


NUCLEAR ORGANIZATION

Microtubule shaping of the nucleus

Nuclei come in many shapes and sizes, although the factors that define this are not clear. Xue *et al.* find that, during *Xenopus laevis* fertilization, changes in sperm nuclear shape are governed by the inhibition of local microtubule assembly by a chromatin-bound factor, dppa2 (developmental pluripotency-associated 2).

Upon interaction with the egg, the sperm pronucleus normally transitions from a compacted crescent-shaped nucleus to one that is decondensed and spherical. Using a proteomics approach, the authors identified dppa2 as a candidate regulator of this process. Polyclonal antibodies against dppa2 confirmed that it localized to chromatin in both interphase and metaphase. In addition, immunodepletion of dppa2 impaired both sperm nuclear assembly and morphology in egg extracts during fertilization, and these effects could be rescued by re-addition of recombinant dppa2.

Fertilization normally correlates with nucleation of microtubules from sperm-associated centrosomes, which then transport the sperm and egg pronuclei to the egg centre for fusion. Xue *et al.* observed that immunodepletion of dppa2 increased the initial growth of microtubules upon the addition of sperm to egg extracts. Moreover, the effects of dppa2 depletion on nuclear morphology were rescued by co-depletion of the chromosomal passenger complex, which is known to prevent nuclear formation and promote spindle assembly in *X. laevis*.

The effects of dppa2 on nuclear formation were through the control of microtubule dynamics: depolymerization of microtubules reversed the effects of dppa2 depletion on nuclear shape, whereas stabilization of microtubules mimicked the effects of dppa2 depletion. This sensitivity to microtubule stability was

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dose-dependent, which indicates that microtubule dynamics must be finely balanced for normal nuclear assembly. The influence of microtubules on nuclear assembly was also restricted to a limited time window. If nocodazole treatment was delayed by 30 minutes, microtubule depolymerization no longer rescued the effects of dppa2 depletion on nuclear shape. Finally, by deleting distinct domains of dppa2, the authors showed that normal nuclear shape required both dppa2-mediated regulation of microtubule assembly and its interaction with DNA.

The authors thus propose that dppa2 must limit local microtubule assembly around chromatin early during fertilization and that this mediates normal nuclear assembly. It remains to be seen how transient microtubule dynamics leave this lasting mark on nuclear morphology and whether this interplay might be relevant in other contexts.

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ORIGINAL RESEARCH PAPER Xue, J. Z. *et al.* Chromatin-bound *Xenopus* Dppa2 shapes the nucleus by locally inhibiting microtubule assembly. *Dev. Cell* **27**, 47–59 (2013)