



SPERMATOGENESIS

Give me a break

Around 10% of sperm from a healthy human male carry visible chromosomal abnormalities. Despite the relevance of this striking statistic to the fertility of males in one generation, and the health of their progeny in the next, we know surprisingly little about the origins and causes of these sperm abnormalities. Sloter *et al.* have developed a fluorescence *in situ* hybridization (FISH) assay to detect specific chromosomal abnormalities in sperm — an assay that will provide new insight into the poor quality of human sperm.

Much of the previous analysis of chromosomal abnormalities in sperm has relied on the hamster-egg method. In this method, sperm are allowed to fuse with hamster oocytes, and when the sperm chromosomes enter metaphase, they are visualized by traditional cytogenetic staining methods. High frequencies of sperm chromosomal abnormalities have been detected in this assay, but it was always possible that the abnormalities seen at metaphase were induced after fusion.

Multicolour FISH methods for the direct analysis of human sperm have been developed over recent years and, in the latest work, Sloter *et al.* have devised an assay that can detect chromosomal breaks and aneuploidy on chromosome 1. Three separate probes are used that hybridize to different satellite DNA loci — two near the centromere (1cen, labelled red and 1q12, blue) and one at the tip of the short arm of the chromosome (1p36, green).

The authors have catalogued a range of chromosomal defects in the mature sperm of four healthy males. In the image (courtesy of A. J. Wyrobek), evidence for a break within the 1q12 chromosomal region is shown. The current assay focuses on one region of the genome, but extrapolation to the whole genome yields an estimate for the number of chromosomal abnormalities in sperm that agrees with previous hamster-egg studies — around 8%. Structural abnormalities, such as chromosomal breaks, tend to occur more frequently than aneuploidy. The position of the breaks could also be assessed, and evidence for chromosomal hotspots (which varied from one individual to the next) was detected. This and other FISH-based assays now set the scene for more detailed analyses of the genetic and environmental factors that influence the occurrence of sperm chromosomal abnormalities.

Mark Patterson

References and links

ORIGINAL RESEARCH PAPER Sloter, E. D. *et al.* Multicolor FISH analysis of chromosomal breaks, duplications, deletions and numerical abnormalities in the sperm of healthy men. *Am. J. Hum. Genet.* **67**, 862–872 (2000)

EVO-DEVO

A leg-up for crickets

The study of fruitflies has yielded huge dividends for our understanding of development, and the comparison of the fruitfly to other insects is proving equally beneficial for understanding morphological evolution. A recent report shows that the difference between the legs of fruitflies and crickets, for example, may depend only on the expression pattern of a single gene.

Crickets and fruitflies belong to two different superorders of the Insecta class. The two-spotted cricket (*Gryllus bimaculatus*) is a hemimetabolous insect — it hatches as a miniature adult and grows until it reaches its adult size. Holometabolous insects, such as the fruitfly *Drosophila melanogaster*, hatch as larvae that contain internal sacs (imaginal discs) from which the adult appendages, such as the wings and legs, develop at metamorphosis.

Flies fly, whereas crickets have a spring in their step thanks to some specialised muscles that are present only in their third pair of legs (the T3 legs). So how do the developmental mechanisms controlling leg development compare in these two insects? Three developmental genes are required for patterning the fruitfly leg: *hedgehog* (*Dmhh*), *wingless* (*Dmwg*) and *decapentaplegic* (*Dmdpp*). Niwa *et al.* have shown that orthologues of these three genes are also present in *Gryllus*, where their expression profiles in the embryo and the leg match very closely those seen in the developing fly. In the *Drosophila* leg imaginal disc and in the cricket leg bud, *wg* is expressed along the ventral side of

the anterior–posterior boundary and Hh protein fills the posterior compartment. The one important exception is the expression of *dpp* in the leg. Instead of being expressed as a strong dorsal strip and a weak ventral one (as in the fly leg disc), *Gbdpp* expression first appears as dots along the dorsal side of the leg bud, and later turns into five circumferential rings. These rings are thought to coincide with the cricket's five leg segments along the proximo–distal axis. Curiously, this circumferential expression of *dpp* breaks down in legs T1 and T2, but is retained in the T3 pair of legs, in precisely those segments that will develop the strong jumping muscles.

This similar expression of the three key patterning genes is important as it suggests a fundamental conservation in the control of leg development, whereas the divergent distribution of *dpp* offers an explanation for differences in leg morphology. This study extends our knowledge of *Drosophila* to one more insect species, but there's still a million or so to go!

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References and links

ORIGINAL RESEARCH PAPER Niwa, N. *et al.* Correlation of diversity of leg morphology in *Gryllus bimaculatus* (cricket) with divergence in *dpp* expression pattern during leg development. *Development* **127**, 4373–4381 (2000)

FURTHER READING Jockusch, E. L. *et al.* Leg development in flies versus grasshoppers: differences in *dpp* expression do not lead to differences in the expression of downstream components of the leg patterning pathway. *Development* **127**, 1617–1626 (2000) | Friedrich, M. Divergent *decapentaplegic* expression patterns in compound eye development and the evolution of insect metamorphosis. *J. Exp. Biol.* **238**, 39–55 (2000)

Gbdpp expression in cricket leg buds: spots in T1/T2 and rings in T3.

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