STEM CELLS

Moving out of the niche

> FGF guides tracheal progenitor cells out of their niche

During tissue homeostasis and after injury, adult stem cells are activated to proliferate and exit their niche — the specific microenvironment in which they reside — to form new tissues. The signals that guide stem cells out of their niche are poorly characterized. Chen and Krasnow now find that fibroblast growth factor (FGF) produced by decaying branches guides progenitor cells to form new tracheal tissue in *Drosophila melanogaster*.

The authors studied tracheal outgrowth during metamorphosis, when the posterior half of the larval tracheal system decays and tracheal imaginal progenitor cells are activated to replace it. By labelling activated progenitor cells and larval tracheal branches with GFP and RFP (red fluorescent protein), respectively, they observed that progenitor cells leave the niche and 'crawl' in clusters along the basal surface of larval tracheal cells. These posteriorly migrating progenitor cells maintain epithelial polarity, form a sac-shaped lumen and differentiate as they crawl; the newly formed pupal abdominal tracheae (PAT) mature as the posterior larval tracheal branches collapse.

So, what guides progenitor cells along specific branches of the larval tracheal system? Expression of a dominant-negative version of the FGF receptor Breathless (Btl), which is known to be expressed in PAT progenitor cells, blocked progenitor cell migration and prevented the formation of new tracheal Branches. Furthermore, the authors found that the Btl ligand branchless (Bnl) was specifically expressed by larval tracheal cells along the progenitor outgrowth path. Bnl expression was dynamic and almost perfectly matched the position and timing of progenitor cell migration, which suggests that Bnl is required for progenitor outgrowth. Indeed, RNAi-mediated knockdown of *bnl* expression reduced or abolished PAT formation. Moreover, ectopic *bnl* expression redirected progenitor cell migration, causing incorrect exit from the niche and/or migration in the wrong direction.

Thus, Bnl FGF guides tracheal progenitor cells out of their niche and into the posterior during tracheal morphogenesis. The decaying larval tracheal branches function both as a source of Bnl and as a substratum for cell migration. This suggests that signals from decaying tissue might be more generally used during tissue repair and homeostasis to direct stem or progenitor cells to appropriate sites.

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ORIGINAL RESEARCH PAPER Chen, F. & Krasnow, M. A. Progenitor outgrowth from the niche in *Drosophila* trachea is guided by FGF from decaying branches. *Science* **343**, 186–189 (2014)

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