Setdb2 restricts dorsal organizer territory and regulates left-right asymmetry through suppressing *fgf8* activity

Summarizing research work partly funded by NSFC, Dr. Chen Zhu of State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, RuiJin Hospital, Shanghai Jiao Tong University and his research team reported on *PNAS* in February 2010 their research findings on dorsal organizer.

According to their paper, dorsal organizer formation is one of the most critical steps in early embryonic development. Several genes and signaling pathways that positively regulate the dorsal organizer development have been identified; however, little is known about the factor(s) that negatively regulates the organizer formation. Here, we show that Setdb2, a SET domain-containing protein possessing potential histone H3K9 methyltransferase activity, restricts dorsal organizer development and regulates left-right asymmetry by suppressing fibroblast growth factor 8 (fgf8) expressions. Knockdown of Setdb2 results in a massive expansion of dorsal organizer markers floating head (flh), goosecoid (gsc), and chordin (chd), as well as a significant increase of fgf8, but not fgf4 mRNAs. Consequently, disrupted midline patterning and resultant randomization of left-right asymmetry are observed in Setdb2-deficient embryos. These characteristic changes induced by Setdb2 deficiency can be nearly corrected by either over expression of a dominant-negative fgf receptor or knockdown of fgf8, suggesting an essential role for Setdb2-Fgf8 signaling in restricting dorsal organizer territory and regulating left-right asymmetry. These results provide unique evidence that a SET domain-containing protein potentially involved in the epigenetic control negatively regulates dorsal organizer formation during early embryonic development.

Their research work was also supported in part by the National Basic Research Program of China, the Science and Technology Commission of Shanghai Municipality, the National High Tech Program for Biotechnology, the Chinese National Key Basic Research Project, the Key Discipline program of Shanghai Municipal Education Commission, in addition to the Grant for Innovation Group of the National Natural Science Foundation of China, and the Shanghai Municipal Commission for Science and Technology.