WNT signaling suppresses oligodendrogenesis via Ngn2-dependent direct inhibition of Olig2 expression

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Abstract
Olig2 transcription factor is essential for the maintenance of neural progenitor cells (NPCs) in the pMN domain and their sequential specification into motor neurons (MNs) and oligodendrocyte precursor cells (OPCs). The expression of Olig2 rapidly declines in newly generated MNs. However, Olig2 expression persists in later-born OPCs and antagonizes the expression of MN‑related genes. The mechanism underlying the differential expression of Olig2 in MNs and oligodendrocytes remains unknown. Here, we report that activation of WNT/β‑catenin signaling in pMN lineage cells abolished Olig2 expression coupled with a dramatic increase of Ngn2 expression. Luciferase reporter assay showed that Ngn2 inhibited Olig2 promoter activity. Overexpression of Ngn2‑EnR transcription repressor blocked the expression of Olig2 in ovo. Our results suggest that down‑regulation of WNT‑Ngn2 signaling contributes to oligodendrogenesis from the pMN domain and the persistent Olig2 expression in OPCs.

Keywords: WNT, β‑catenin, Oligodendrocyte, Ngn2, Olig2

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from a few dorsally-derived [15–17] OPCs were generated (Fig. 1a), demonstrating that WNT activation promotes Ngn2 expression. To confirm that expression in the electroporated side at cE7 (Additional file 1: Fig. S1). However, the number of Ngn2-positive cells was dramatically increased within the ventral ventricular region in Olig2 expression (Fig. 1d), mimicking the effect of full-length Ngn2. This finding demonstrated that Ngn2 inhibits Olig2 expression by its transcriptional repressor activity.

In conclusion, our results suggest that WNT signaling up-regulates the expression of Ngn2, and Ngn2 in turn inhibits Olig2 expression and oligodendrogenesis during MN specification (Fig. 1e).

**Supplementary information**

Supplementary information accompanies this paper at https://doi.org/10.1186/s13041-020-00696-0.

**Additional file 1:** Supplementary materials and results.

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Not applicable.

**Authors’ contributions**

ZMD conceived the project. MJ, DY, BX, HH, WL and ZMD performed the experiments. MJ, DY, BX, HH, MQ, WL and ZMD analyzed the data. MQ and ZMD supervised the project. MJ, MQ and ZMD wrote the paper with input from the other authors. All authors read and approved the final manuscript.

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**Availability of data and materials**

All data generated during this study are included in this article.

**Ethics approval and consent to participate**

The use of animals was approved by the Committee on Laboratory Animals, Hangzhou Normal University.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no conflict of interest.

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