



# CDB SEMINAR

## Ruth Arkell

Australian National University

Monday, November 5

16:00~17:00 A7F CDB Conference Room

### **Zic2 is required for prechordal plate development in the mouse**

#### **Summary**

The Zic genes are the vertebrate homologues of the Drosophila pair rule gene odd paired and contain a zinc finger domain with DNA and protein binding capabilities. Of the five mammalian Zic genes, 3 are expressed during mouse (Zics 2,3 and 5) and the function of each of these is being investigated using mouse models that carry coding region point mutations. ZIC2 is associated with a defect of forebrain development, known as Holoprosencephaly (HPE), in humans and mouse, yet the mechanism by which aberrant ZIC2 function causes classical HPE is unexplained. The zinc finger domain of all mammalian Zic genes is highly homologous with that of the Gli genes, which are transcriptional mediators of Shh signaling. Mutations in Shh and many other Hh pathway members cause HPE and it has been proposed that Zic2 acts within the Shh pathway to cause HPE. We have investigated the embryological cause of Zic2-associated HPE and the relationship between Zic2 and the Shh pathway using mouse genetics. We show that Zic2 does not interact with Shh to produce HPE. Moreover, molecular defects able to account for the HPE phenotype are present in Zic2 mutants before the onset of Shh signaling. Mutation of Zic2 causes HPE via a transient defect in the function of the organiser region at mid-gastrulation which causes an arrest in the development of the prechordal plate (PCP), a structure required for forebrain midline morphogenesis. The analysis provides genetic evidence that the PCP develops via a multi-step process and that the mouse organiser undergoes a molecular transition during gastrulation.

#### **Host:**

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