outgrowth obtained *in vivo* from a single mouse mammary stem cell (left), and an endbud from one such outgrowth (right). Images reprinted with permission from *Nature*.

The two groups started their work unbeknownst to each other, but then kept in touch and were gratified to learn their findings correlated. "Overall it was an ideal collaboration, and it is very reassuring to see many of the key concepts validated by different approaches in the two studies," says Eaves.

Eaves' group has performed gene expression analysis of the stem cells and found that the mammary epithelium contains another population of progenitors. Visvader's group found that mammary stem cells are expanded in a mouse model of tumorigenesis, supporting the concept that breast cancer could originate from so-called 'cancer stem cells'.

Both groups now intend to purify these cells further. And then they will go after human mammary stem cells, a goal that holds new challenges. For example, the transplant strategy is much less efficient with human cells, and there is no reason to believe that the markers will be the same.

Nonetheless, useful markers for mammary stem cells are finally available and both Visvader and Eaves are confident that they will be used. "Hopefully it will provide a very good and useful framework for other mammary cell biologists," says Visvader, "the two papers together should at least do that."

Veronique Kiermer

RESEARCH PAPERS

Shackleton, M. *et al.* Generation of a functional mammary gland from a single stem cell. *Nature* **439**, 84–88 (2006).

Stingl, J. *et al.* Purification and unique properties of mammary epithelial stem cells. *Nature;* published online 4 January 2006.