Figure 1 How blood vessels develop. **a**, Arteries and veins are formed from precursor cells called angioblasts, which are initially found in the lateral posterior mesoderm (a tissue in the periphery of the embryo). Zhong *et al.*¹ show that, in zebrafish, angioblasts that express the proteins Notch and Gridlock will contribute to arteries. Those that do not express these proteins will contribute to veins. **b**, Once committed to forming arteries or veins, the cells migrate towards the midline and coalesce to form the appropriate blood vessel. The figure shows a cross-section of an embryo.

blasts in the LPM with a fluorescent tag and monitoring their fate. This appeared to be predetermined: all the progeny of a given angioblast ended up in either the aorta or a vein, but not both. Zhong *et al.* then looked at whether *gridlock* prompts angioblasts to form arteries. They decreased levels of the Gridlock protein by using modified antisense oligonucleotides, and found a dose-dependent reduction in the size of the aorta, and an increase in the adjacent vein. Reciprocally, increasing Gridlock activity by injecting *gridlock* messenger RNA into early embryos decreased the size of the vein (though it did not increase the size of the aorta). The implication is that angioblasts make up a limited pool of precursors whose default fate is venous, and that the expression of *gridlock* suppresses the venous characteristics and helps to drive the precursors towards forming an aorta.

Transcriptional repressors that are related to Gridlock can be expressed in response to signals from the Notch family of receptor proteins. To find out whether this applies to Gridlock as well, Zhong *et al.* injected either an activated form of Notch1 or an inhibitor of the Notch1 signalling pathway into zebrafish embryos. They found that activation of the pathway by Notch1 induced the expression of *gridlock*, whereas suppression of the pathway both reduced *gridlock* expression and disrupted the formation of the aorta.

Another study⁵, by Lawson *et al.*, had already implicated the Notch pathway in arterial fate, particularly in the expression of artery-specific proteins such as ephrinB2. But these authors found that certain arterial characteristics — such as the expression of ephrinB2 — could be ablated even when *gridlock* expression was maintained, raising questions about where *gridlock* comes into artery determination. These findings can be reconciled with those of Zhong *et al.* if one assumes that the response to *gridlock* is dose dependent, as indeed Zhong *et al.*'s results suggest. So, the total absence of *gridlock*

results in the default venous fate and obliteration of the aorta. Partial expression of *gridlock* (as may have occurred in Lawson *et al.*'s study) allows some characteristics of an artery to develop, but not all, as reflected by the lack of expression of proteins such as ephrinB2.

It seems, then, that the Notch/Gridlock pathway predetermines the fate of angioblasts (Fig. 1). Of course, questions remain. How, for example, do these precursors migrate to the appropriate site and then coalesce only with similarly fated cells? The ephrin proteins and their receptors are known to be involved in the migration and sorting of other cell types, and seem likely to help maintain the identities of different blood-vessel precursors. But do they act in the LPM, in the migration pathway, or in blood vessels themselves?

Moreover, although the nature of vascular cells may indeed be predetermined by a genetic programme before blood flow begins, many studies of vessel transplantation in embryos and adults have indicated that vessels can remodel and switch their identity. Indeed, surgeons commonly transplant the saphenous vein into segments of diseased arteries. It will be fascinating to look at the involvement of proteins such as Notch1 and Gridlock during cellular reprogramming in the course of arterial disease and in transplanted veins. With this in mind, we now need to find out if the zebrafish work can be translated to mammals. Stay tuned for further gridlock alerts!

Gavin Thurston and George D. Yancopoulos are at Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591, USA. e-mails: gavin.thurston@regeneron.com george@regeneron.com

1. Zhong, T. P., Childs, S., Leu, J. P. & Fishman, M. C. *Nature* **414**, 216–220 (2001).
2. Wang, H. U., Chen, Z. F. & Anderson, D. J. *Cell* **93**, 741–753 (1998).
3. Weinstein, B. M., Stemple, D. L., Driever, W. & Fishman, M. C. *Nature Med.* **1**, 1143–1147 (1995).
4. Zhong, T. P., Rosenberg, M., Mohideen, M. A., Weinstein, B. & Fishman, M. C. *Science* **287**, 1820–1824 (2000).
5. Lawson, N. D. *et al.* *Development* **128**, 3675–3683 (2001).

Daedalus

Vacuum in miniature

Meredith Thring once proposed a domestic robot to operate other machines, such as the vacuum cleaner, but was unable to give it human intelligence. Annoyed by the vacuum cleaner, Daedalus is now scaling it down. His ideal is a dedicated, chip-operated cleaner maybe only 3 cm across. Unlike bigger machines, it will need no operator, and will run continuously, like a diminutive pet. On tiny wheels it will nose along the carpet, sucking vigorously at everything that seems foreign to its environment. It will pack loose dust, skin particles and fibre into a little sack.

Like W. Grey Walter's old *Machina habilis*, the new microcleaner will be alert to the state of charge of its batteries. When they are low, or when its sack is full, it will head back to an illuminated or otherwise designated charging base. There the microcleaner will acquire electricity and dump its haul of rubbish, ideally in a box that can be disposed of when full.

A small vacuum device can be far more effective than a larger version, and can study possible waste more carefully. Modern chips allow a microcleaner to be quite flexible in its approach. An ultrasonic sensor will tell it where it is at all times. It will map an entire room into parallel tranches — several hundred tracks and many hundred of metres to be covered at maybe a metre every few minutes, perhaps at night if it is quiet enough. It will avoid cats, papers, feet and so on, remembering to revisit the site later. It will soon learn the regular occupants of the room (such as the furniture) and their degree of permanence.

The microcleaner should effortlessly displace bigger and clumsier machines. It will run all the time, cleaning an entire room in about a week, far more efficiently than any hand-held device. Then it will start again. Its owner will merely have to dispose of the dust and fluff it piles up at its charging-station. Unlike traditional machines it will need no operator, and it will tirelessly revisit sites temporarily denied to it.

Each room or pair of rooms will have its own cleaner. A household kitchen or dining-room will have a model that specializes in various sorts of spilt food; a factory will have one that knows how best to remove the particular swarf or waste it will find. The discriminating microcleaner will remove green fluff from a red carpet, but not from a mixed one. But mud, loose fluff, superfluous food, loose tea-leaves and metal turnings will be removed wherever they are.

David Jones