Review of the Ph.D. Thesis by Naoko Dupačová-Fujimura:

The Role of Wnt signaling in embryonic development

The Ph.D. Thesis by N. Dupačová-Fujimura focuses on the developmental role of Wnt signaling with emphasis on the role of the Wnt/β-catenin signaling during telencephalon and eye early development in mouse embryos. The Thesis is supported by results of the research work performed at the Department of Transcriptional Regulation, Institute of Molecular Genetics, Academy of Sciences CR, under supervision by Dr. Zbyněk Kozmík. The research insisted in systematic and detailed studies on the molecular control of an eye early development in the mouse model, effectively combining the modern methods of molecular biology with descriptive embryological knowledge. Such an approach has brought excellent results based on well-founded correlation of the acquired molecular data with morphogenesis of appropriate structures. The results gave rise to three papers published in prestigious impacted journals, their total IF = 11.93 - N. Dupačová-Fujimura is the first author in two of them. In addition, she has published still one paper, which has not been included in the present thesis.

The present Thesis has a form of a set of publications accompanied by a brief text. The text written in English is well readable and comprehensive. The Thesis is structured in accordance with the rules and includes three inserted papers.

The Abstract (in both English and Czech) summarizes the Thesis content.

The part Introduction presents, it its first chapter, the state of knowledge on the Wnt signaling, its principle, types, Wnts antagonists and agonists, and on the Wnt/ β-catenin signaling during embryonic development in particular. The second and third parts of the Introduction summarize the knowledge on the vertebrate eye and telencephalon development and its molecular control, with emphasis on the available data on the involvement of Wnt signaling. The content of Introduction logically leads to the presentation of a brief rationale and setting out of three aims, which are tangibly and clearly formulated.

The part Material and Methods is represented by enumeration of methods applied.

The part Results and Discussion comprises commentary related to the following inserted 3 papers, which had successfully passed the peer-review process in the impacted journals. The comments further elucidate rationale and sequence of particular steps of research works.

The presented Conclusions answer the Aims.

I have just few minor comments concerning formal aspects of the Thesis that in no way decrease its high quality:

In the text, there is introduced a classical (textbook) description of eye development supported by references of recent papers (e.g. Chow and Lang, 2001; Grainger et al, 1997). A reader-beginner can get an impression that embryological knowledge on eye development is very fresh, although, for example, the interaction between protrusion of the forebrain and surface ectoderm to form eye cup and lens primordia was described by B. Sharp in 1885 (according to Pubmed).

The chapter called Aims and Hypothesis could better be only called Aims, since hypotheses are not explicitly formulated there. (Particular hypotheses are presented in Results and Discussion, and in the papers themselves).

It might also be useful for a reader to find the following information in the Thesis – the enumeration of the mouse lines employed in the studies (in Material and Methods); the list of included publications by N. Dupačová-Fujimura with IF value (such a list is present in Thesis

Summary) and with a specification of author's personal contribution in each study; emphasizing of the importance and impact of the findings achieved in frame of the Ph.D. project (in Conclusions).

In the Thesis text, references in parentheses are ranked alphabetically instead of chronological ranking.

Refs Dimanlig et al, 2001 and Wilians (Wiliams?) et al, 1998 are introduced on page 18 in the Thesis, but missing in the list of references.

The authors'names starting with Ch (pp. 90-91) should probably be listed in frame of "C" in English written References.

The very interesting data of the Thesis gave rise to some questions:
- Is there an explanation for why are the nuclei of RPE resistant to DAPI labeling in gain-of-function mutants in Fujimura et al, 2009, Fig. 5 F,H,K,L?
- The abnormally folded neural retina (NR) in the gain-of-function mutants (e.g. Fig. 7P in Fujimura et al, 2009) seems to have twice more extent area than the NR in WT animals (e.g. Fig. 7O). How can be such an increase in area explained? Could not correspond, at least partially, the proximally located layer of the NR to transdifferentiated RPE (compare the retina shape on Fig. 7L,N,P,R with Fig. 2H)?
- Is there any explanation for why is such a strong staining present in the surface ectoderm so far around the lens placode on Fig. 1, Machon et al, 2010?
- Just a technical question: Was the treatment and storage time before sectioning identical in the two groups of specimens E10.5-11.5 and E13.5-15.5, which exhibit different aspect of tissues on sections (Fujimura et al, 2009, Figs 2A-D versus 2E-H, or Fig. 6A-D versus 6E-H)?

Conclusion: The Ph.D. Thesis by N. Dupačová-Fujimura has brought valuable and high quality data on molecular control of the eye early development in the mouse, especially on the Wnt/β-catenin signaling, and on the functional interaction between canonical Wnt signaling and Pax6. The Thesis, as well as the Thesis Summary, are very well readable and comprehensively written, comprising the papers published in impacted journals with total IF=11.93. The employed methods document a large spectrum of theoretical and practical knowledge achieved during realization of the Ph.D. project. The accompanying text supported by more than 300 references evidences that the author is very well versed in the problematic and knows to synthesize and integrate the existing literary data with the data achieved by own research work. By the present Thesis, N. Dupačová-Fujimura has demonstrated disposition for self-reliant research work.
In conclusion, this Ph.D. Thesis is recommended for its defense.

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