ly? Using mutants of the insulin signalling pathway, Teleman and Cohen induced the imaginal disc to grow faster (or slower) on one side of the DPP stripe and at the normal rate on the other side. The end result was that the DPP gradient accommodated these changes, so that the slope of the gradient varied depending on the size of the cellular field. Teleman and Cohen propose that this might be explained by the presence of a DPP sink at the edge of the disc.

Together, these studies provide detailed insight into the way a morphogenetic gradient is formed and how pattern formation by morphogens is coordinated with growth. Given the conservation of the morphogens and their signalling pathways, these insights will have very general relevance for understanding morphogenetic gradients in vertebrate development.

Mark Patterson

References and links

ORIGINAL RESEARCH PAPERS Teleman, A. & Cohen, S. M. Dpp gradient formation in the *Drosophila* wing imaginal disc. *Cell* **103**, 971–980 (2000) | Entchev, E. V. *et al*. Gradient formation of the TGF-β homolog Dpp. *Cell* **103**, 981–991 (2000)

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the basic contractile unit in striated muscle — and found one more mutation in a critical region of the troponin T gene (*TNNT2*). Troponin T regulates the interaction between myosin and actin. On the basis of the known structural properties of the residues that are mutated in TNNT2 and MYH7, Kamisago *et al.* predict that all three mutations will impair the contractile function of cardiac muscle.

Mutations in *MYH7* and *TNNT2* have previously been found in hypertrophic cardiomyopathy, the pathology of which is quite different from dilated cardiomyopathy. Functional studies of some of the hypertrophic cardiomyopathy mutations indicate that they might enhance, rather than impair, the contractile function of cardiac muscle.

Overall, defects in a single cellular component — the cardiac sarcomere — appear to unite two distinct pathologies. The implication is that sarcomere abnormalities will be a more common cause of cardiac dysfunction than previously suspected, and that the sarcomere is therefore an attractive target at which to aim new ideas about therapeutic intervention.

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References and links

ORIGINAL RESEARCH PAPER Kamisago, M. *et al*. Mutations in sarcomere protein genes as a cause of dilated cardiomyopathy. *N. Engl. J. Med.* **343**, 1688–1696 (2000)

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IN BRIEF

HUMAN GENETICS

Mutations in *Cdh23*, encoding a new type of cadherin, causes stereocilia disorganization in waltzer, the mouse model for Usher syndrome type 1D.

Di Palma, F. *et al*. *Nature Genet.* **27**, 103–107 (2001)

Mutation of *CDH23*, encoding a new member of the cadherin gene family, causes Usher syndrome type 1D.

Bolz, H. *et al*. *Nature Genet.* **27**, 108–112 (2001)

Cloned mouse mutant genes often provide new candidates for human genetic disorders, as these studies well exemplify. By positional cloning, Di Palma *et al.* identified a novel cadherin gene, *Cdh23*, as a candidate for the deaf waltzer mouse mutant, and found it was mutated in three waltzer alleles. In the neurosensory epithelium, *Cdh23* expression is restricted to the inner and outer hair cells, where its loss in waltzer mice causes stereocilia disorganization and hearing impairment. The human orthologue of *Cdh23* maps to the region implicated in Usher syndrome type 1D (USH1D), a human disease characterized by hearing and retinal defects. So the group's collaborators, Bolz *et al.*, tested *CDH23* as a candidate gene for the disease and found four different *CDH23* mutations in USH1D patients. Further studies in waltzer mice promise new insights into the molecular pathology of USH1D.

IMMUNOGENETICS

The antibacterial arm of the *Drosophila* innate immune response requires an IκB kinase.

Lu, Y. *et al. Genes Dev.* **15**, 134–146 (2001)

Both in flies and in mammals, different microbial components activate different signalling pathways of the innate immune response. The *Drosophila ird5* gene was identified in a screen for mutants with defective immune responses; in its absence, the anti-fungal response is normal, but flies fail to induce six antibacterial peptide genes in response to infection. The product of the *ird5* gene is homologous to the mammalian IκB kinases and is required for the activation of Relish, one of the three known NF-κB family members in flies.

GENE THERAPY

Glucose-dependent insulin release from genetically engineered K cells.

Cheung, A. T. *et al*. *Science* **290**, 1959–1962 (2000)

To tackle diabetes using gene therapy, one of the main challenges is to regulate the expression of insulin in response to glucose (see last month's Highlights for another approach to this). Cheung *et al.* constructed a transgene comprising the human insulin gene and the control region of the glucose-dependent insulinotropic polypeptide (GIP). GIP is expressed in specialized, glucose-responsive gut cells, known as K cells, with kinetics that are very similar to insulin expression. The insulin transgene was expressed in K cells of transgenic mice in a glucose-dependent fashion. Notably, the transgene could also rescue the diabetic phenotype of a chemically induced mouse diabetes model.