

REVIEW

By a member of the Dissertation Council

on the dissertation of Pavel Mikhailovich Docshin titled “Notch-Dependent Mechanisms of Functional Regulation of Cardiac Mesenchymal Cells in Acute Infarction and Malformations”, submitted for the degree of Candidate of Biological Sciences in the specialty 1.5.22 – Cell Biology.

General Overview of the Work

The dissertation by Pavel Mikhailovich Docshin focuses on the study of the Notch signaling pathway as a key regulator of cardiac mesenchymal cell function under conditions of hypoxia and myocardial remodeling. This work is highly relevant in the context of advancing molecular medicine and regenerative approaches to cardiovascular diseases.

The dissertation comprises 142 pages, including 45 figures. It consists of an introduction, three chapters, conclusions, and references, with a bibliography of 229 sources. The structure of the work is logical, and the results are thoroughly discussed in the context of existing scientific literature.

Significance and Originality

The study addresses an essential scientific problem: understanding the molecular and cellular mechanisms underlying myocardial remodeling. The author has made significant contributions to the field, including:

- Elucidating the role of the Notch signaling pathway in regulating the proliferative and migratory properties of cardiac mesenchymal cells under hypoxic stress.
- Establishing the interaction between Notch and BMP signaling pathways in mediating endothelial-to-mesenchymal transition.
- Providing novel insights into the molecular processes in cardiac mesenchymal cells derived from tissues with congenital heart defects, such as tetralogy of Fallot.

These findings expand our understanding of the cellular mechanisms driving myocardial repair and provide a foundation for further research into targeted therapies for heart disease.

Strengths and Methodological Rigor

The study employs a broad range of cutting-edge methodologies, including:

- Lentiviral transduction for precise modulation of Notch signaling.
- Co-culture systems to study intercellular interactions.
- Real-time PCR for detailed expression analysis of key signaling genes.
- Advanced bioinformatics tools to investigate pathway activation and regulatory networks.

The robustness of these methods and the reproducibility of the results underscore the high quality of the experimental work.

Comments and Suggestions

1. The data on tetralogy of Fallot provides an intriguing perspective. Could the author expand on how the altered Notch signaling observed in congenital heart defects might inform regenerative strategies for adult cardiac diseases?
2. Beyond lentiviral transduction, what other strategies (e.g., small molecules or CRISPR-based tools) might the author suggest for modulating Notch activity in cardiac cells?

Conclusion

Pavel Mikhailovich Docshin's dissertation represents a well-structured, thoroughly conducted investigation of the Notch signaling pathway in cardiac mesenchymal cells. The results are original and impactful, contributing to the fields of cellular biology and regenerative medicine.

The dissertation meets the criteria for scientific rigor and novelty, and I firmly recommend awarding Pavel Mikhailovich Docshin the degree of Candidate of Biological Sciences in the specialty 1.5.22 – Cell Biology.

Member of the Dissertation Council,
PhD, Professor



Kang Xu

Date: November 20, 2024