IN BRIEF

ZEBRAFISH MODELS

Removal of dystroglycan causes severe muscular dystrophy in zebrafish embryos.

Parson, M. J. *et al. Development* **129**, 3505–3512 (2002)

Muscular dystrophy (MD) often results from the disruption of a complex that links muscle cells to the extracellular matrix. To model the disease, dystroglycan — a central component of this complex — had been knocked out in mice, but they die in early embryogenesis. Parson *et al.* turned to zebrafish and used morpholinos to knock down dystroglycan in this species. Mutant fish were viable and had a muscle-specific phenotype, indicating the potential of zebrafish as a model of MD.

HUMAN GENETICS

Presence of large deletions in kindreds with autism.

Yu, C. E. *et al. Am. J. Hum. Genet.* **71**, 100–115 (2002)

To identify autism susceptibility genes, Yu *et al.* carried out linkage analysis on a sample of 105 families that included two or more affected sibs. Segregation analysis pointed to four 5–260-kb deletions, some of which were complex, that associated with the trait. When tested in control families, three out of four deletions were specific to the autistic families, further implying that new susceptibility loci might lie in the deleted regions.

CANCER GENETICS

Ptprj is a candidate for the mouse colon-cancer susceptibility locus *Scc1* and is frequently deleted in human cancers.

Ruivenkamp, C. A. L. *et al*. *Nature Genet.* **31**, 295–300 (2002)

As most cancers are sporadic, identifying human cancer susceptibility genes is an urgent goal. Ruivenkamp *et al.* now report their positional cloning of the gene that underlies the mouse *Scc1* (susceptibility to colon cancer 1) locus — the first-time cloning of a cancer QTL. *Ptprj* encodes a receptor-type protein tyrosine phosphatase that has several characteristics of tumour-suppressor genes. Moreover, human colon, lung and breast cancers show frequent *PTPRJ* deletions, missense mutations and loss of heterozygosity, indicating its likely importance in the aetiology of several human cancers.

GENOME EVOLUTION

Genome size reduction through illegitimate recombination counteracts genome expansion in *Arabidopsis*.

Devos, K. M. *et al*. *Genome Res*. **12**, 1075–1079 (2002)

Species of flowering plants are known for varying greatly in genome size, largely due to genome duplication and retrotransposon activity. So what stops these genomes from becoming ever bigger? This work shows that illegitimate recombination is able to keep in check the size of the *Arabidopsis thaliana* genome and can do so fivefold more effectively than unequal homologous recombination.

DEVELOPMENTAL BIOLOGY

Out on a limb

That the early development of vertebrate external genitalia resembles that of vertebrate limbs is a little known fact — but then this aspect of vertebrate development is rarely the focus of research. It was previously shown that fragments of the developing genital region harbour a signalling activity akin to the zone of polarizing activity in the vertebrate limb. These findings are now extended by Perriton and colleagues, who show that external genitalia are patterned by signals that emanate specifically from the urethral epithelium and that Sonic hedgehog (Shh) has a key role in genital development.

Previous work that highlighted the developmental similarity between limbs and external genitalia implicated the genital tubercle — the region that gives rise to the penis and clitoris — as a source of mild polarizing activity. But because the grafts contained the urethral epithelium and the genital mesenchyme it was unclear which tissue provided the signal. When Perriton *et al.* grafted each tissue separately onto chick limb buds they saw mirror-image duplication of digits — a hallmark of polarizing activity — but only in the case of the urethral epithelium, proving that this was the true source of the patterning signals. Additionally, some morphological features of the induced limb suggested that the urethral epithelium can drive tissue movements that are characteristic of genital morphogenesis.

So, what is the molecular basis of this signal? Out of 30 genes involved in limb development, 26 were also expressed in the genital tubercle, further supporting the existence of a common developmental mechanism. The authors focused on one of the two signalling molecules that were expressed in the developing urethra — Shh — and found that, although the outgrowth of the genital region was initiated, it wasn't maintained in *Shh*$^{-/-}$ mouse embryos. The expression of *Fgf8*, *Bmp4*, *Wnt5a* and *Fgf10* — genes that, together with *Shh*, pattern the vertebrate limb — was either downregulated or not detectable in the external genitalia of *Shh*$^{-/-}$ mice. The authors also showed that excessive apoptosis contributes to a lack of the genital outgrowth in *Shh*$^{-/-}$ mice.

These results implicate *Shh* as the main urethral signal that is essential for external genital development. The authors showed that genital development is not maintained in the absence of *Shh* because normal patterning and growth fail. These findings substantially extend our understanding of genital development. The hope is that they will encourage more research into this often-neglected area of development.

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References and links

ORIGINAL RESEARCH PAPER Perriton, C. L. *et al*. Sonic hedgehog signaling from the urethral epithelium controls external genital development. *Dev. Biol.* **247**, 26–46 (2002)