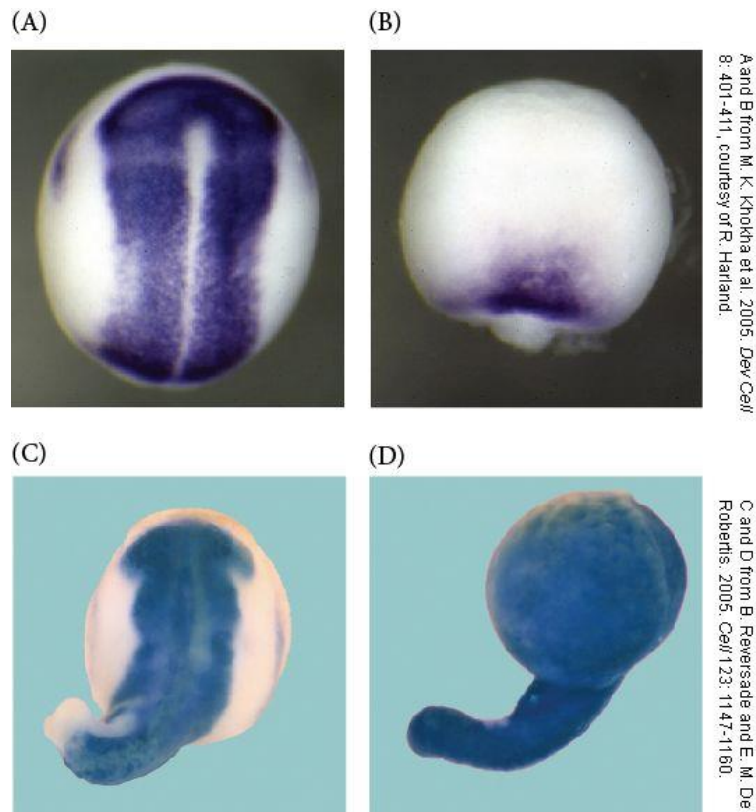


# The Experiments That Confirmed Ectodermal Bias

In 2005, two important sets of experiments confirmed the importance of blocking BMPs to specify the nervous system. First, Khokha and colleagues (2005) used antisense morpholinos to eliminate three BMP antagonists (Noggin, Chordin, and Follistatin) in *Xenopus*. The resulting embryos had catastrophic failure of dorsal development and lacked neural plates and dorsal mesoderm (Figure 1A, B). Second, Reversade and colleagues blocked BMP activity with antisense morpholinos (Reversade et al. 2005; Reversade and De Robertis 2005). When they simultaneously blocked the formation of BMPs 2, 4, and 7, the neural tube became greatly expanded, taking over a much larger region of the ectoderm (Figure 1C). When they did a quadruple inactivation of the three BMPs *and* ADMP (another protein of the BMP family), the entire ectoderm became neural (Figure 1D). Thus, the epidermis is instructed by BMP signaling, and the organizer specifies the ectoderm above it to become neural by blocking that BMP signal from reaching the adjacent ectoderm.

In the absence of BMP signaling, the FoxD4 transcription factor becomes expressed in the presumptive neural ectoderm. It initiates a pathway that leads to the stabilization of neural identity in most of the induced ectodermal cells, while allowing the formation of an immature, stem cell-like state in other induced cells (see Rogers et al. 2009; Klein and Moody 2015).



**Figure 1** Control of neural specification by levels of BMPs. (A,B) Lack of dorsal structures in *Xenopus* embryos whose BMP-inhibitor genes *chordin*, *noggin*, and *folliculin* were eliminated by antisense morpholino oligonucleotides. (A) Control embryo with neural folds stained for the expression of the neural gene *Sox2*. (B) Lack of neural tube and *Sox2* expression in an embryo treated with the morpholinos against three BMP inhibitors. (C,D) Expanded neural development. (C) The neural tube, visualized by *Sox2* staining, is greatly enlarged in an embryo treated with antisense morpholinos that destroy BMPs 2, 4, and 7. (D) Complete transformation of the entire ectoderm into neural ectoderm (and loss of the dorsal-ventral axis) by inactivation of ADMP as well as BMPs 2, 4, and 7.

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