This wound response enhancer didn't require the activity of signalling pathways involved in innate immunity (which protect against infections through wounding), nor did it require the zygotic functions of Jun N-terminal kinase (JNK), Jun or Fos, which are involved in dorsal closure during embryogenesis. What, then, binds to the enhancer region?

One protein isoform encoded by *grh* — Grh-N — is expressed in barrier epithelia, and zygotic mutations in *grh* result in a phenotype similar to *Ddc* and *ple* mutants. The authors therefore tested a potential function for Grh-N in activating the –1.4-kb *Ddc* wound response element. The –1.4-kb *Ddc* reporter was only weakly activated in aseptically wounded *grh*-mutant embryos, and such wound sites couldn't regenerate normal cuticle.

As well as two evolutionarily conserved sites that bind the Grh transcription factor, the *Ddc* wound response enhancer contains several other consensus binding sites for other transcription factors, including activator protein-1 (AP-1) and ETS, as well as a GGGGGATT motif. A 3-kb fragment of *ple* also includes such sites, and strongly activates reporter expression around wounds.

McGinnis and colleagues also noticed an increase in phosphotyrosine staining and ERK activation in cells near aseptic wounds. ERK was activated in sites surrounding embryonic wounds within 30 minutes of injury. ERK was still activated in *grh* mutants, but inhibiting ERK activation decreased the activation of the *Ddc* wound response reporter. So ERK might somehow transduce the wound signal to Grh, and the aim is to find out how. Once Grh binds to, and activates, *Ddc* and *ple* near wounds, crosslinking molecules that repair the epithelial barrier kick into action. In another study in *Science*, Ting *et al.* report that a mouse orthologue of *grh*, *Grainy head-like-3* (*Grhl3*), is needed to form and maintain the epidermal barrier in mice. One target of Grhl3 is the gene for transglutaminase-1, an enzyme that, like the *Ddc* and *ple* gene products, is involved in crosslinking epidermal proteins.

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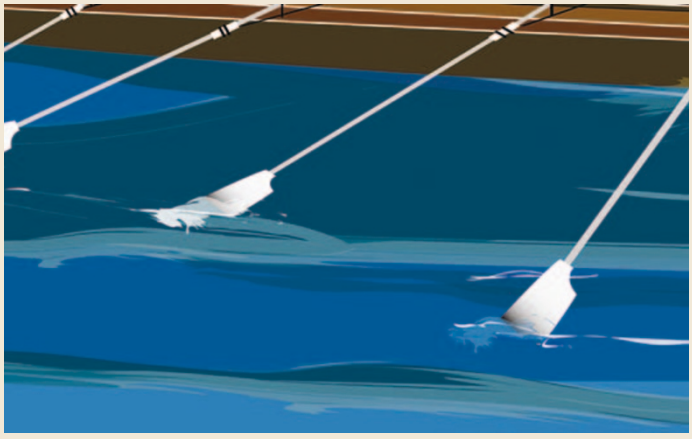
References and links

ORIGINAL RESEARCH PAPER Mace, K. A., Pearson, J. C. & McGinnis, W. An epidermal barrier wound repair pathway in *Drosophila* is mediated by *grainy head*. *Science* **308**, 381–385 (2005)

FURTHER READING Ting, S. B. *et al.* A homolog of *Drosophila* grainy head is essential for epidermal integrity in mice. *Science* **308**, 411–413 (2005)



is the challenge for the future. It will be interesting to determine exactly how the movements of kinesin and dynein are coordinated, as well as how several kinesins or dyneins can work together to bring about the rapid movement of cargo.

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References and links

ORIGINAL RESEARCH PAPER Kural, C. *et al.* Kinesin and dynein move a peroxisome *in vivo*: a tug-of-war or coordinated movement? *Science* 14 Apr 2005 (doi:10.1126/science.1108408)

FURTHER READING Mallik, R. & Gross, S. P. Molecular motors: strategies to get along. *Curr. Biol.* **14**, R971–R982 (2004)

WEB SITE

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IN BRIEF

CELL CYCLE

PPM1D dephosphorylates Chk1 and p53 and abrogates cell cycle checkpoints.

Lu, X., Nannenga, B. & Donehower, L. A. *Genes Dev.* 3 May 2005 (doi:10.1101/gad.1291305)

The ataxia-telangiectasia mutated (ATM) and ataxia-telangiectasia and Rad-3 related (ATR) kinases phosphorylate various targets, including p53 and Chk1, following DNA damage. Lu *et al.* reported that the serine/threonine phosphatase PPM1D/Wip1, which is induced by p53, dephosphorylates Chk1 and p53. Overexpression of PPM1D inhibited both S-phase- and G2–M-damage-induced checkpoints, so PPM1D might restore cell-cycle homeostasis after completion of DNA repair.

SIGNALLING

JNK extends life span and limits growth by antagonizing cellular and organism-wide responses to insulin signalling.

Wang, M., Bohmann, D. & Jasper, H. *Cell* **121**, 115–125 (2005)

In *Drosophila melanogaster*, calorie restriction extends lifespan by relieving the inactivation by insulin/insulin-like growth factor signalling (IIS) of Foxo to allow Foxo target-gene activation. Foxo also translocates to the nucleus in response to oxidative stress. The authors showed that Jun N-terminal kinase (JNK) signalling, which in *D. melanogaster* confers tolerance to oxidative stress and extends lifespan, induces Foxo nuclear localization and Foxo-dependent stress-response genes by antagonizing IIS. JNK also downregulates the production of *D. melanogaster* insulin-like peptide-2, thereby inhibiting IIS.

MORPHOGENS

Lipoprotein particles are required for Hedgehog and Wingless signalling.

Panáková, D. *et al. Nature* **435**, 58–65 (2005)

How do lipid-anchored Wingless/Wnt and Hedgehog (Hh) induce long-distance target-gene expression? Panáková *et al.* showed that Wingless and Hh, as well as glycosylphosphatidylinositol (GPI)-linked proteins, associate and colocalize with the lipoprotein lipophorin, which is needed for lipid transport and long-range Hh and Wingless function. Lipid-linked morphogens and GPI-linked proteins are therefore moved (rather than simply released) by binding to lipoprotein particles.

DEVELOPMENT

FGF signal interpretation is directed by Sprouty and Spred proteins during mesoderm formation.

Sivak, J. M., Petersen, L. F. & Amaya, E. *Dev. Cell* **8**, 689–701 (2005)

These authors identified two Sprouty and two Spred genes in *Xenopus laevis*, and showed that, in the early embryo, they inhibit distinct pathways mediated by fibroblast growth factor. The Sprouty proteins inhibit the activation of protein kinase Cδ, Ca^{2+} signalling and morphogenesis, whereas the Spreds inhibit the activity of mitogen-activated protein kinase and mesoderm specification. Their differential expression provides a putative mechanism to coordinate mesoderm formation and cell movements.