**INTRODUCTION**

**Zinc Finger of the Cerebellum genes (ZIC)**
- Family of Transcription Factors (TFs) sharing 5 highly conserved Cys2His2-zip Zinc Fingers.
- Perform functions at early and late stages of neural development.

**ZIC2 associated holoprosencephaly (HPE)**
- HPE is the most common brain congenital malformation (1/2000 conceptuses): incomplete cleavage of the prosencephalon affecting the correct separation of the two brain hemispheres and facial structures.

**Mouse embryonic stem cells (mESCs) as a tractable in vitro model**
- Strong points:
  - Retention of high amount of cells required for different genomic approaches such as RNA-seq or Chromatin Immunoprecipitation Sequencing (ChIP-seq)
  - No ethical restrictions
  - Easy to modify genetically to model a broad range of diseases

**ZIC2 as a Transcriptional Regulator**

**RESULTS**

3.1. Zic2 knock-out leads to an upregulation of dorsal genes and a downregulation of ventral ones in AntNPCs.

3.2. Generation of Zic2-Flag-HA tagged cell lines by CRISPR-Cas9

3.3. FH6 mESC line shows similar Zic2 expression levels than WT mESC line

3.4. FH6 mESC line is valid for Zic2 ChIP

**CONCLUSIONS**

- The loss of ZIC2 disrupts dorsalventral patterning during the differentiation of mESCs into AntNPCs.
- In our in vitro differentiation model, Zic2 knock-out leads to a drastic downregulation of roof plate markers Lmx1a and Lmx1b in AntNPCs.
- The generated Zic2-Flag-HA tagged mESC line (FH6) can be used as an important tool to investigate ZIC2 function using various experimental approaches (ChIP, IP).

**PERSPECTIVES**

Integration of data obtained from different global approaches in order to...

- RNA-seq
- ZIC2 ChIP-seq
- Histone marks ChIP-seq
- Immunoprecipitation-Mass Spectrometry (IP-MS)

...obtain a complete picture of ZIC2 function during neural differentiation.