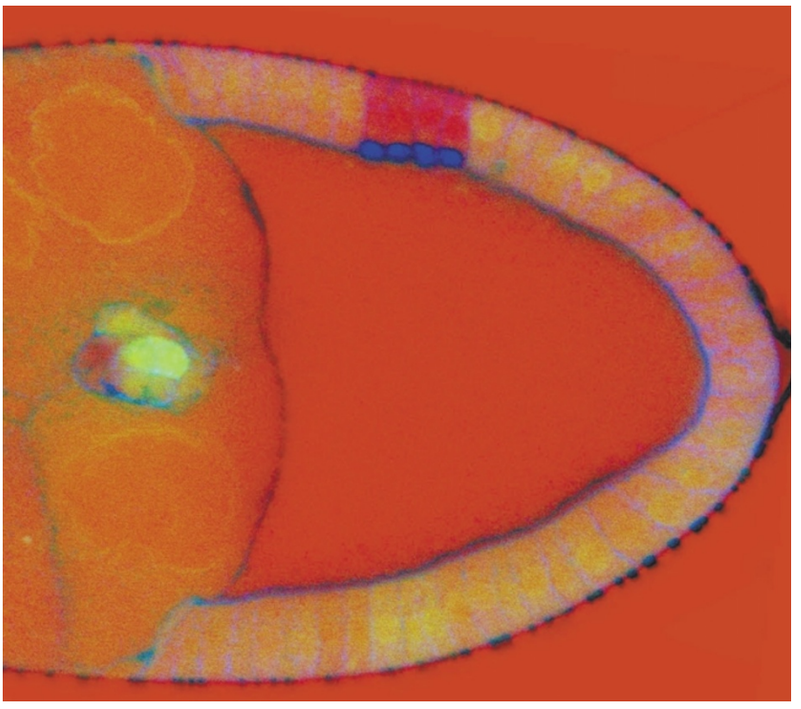

organization. Ena clones, however, lose actin filaments.

Given that mammalian Abl binds CAP and antagonizes the function of Ena, Baum and Perrimon went on to determine whether CAP/Abl/Ena act together to control the level and localization of F-actin. Epistatic experiments allowed them to place Ena genetically downstream of CAP in regulating actin organization, as loss of CAP leads to a change in the localization of both Ena and Abl.

Therefore, it seems that the action of actin-regulatory proteins within an intact organism is very similar to the system previously observed in mammalian cells. CAP, in collaboration with Abl, inhibits actin polymerization, whereas Ena acts in the opposite way. This set of genes acts together to ensure the correct levels of actin are made and localized to their proper locations, and so they ensure the cap always fits.

Sarah Greaves, Senior Editor,
Nature Cell Biology

References and links

ORIGINAL RESEARCH PAPER Baum, B. & Perrimon, N. Spatial control of the actin cytoskeleton in *Drosophila* epithelial cells. *Nature Cell Biol.* **3**, 883–890 (2001)

WEB SITE Perrimon lab:
http://genetics.med.harvard.edu/~perrimon/

location of immunoglobulin alleles in mature B cells was revealed by combining immunofluorescence and fluorescence *in situ* hybridization (FISH) techniques.

Resting primary B cells were stimulated to proliferate, causing the recruitment of Ikaros to heterochromatic regions. In almost all the cells observed, only one *IgH* allele was associated with Ikaros-containing centromeric domains. Similarly, three of the four possible light chain alleles were centromeric. By contrast, neither *IgH* allele was found in association with centromeric domains in progenitor B-cell clones, indicating that non-equivalent nuclear localization of immunoglobulin alleles is acquired during B-cell development. Using specific messenger RNA probes, the authors confirmed that mature B cells express only one allele, which is consistently the non-centromeric allele.

In terms of transcription, centromeres are relatively inactive regions of the nucleus. The authors propose that during B-cell proliferation, the centromeric recruitment of immunoglobulin alleles excluded during development helps to keep them quiet — crucially maintaining the monospecificity of a B-cell clone.

Jen Bell, Associate Editor,
Nature Reviews Immunology

References and links

ORIGINAL RESEARCH PAPER Skok, J. A. *et al.* Nonequivalent nuclear location of immunoglobulin alleles in B lymphocytes. *Nature Immunol.* **2**, 848–854 (2001)

WEB SITE Amanda Fisher's lab:
http://www.csc.mrc.ac.uk/research/Lymphocyte/Development.html

DEVELOPMENT

Muscle bound

The mysterious biochemical network that determines how one cell in the developing embryo becomes muscle whereas an adjacent cell becomes skin or bone is beginning to be revealed. Reporting in *Science*, Emerson and colleagues describe how the main function of the enzyme QSulf1 is to modify the signalling co-factors, heparan sulphate proteoglycans (HSPGs). This allows a cell to respond to molecular signals, such as Wnt, and transform into muscle instead of skin or bone.

The researchers highlight how the discovery of QSulf1 sheds light on mechanisms that can regulate responses to developmental signals for embryo patterning. Although the developmental signalling molecules that control embryo patterning for body-plan specification are well known, the mechanisms behind the spatially localized responses to these signals within the developing embryos are less understood.

One candidate for embryo-patterning regulation was HSPGs, as they are localized to the cell surface where they influence diverse developmental signals. In addition, the sulphation states of *N*-acetyl glucosamine residues in heparan sulphate moieties of HSPGs influence their activities in fibroblast growth factor (FGF) and Wnt signalling. However, the mechanism through which HSPG sulphation could be achieved was unclear.

The researchers first identified the enzyme QSulf1 by screening quail embryos for genes that are expressed when Sonic hedgehog (Shh) signalling is activated — precisely at the time when presomitic mesoderm epithelializes to form somites. QSulf1 is part of an evolutionarily conserved protein family that is related to heparin-specific *N*-acetyl glucosamine sulphatases. *In situ* hybridization studies showed QSulf1 was coexpressed with the muscle-specification genes *Myf5* and *MyoD* in the Shh-responsive epaxial muscle progenitors — which give rise to the deep-back and intercostal muscles of the adult — of newly formed somites.

Antisense inactivation of QSulf1 resulted in the specific inhibition of *MyoD*, but not *Myf5*, in the epaxial somite muscle progenitors and did not disrupt expression of *Pax3* or *Pax1* in the ventral somite. As *Myf5*, *Pax3* and *Pax1* are Shh-response genes, the researchers concluded that QSulf1 does not function in Shh signalling.

However, *MyoD* is Wnt-inducible, indicating QSulf1 might be involved in Wnt signalling, which is controlled by HSPGs — the likely substrate of QSulf1 activity. Co-transfection studies showed that QSulf1 is localized on the cell surface, and reporter gene assays in C2C12 myogenic progenitor cells found that QSulf1 regulates HSPG-dependent Wnt signalling through a mechanism that requires its catalytic activity, providing evidence that QSulf1 regulates Wnt signalling through desulphation of cell-surface HSPGs.

The researchers propose that QSulf1 could function in a two-step mechanism to regulate HSPG-dependent Wnt signalling. Wnts in the extracellular matrix could bind widely to heparan sulphate moities on cell-surface HSPGs, but only cells expressing QSulf1 on their surface would desulphate heparan sulphate to locally release HSPG-bound Wnts, allowing Wnt to activate regulatory genes, which give the instructions to become muscle progenitor cells.

Simon Frantz

References and links

ORIGINAL RESEARCH PAPER Dhoot, G. K. *et al*. Regulation of Wnt signaling and embryo patterning by an extracellular sulfatase. *Science* **293**, 1663—1666 (2001)

FURTHER READING Iozzo, R. V. Heparan sulfate proteoglycans: intricate molecules with intriguing functions. *J. Clin. Invest.* **108**, 165–167 (2001)