IN THE NEWS

Egg-citing fertility finding

For a long time scientists have been puzzled by the difference between male and female reproductive biology; why do males make fresh sperm daily, yet females are born with all the eggs they will ever have? The dogma was that female mammals lack renewing egg stem cells. But now an astonishing discovery by Jonathan Tilly and his team at Massachusetts General Hospital, USA, shows that germline stem cells do exist.

Tilly and colleagues studied the number of dying follicles — the tiny sacs in which eggs grow — in female mice, which are fertile for more than a year. Surprisingly, follicles died so rapidly that mice should have become infertile after only weeks. This provided indirect evidence that new egg cells were being produced.

When fragments of ovaries from normal mice were transplanted into transgenic mice that expressed fluorescent protein in all cells, glowing follicles were observed in the transplanted tissue after a few weeks, which confirmed that new eggs can develop from existing stem cells.

"We had a six-month period of disbelief, when we had trouble digesting the whole thing," claims Tilly. "The shock people may feel on seeing this paper, trust me, we went through it as well." (*The New York Times*, 11 March 2004).

The researchers are confident that they will find germline stem cells in human ovaries, which would open the way to treating infertility problems. "Women could essentially grow back their ovaries after [chemo]therapy." says Tilly. "The possibilities are almost too numerous to mention." (*NewScientist.com*, 10 March 2004).

Emma Croager

DEVELOPMENTAL BIOLOGY

Molecular relay

The concept of morphogens has been one of the most significant additions to our understanding of developmental biology over the past half-century or so. The idea is that these signalling molecules are secreted by one set of cells and then move away, forming a gradient that other cells can use to work out where they are in the embryo, and so what they should become. But how exactly do morphogens move? There are several theories — ranging from diffusion to active transport through each cell — and each has some support from studies of particular morphogens. Now, writing in *Development*, Lin and colleagues add more flesh to the idea that morphogens can be passed from one cell to another in a molecular relay.

The authors studied the Hedgehog signalling protein, which is involved in tissue patterning in many different animals. Another protein, Tout-velu (Ttv), is known to be needed for Hedgehog to move across fields of cells in fruitflies. This requirement was assumed to be related in some way to Ttv's ability to modify simple precursors to generate cell-surface heparan sulphate proteoglycans (HSPGs). So Lin and co-workers first sought to identify the HSPGs that are required for Hedgehog signalling.

One category of HSPGs comprises the glypicans Dally and Dally-like (Dly), so the authors generated null alleles of the genes encoding these proteins. They found that Dally and Dly are needed, but seem to function redundantly, in Hedgehog signalling in fruitfly wings: inactivating both proteins together, but not either one alone, produced a phenotype similar to that resulting from loss of Hedgehog. Using western-blot analysis, the group also showed that Dally and Dly are substrates of Ttv. Together, these findings indicate that Ttv probably exerts its effects on Hedgehog signalling through these proteins.

So what might Dally and Dly do? In the developing wing disc, Hedgehog usually moves from its source in the posterior compartment to receiving cells in the anterior compartment. But when Lin and co-workers generated a narrow band of Dally- and Dly-deficient cells between the signalling and receiving cells, a particular transcriptional response to Hedgehog was not detected in the recipients. This hints that Hedgehog does not diffuse freely, but, rather, must be relayed from one cell to another, in a manner that is dependent on Dally and Dly. The authors also showed that Hedgehog is unlikely to be transported into each cell and out the other side: when endocytosis was inhibited by mutating the motor protein dynamin, Hedgehog signalling was not reduced.

So the authors propose that, when Hedgehog is released from the cells that produce it, it latches on to Dally and Dly on the cell surface. A concentration variation ensures that Hedgehog is driven down the gradient from one HSPG to another, and from one cell to another. Further work is now needed to refine the details of this theory, and to see whether other models for Hedgehog transport still apply — these findings don't, for instance, rule out the possibility that receiving cells can extend long 'fingers' to pick up the signal.

Amanda Tromans

References and links

ORIGINAL RESEARCH PAPER Han, C. *et al. Drosophila* glycipans control the cell-to-cell movement of Hedgehog by a dynamin-independent process. *Development* **131**, 601–611 (2004)