МЕДИЦИНСКИ УНИВЕРСИТЕТ - ВАРНА
„Проф. д-р Параскев Стоянов“
Ул.“Марин Дринов“ 55, Варна 9002, България
Тел. : 052/ 65 00 57, Факс: 052/ 65 00 19
e-mail: uni@mu-varna.bg, www.mu-varna.bg

MEDICAL UNIVERSITY - VARNA
“Prof. Dr. Paraskev Stoyanov”
55, Marin Drinov Str., 9002 Varna, Bulgaria
Tel.: +359 52/ 65 00 57, Fax: + 359 52/ 65 00 19
e-mail: uni@mu-varna.bg, www.mu-varna.bg

Fund “Nauka” Project № 19025 Resume – Competition-Based Session 2019:

“Astrocytic heterogeneity and transcription factor ZBTB20 expression in glial cell subpopulations of human telencephalon”

Project leader: Assoc. prof. Irina Ivanova Stoyanova-van der Laan, MD, PhD

Michailova VD, Genev PI, Tonchev AB, Zhekova VG, Bukovinov DD, Angelov IA, Stoyanova II

Astrocytes are brain glial cells that perform various functions in the Central Nervous System (CNS): Two major morphological types of astrocytes are known: fibrous, in the white matter and protoplasmic, in the gray matter. GFAP (glial fibrillary acidic protein) is a standard marker used to for identify CNS astrocytes. Most of the data available about the morphology of the astrocytes has been obtained from experiments in rodents. However, studies in the primate brain suggest the existence of primate specific astrocyte features. For example, a study on the expression of CD44 (membrane protein and extracellular matrix receptor) classifies astrocytes into two main subtypes: $CD44^{+}$ with long processes and $CD44^{+}$ without long processes. Some of these cells express GFAP, while others do not. The latter, according to their morphology and immunohistochemical phenotype, have the characteristics of both protoplasmic and fibrous astrocytes, which suggest heterogeneity of the human astrocytes.

In this project, we plan to investigate the expression of transcription factor ZBTB20 in human brains. In adult brain, ZBTB20 is expressed in the hippocampal pyramidal neurons. However, evidence in mice suggests it is also expressed in cortical glia. We aim to investigate the cell types which express ZBTB20 in adult human cerebral cortex under normal conditions. To this aim, we shall investigate brain tissue from autopsies of deceased patients without evidence for neurological disease. Images obtained after immunofluorescence staining will be quantitatively evaluated and subjected to additional statistical analysis. With this study, we hope to shed additional light on the heterogeneity of the glial subpopulations in the human brain.

Key words: Human telencephalon, astrocytes, heterogeneity, ZBTB20

Achieved results:

The transcription factor ZBTB20 is expressed in neural progenitor cells during mouse brain development, where it plays a role in the switch from neurogenesis to gliogenesis. However, in the adult brain there is a differential expression of Zbtb20: in rodents, only the hippocampal pyramidal neurons are positive, while in the cortex Zbtb20 expression is limited to the glial cells. In the adult human brain ZBTB20 has been studied only in the hippocampus and detected in the pyramidal neurons. The ZBTB20 expression in the cerebral cortex of adult

humans has not been investigated yet. We studied the expression of ZBTB20 in human autopsied brains without prior neurological disease. We examined areas of the motor cortex. The specimens were double immunostained for detection of the transcription factor ZBTB20 in combination with glial fibrillary acidic protein (GFAP), marker for astrocytes; with the neuronal marker Neuronal nuclei (NeuN); with the endothelial marker CD34; with ionized calcium-binding adapter molecule 1 (IBA1), marker for microglia and with SRY-related HMG-box 10 (SOX10), marker for oligodendrocytes. Immunofluorescent images were qualitatively and quantitatively analyzed. ZBTB20 expression was not detected in either cortical neurons or microglia. Strong expression of the transcription factor was observed in astrocytes, predominantly located in the molecular layer. In the deeper layers, as well as in the white matter, a limited number of astrocytes was also ZBTB20 positive. ZBTB20 expression was also present in some of the perivascular astrocytes. Additionally, we found ZBTB20 positive oligodendrocytes localized mainly around neurons in the cerebral cortex, but co-expression of ZBTB20 and SOX10 was observed also in white matter glial cells. These results suggest heterogeneity of the cortical glial population based on the expression of ZBTB20. Further, these data prompt to the conclusion that ZBTB20 plays a role not only in the neurogenesis but also in the gliogenesis in human.