SUPPLEMENTARY FIGURES

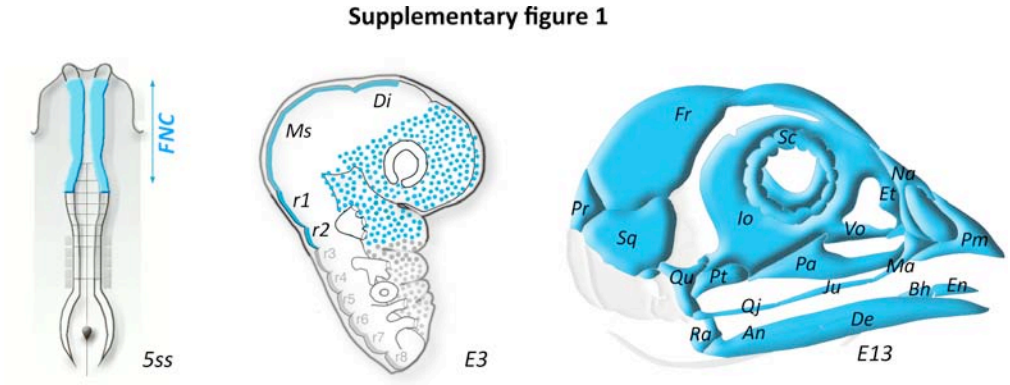

Fig. S1: **Contribution of the FNC to head development.** At 5ss, the FSNC (cyan) extends from the mid-diencephalon down to r2. At E3, FSNC cells populate the nasofrontal and maxillo-mandibular regions. At E13, the craniofacial skeleton is derived from the FNC. An, angular; Bh, basihyal; De, dentary; Di, diencephalon; En, entoglossum; Et, ethmoid; Fr, frontal; Io, interorbitary septum; Ju, jugal; Ma, maxilla; Ms, mesencephalon; Na, nasal; Pa, palate; Pm, pre-maxilla; Pr, parietal; Pt, pterygoid; Qj, quadrato-jugal; Qu, quadrate; Ra, retro-articular process; Sc, sclerotic ossicles; r1, rhombomere 1; r2, rhomobomere 2; Sq, squamosal; Vo, vomer.

Supplementary figure 2

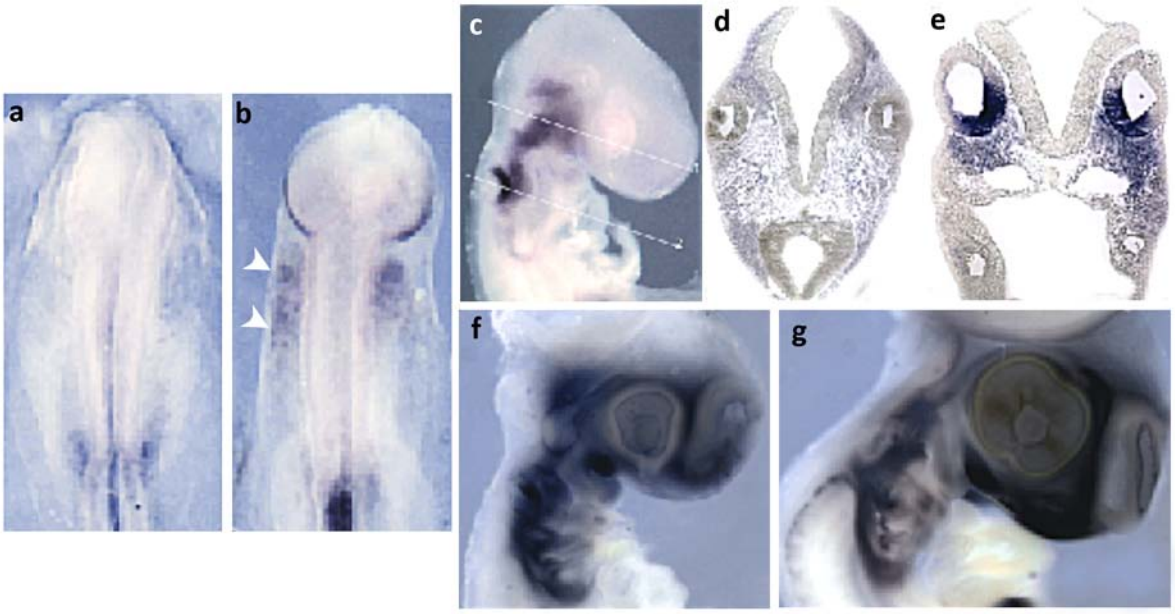

Fig. S2: *Six2* gene expression pattern. Hybridization of *Six2* in (**a**) 5ss, (**b**) 10ss, (**c**) 25ss, (**f**) E4 and (**g**) E5 chick embryos. Note the *Six2* expression in the (**d**) peri-optic and (**e**) peri-otic NC-derived mesenchyme on sections.

Supplementary figure 3

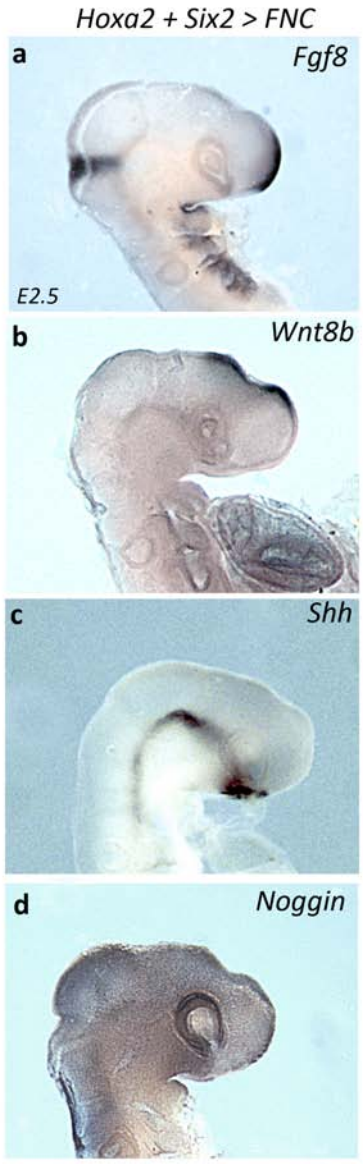

Fig. S3: Six2 can overcome the molecular defects resulting from Hoxa2 activity. Six2 supplementation in *Hoxa2*-transfected embryo can bypass the detrimental effect of Hoxa2 on the expression of (**a**) *Fgf8*, (**b**) *Wnt8b*, (**c**) *Shh* and (**d**) *Noggin*.

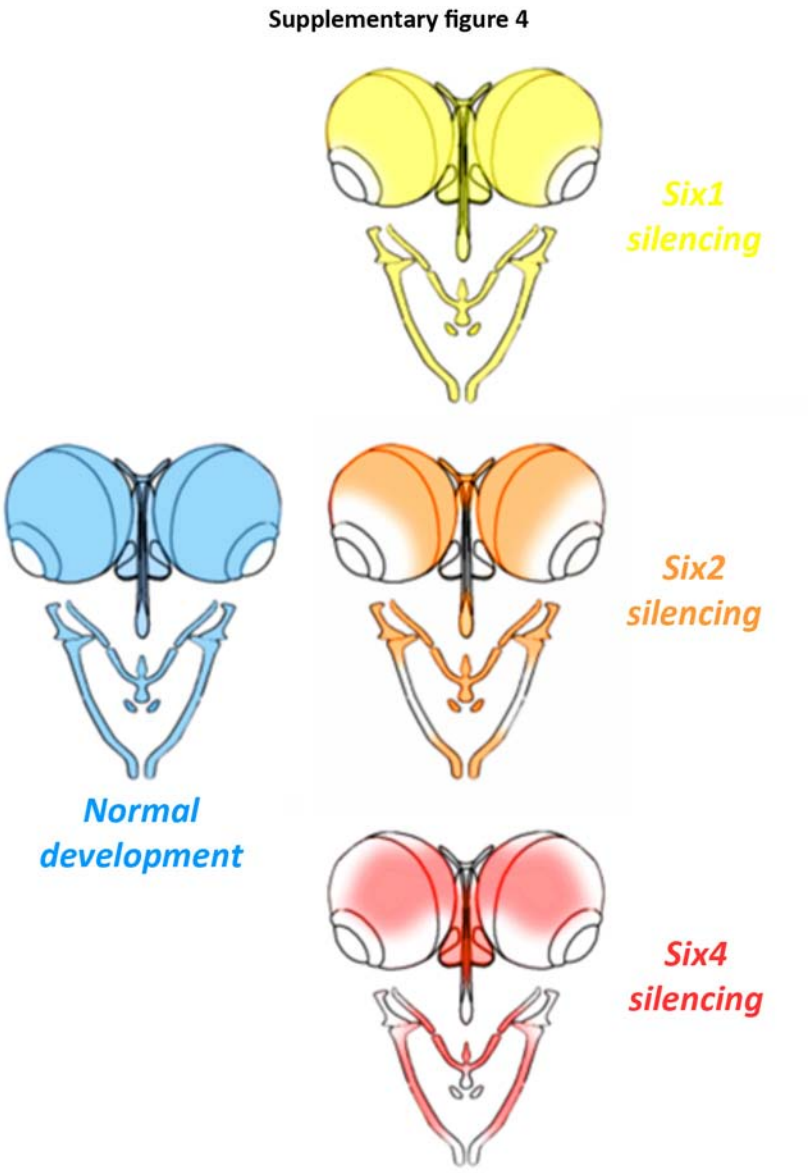

Fig. S4: Effects of *Six* gene silencing. Schematic diagram of the normal skeleton (blue) and the defects resulting from *Six1* (yellow), *Six2* (orange), and *Six4* (red) silencing.

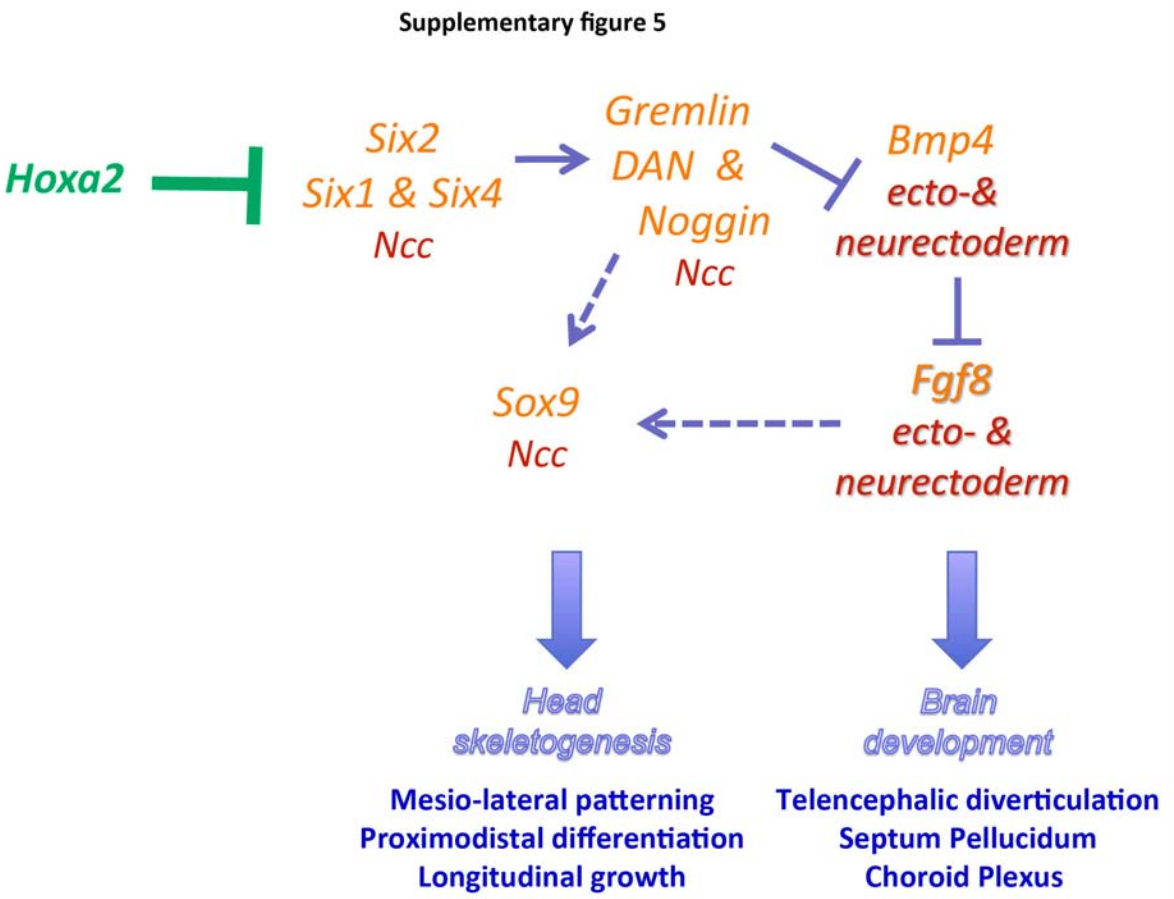

Figure S5: Proposed model. Summary of the epistatic relationship linking *Six* gene expression in FSNC cells to the morphogenetic control of head and brain development through the regulation of Bmp signaling. The forced expression of *Hoxa2* represses *Six1-2-4* expression, leading to an overall decrease in the production of Bmp antagonist by FNC cells. Reciprocally, this condition entails an increase in Bmp activity in the ectodermal compartments, thus inhibiting Fgf8 activity in the ANR. This results in detrimental effects on brain development and inhibits *Sox9* expression, hence preventing head skeletogenesis.