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Maternal impact of chromatin reorganization

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In the early phases of embryonic development, extensive remodeling of condensed maternal and paternal gamete DNA occurs. The genes and related proteins responsible for chromatin reorganization are well characterized in vertebrates, such as *Xenopus laevis*, but have been unclear in mammals. In the April 25 *Science*, Kathleen Burns and colleagues at *Baylor College of Medicine*, Houston, show that nucleoplasmin 2 (NPM2), an oocyte-specific nuclear protein, is crucial in chromatin organization and post-fertilization development in mice (*Science* 2003, **300**:633-636).

Using *Xenopus* NPM2 as a template, Burns *et al.* isolated the murine NPM2 ortholog. In situ hybridization showed that expression of the NPM2 protein was limited to growing oocytes. To study the NPM2 activity, they used embryonic stem cell technology to generate homozygous NPM2-null mice. Although *Xenopus* NPM2 decondenses sperm DNA, the same process seems to proceed without NPM2 in mice, as NPM2-null males were fertile and normal. In contrast, NPM2 knockout females were found to be subfertile or infertile. Analysis of fertilization and post-fertilization events in vitro and in vivo revealed impaired early embryo development, mostly due to failure of the one-cell to two-cell transition. Examining oocytes and eggs from NPM2-null females, they detected gross defects, including an absence of coalesced nucleolar structures and loss of heterochromatin and deacetylated histone H3 that normally circumscribe nucleoli in oocytes and early zygotes, respectively.

NPM2 is one of a family of oocyte-derived proteins for which a role in zygote development has been demonstrated. "In the future it will be important to define the functional domains of NPM2... and to assess whether NPM2-gene mutations may cause infertility in women," conclude the authors.

References

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