

Journal club



FEARLESSLY TACKLING THE ORGANIZER

“What should I read?” is the classic question I receive from new undergraduates entering the laboratory. Last time, I opted for three old papers that profoundly influenced me during my postdoctoral studies in the late 1990s. These papers were the first steps of a formidable challenge: understanding how the Spemann organizer builds the vertebrate body. I recommended these papers not out of nostalgia, but because they still remind me that fearlessness in exploring the biological power of genes and elegance in experimental design are key to tackling daring biological questions — as is faith that simple solutions may be found for what was deemed impossible.

In the first paper, Smith and Harland described how they cloned noggin, the first factor secreted from the organizer. They first detected signs of organizer-like activity simply by

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microinjecting total poly(A)⁺ mRNA into ventralized embryos. To identify the mRNA responsible for this activity, they then tested progressively smaller pools of cloned cDNA down to the single ‘positive pick’. This ‘expression cloning’ approach became a blockbuster strategy, adopted by many to identify new genes using solely a cDNA library and a bioassay.

The breakthrough for the field came with the identification of chordin and its neural induction capacity by Sasai *et al.* Chordin — or noggin — induced the formation of the central nervous system in naive *Xenopus laevis* cells, and this could be reversed by bone morphogenetic protein 4 (bmp4). These findings were in accordance with the elegant genetic studies in *Drosophila melanogaster* by Ferguson and Anderson. They had found that doubling the copies of the bmp4 homologue *decapentaplegic* enhanced the body patterning defects of mutants in *short gastrulation*, the chordin homologue. Thus, the genetic framework for embryonic induction was evolutionarily conserved.

Thanks to these experiments, an old field was finally mature — its mechanistic dissection led to our current understanding of the organizer as a source of antagonists for BMP, transforming growth factor- β and WNT growth factors. From the wonder in my student’s eyes, it is true that good stories never age.

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ORIGINAL RESEARCH PAPERS Smith, W. C. & Harland, R. M. Expression cloning of noggin, a new dorsalizing factor localized to the Spemann organizer in *Xenopus* embryos. *Cell* **70**, 829–840 (1992) | Sasai, Y. *et al.* Regulation of neural induction by the Chd and Bmp-4 antagonistic patterning signals in *Xenopus*. *Nature* **376**, 333–336 (1995) | Ferguson, E. L. & Anderson, K. V. Localized enhancement and repression of the activity of the TGF- β family member, *decapentaplegic*, is necessary for dorsal-ventral pattern formation in the *Drosophila* embryo. *Development* **114**, 583–597 (1992)

FURTHER READING De Robertis, E. M. Spemann’s organizer and the self-regulation of embryonic fields. *Mech. Dev.* **126**, 925–941 (2009)