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Nanos keeps its job

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David Secko
Email: dmsecko@interchange.ubc.ca

The *Drosophila* gene nanos was first identified as an RNA-binding protein whose absence prevented primordial germ cells (PGCs) from migrating to the gonad, resulting in a loss of functional germ cells. Subsequently, a variety of *nanos* homologs have been found in other systems, including a single mouse nanos gene (*nanos*1), the disruption of which had no affect on PGCs or germ cell development. The mechanism for specifying and maintaining PGCs in mice has been unclear, but it was suspected that other *nanos*-related genes might exist. In the August 29 Science, Masayuki Tsuda and colleagues at the National Institute of Genetics report the identification of two additional mouse *nanos* genes and show their requirement for germ cell development (*Science* 2003, **301:**1239-1241).

Tsuda *et al*. identified two homologs of the mouse *nanos*1 gene by searching the human genome for a conserved zinc finger motif. These two genes - *nanos*2 and *nanos*3 - were expressed in the developing mouse gonads, suggesting the potential for these genes to be involved in germ cell development. The authors then generated viable heterozygous and homozygous knockout mice, showing no major abnormalities, expect in the gonads. When examined, *nanso*2-null mice had testes weighing only 30% of a wildtype mouse, but the female mice had fully developed gonads. The embryonic male gonads of these mice showed a reduction in the number of germ cells, with none detectable after 4 weeks (during this time, apoptotic cells were detectable as TUNEL-positive cells). In contrast, *nanos*3-null mice showed a reduction in the size of both the ovaries and testes, with no germ cells being detectable. Tsuda *et al*. examined the PGCs of *nanos*3-null mice by alkaline phosphatase staining and revealed an initially equal number of PGCs in wildtype and *nanos*3-null mice that was, however, reduced during PGC migrations in the null mice. This suggests that *nanos*3 is important for the "maintenance of PGCs by supporting their proliferation and/or by suppression of cell death."

"We have demonstrated here an evolutionarily conserved function of Nanos proteins in germ cell development," conclude the authors. This may have important implications in our understanding of sterility and infertility in humans.

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