Reissner fibre-induced urotensin signalling from cerebrospinal fluid-contacting neurons prevents scoliosis of the vertebrate spine

Tuesday, 9 Jun 2020

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Published in *Biology Open 2020* on 18 May 2020

Abstract

Reissner fibre (RF), discovered by the 19th-century German anatomist Ernst Reissner, is a filamentous structure present in cerebrospinal fluid (CSF). RF forms by aggregation of a glycoprotein called SCO-spondin (Sspo), but its function has remained enigmatic. Recent studies have shown that zebrafish *sspo* mutants develop a curved embryonic body axis. Zebrafish embryos with impaired cilia motility also develop curved bodies, which arises from failure of expression of urotensin related peptide (*urp*) genes in CSF-contacting neurons (CSF-cNs), impairing downstream signalling in trunk muscles. Here, we show that *sspo* mutants can survive into adulthood, but display severe curvatures of the vertebral column, resembling the common human spine disorder idiopathic scoliosis (IS). *sspo* mutants also exhibit significant reduction of *urp* gene expression from CSF-cNs. Consistent with epinephrine in CSF being bound by RF and required for *urp* expression, treating *sspo* mutants with this catecholamine rescued expression of the urp genes and axial defects. More strikingly, providing Urp2, specifically in the CSF-cNs, rescued body curvature of *sspo* homozygotes during larval stages as well as in the adult. These findings bridge existing gaps in our knowledge between cilia motility, RF, Urp signalling and spine deformities, and suggest that targeting the Urotensin pathway could provide novel therapeutic avenues for IS.

Figure

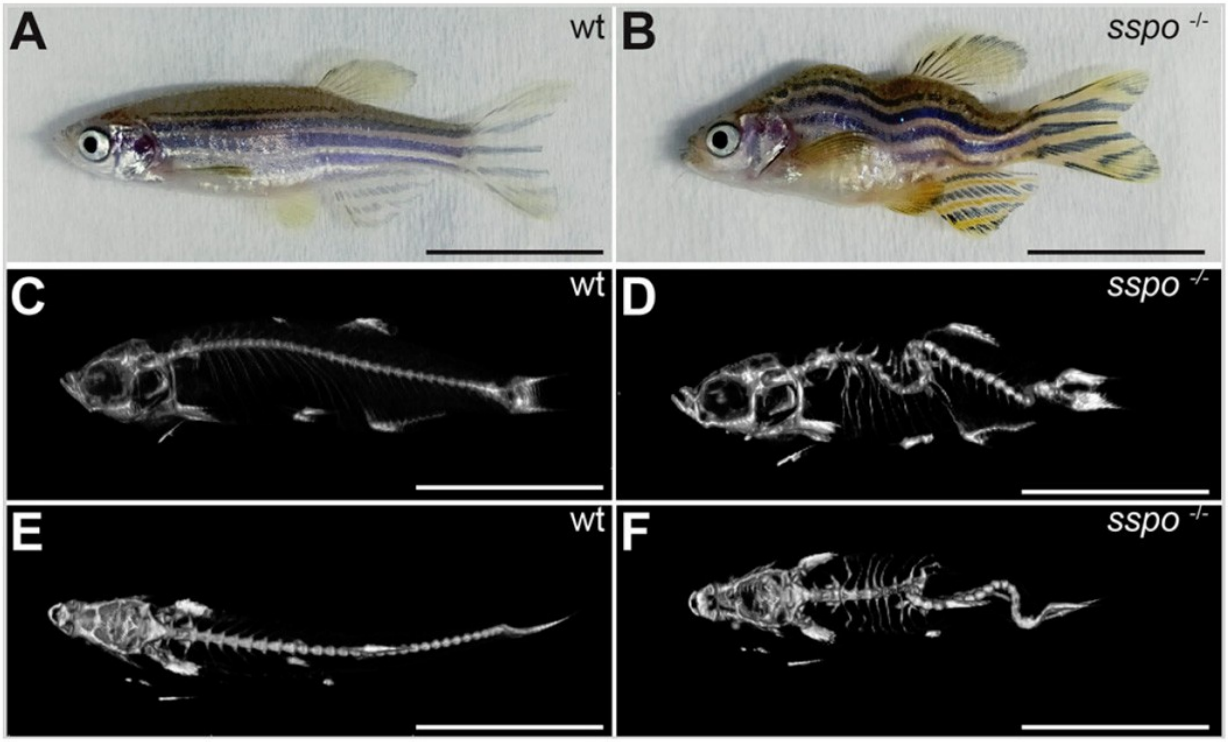

Figure Legend:
***sspo* mutants develop into adults with scoliotic spines.** (A) A wild-type adult zebrafish. (B) An *sspo* mutant. Note the curved malformations of the trunk and tail. (C) MicroCT scan image of a wild-type zebrafish (lateral view). (D) MicroCT scan image of an *sspo*-mutant zebrafish (lateral view). Note the dorso-ventral curvatures of the spine. (E) MicroCT scan image of the wild-type zebrafish (dorsal view). (F) MicroCT scan image of the *sspo*-mutant zebrafish (dorsal view). Note the lateral curvatures of the spine. All fish were 3 months of age. Two fish were analysed for each genotype. Scale bars: 1 cm.

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Cilia, Reissner Fiber and Crooked Spines - the Node

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