



Fund “Nauka” Project № 25013 Resume – Competition-based Session 2025:

“Light- and electron-microscopic phenotyping of progenitor cell populations expressing the transcription factor ZBTB20 in the human subpallium during fetal development”

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ZBTB20 is a transcription factor with a key role for the development of neurons and glia in the central nervous system. Experimental change in its levels of expression leads to significant defects in the neocortex, hippocampus, and the olfactory bulb. ZBTB20 is expressed in the murine subpallium and is important for the normal development of the cortical interneurons. The interneurons are significantly more numerous and better connected in primates. Much less is known about its expression and role in primates, especially humans. A mutation of ZBTB20 leads to a rare neurodevelopmental disorder known as Primrose syndrome. In contrast to the murine subpallium, different cytoarchitecture and a prolonged period of neurogenesis of the cortical interneurons are observed in humans, which is associated with the greater number of cortical interneurons in humans. According to preliminary data, there is significant expression of ZBTB20 in the human subpallium as well. These observations led to investigation and phenotypization of the ZBTB20-positive (+) cells in the human subpallium. To achieve this goal, a combination of the already well-established immunofluorescence protocol for human fetal tissues with electron microscopy and immunogold particles will be used to analyze the ZBTB20+ cells at the ultrastructural level. These studies will be conducted at two primary time points: approximately sixteenth and twenty-fourth gestational weeks, which will allow the investigation of a shift in the functions of ZBTB20 during different periods of fetal development. Additionally, the nuclear localization of ZBTB20 will be of interest, as it has not been studied. This research will provide ultrastructural data about the association of the transcription factor ZBTB20 with euchromatin or heterochromatin, which is crucial for the mechanism of action of ZBTB20 as a transcriptional repressor like zinc-finger transcription factors of other families.

Expected results:

1. The role of ZBTB20 during human subpallium development will be elucidated through the phenotyping of ZBTB20+ cell populations based on immunofluorescent and electron-microscopic features;

2. An algorithm will be established for the study of the human fetal brain using electron microscopy;
3. The interaction of ZBTB20 with different intranuclear compartments will be detected at the ultrastructural level.