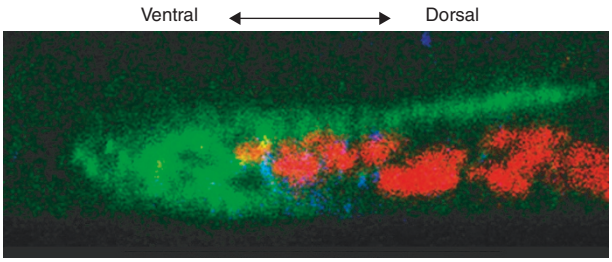
Getting a straight boundary

The development of any organism relies on the formation of boundaries between homogeneous populations of cells. These boundaries generate compartments of cells that do not intermingle. Work recently published in *Cell* by Marco Milán, Stephen Cohen and colleagues (*Cell* **106,** 785–794, 2001) identifies two transmembrane proteins with leucine-rich repeats, known as Capricious (Caps) and Tartan, that contribute to this process.

Formation of the dorsal/ventral compartment boundary in *Drosophila melanogaster* has been extensively studied to understand how cells are separated into different populations and lineages. The transcription factor Apterous (Ap) is required for the formation of the dorsal/ventral boundary and is expressed in the dorsal wing compartment. Ap controls the expression of genes regulating the development of the boundary and is essential for the development of the entire dorsal wing compartment. It has long been postulated that cells in different compartments of the *Drosophila* wing have altered affinities for one another, but this has not yet been confirmed.

Cohen and colleagues showed that both *caps* and *tartan* are expressed only in the dorsal compartment of the wing, and that this expression relies on *apterous*. Interestingly, when clones of cells expressing *caps* or *tartan* are generated in the ventral compartment of the wing, these clones try to migrate towards the dorsal compartment. The clones actually push into a stripe of Wingless at the dorsal/ventral boundary and move it dorsally. This stripe is required for supporting the growth and patterning of the wing and is a consequence of dorsal/ventral boundary formation. If the clones expressing *caps* or *tartan* are made early enough in development, the dorsal/ventral boundary is severely distorted.



Marco Milán and Stephen Cohen

As Caps and Tartan seem to have no effect on homophilic adhesion, Milán *et al.* propose that both molecules interact with an unknown protein expressed in the dorsal compartment. One insight into how these proteins might lead to cell sorting comes from analysing ventral clones expressing *caps* under the confocal microscope. Under the microscope these clones have membrane-bound cellular processes that extend towards the dorsal comparment (see figure, Caps protein (green), *wingless* (blue), *apterous* (red)). These processes are quite possibly filopodia and could act to increase the affinity of cells within the dorsal compartment for one another.

The identification of these two proteins, which seem to mediate the affinity between cells of separate compartments, opens the way to further insight into how cells of different lineage separate from each other.

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The expanding world of oxidative protein folding

Hiroshi Kadokura and Jon Beckwith

An ever-expanding and diverse collection of proteins and small molecules is involved in the pathways leading to protein disulphide bond formation. However, the origin of oxidative power for this process in the eukaryotic endoplasmic reticulum has remained mysterious. It has now been shown that in the yeast endoplasmic reticulum (ER), the catalyst Erv2p, a member of the Erv1p/ALR protein family, uses molecular oxygen directly to contribute oxidizing equivalents for disulphide bond formation.

Disulphide bond formation is a crucial step in the folding of many secretory proteins. This process ordinarily occurs in specialized subcellular compartments: the periplasm of Gram-negative bacteria and the endoplasmic reticulum (ER) of eukaryotes. Early experiments by Anfinsen and co-workers[1] suggested that disulphide bond formation was simple: the joining of two cysteine residues in proteins required only an environment in which oxygen or a molecule such as oxidized glutathione was present. However, later studies in *Escherichia coli* and *Saccharomyces cerevisiae* made it clear that oxidative enzyme catalysts were necessary for disulphide bond formation in vivo in both prokaryotes and eukaryotes[2,3]. Further investigation of these systems has revealed that a process originally considered to be simple and spontaneous exhibits extraordinary complexity and entails a host of cellular proteins and small molecules involved in electron transfer. In last month's issue of *Nature Cell Biology*, Kaiser and colleagues further illuminate the process in yeast with the discovery that molecular oxygen interacts directly with a luminal ER protein, Erv2p, to provide oxidizing potential for disulphide bond formation[4]. Their results open up many new questions about the role of the large Erv1p/ALR family of proteins.