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Fund “Nauka” Project № 24026 Resume – Autumn Competition-based Session 2024:

“Discovery of novel markers for progenitor cells in the adult primate brain through analysis of genes with increased postischemic expression in the stem cell niches”

Project leader: Chief assist. Doctor Martin Nikolaev Ivanov, PhD

Adult neurogenesis is the process by which new neurons are formed from neural stem cells in specific regions of the brain known as “neurogenic niches”. These areas include the subventricular zone of the lateral ventricle (SVZ) and the subgranular zone of the hippocampal dentate gyrus (SGZ). The SVZ extends from the anterior horn of the lateral ventricle (anterior SVZ, SVZa) to the temporal/ inferior horn (inferior SVZ, SVZi). Stem cells in the SVZa can produce neurons, while progenitors in the SVZi primarily generate glial cells. Previous research of the project team has shown that cerebral ischemia leads to differential changes (increases or decreases) in the expression of approximately 1000 genes in the SVZa and SVZi. Bioinformatics analyses have revealed that genes whose expression increases after ischemia in either zone (SVZa or SVZi) are functionally associated with progenitor cells and their biology.

In this project, the aim is to investigate only those genes whose expression increases after ischemia in both stem cell niches: SVZa and SVZi. These genes have a high potential to serve as markers for stem cells. To achieve this goal, samples from adult primates (monkeys) subjected to global cerebral ischemia will be used. Cerebral hypoxia stimulates the transcription of genes that promote the cell division and differentiation of stem cells in the brain. Previous bioinformatics analyses of RNA sequencing have identified genes whose expression increases in the SVZa and SVZi after ischemia. In this project, we propose to examine a significant portion of these over 130 genes at a cellular resolution level: analysis through in situ hybridization (ISH) of tissue sections from normal and ischemic tissues of SVZa and SVZi.

The gene expression in the neurogenic zone SVZa and the non-neurogenic zone SVZi will be compared. The identification of the same genes with increased expression in both zones would indicate an important role of these genes in cellular processes common to both regions. Primarily, the goal is to identify one or more of these genes as new potential markers for stem/progenitor cells in the primate brain, which can subsequently be validated in humans.

За да постигнем поставената цел, предвиждаме следните задачи:

(1) Идентифициране на гените, увеличени и двете зони (SVZa и SVZi) след исхемия.
(2) Генериране на in situ проби за максимален възможен брой, около 25% от 130-те увеличени гени в SVZa и SVZi (30-35 гена)
(3) Провеждане на in situ хистологичен анализ на експресията на минимум 10 гена, чиято експресия е увеличена както в SVZa, така и в SVZi при контролни и исхемични маймуни.
(4) Обобщение на резултатите и идентифициране на нови маркери за стволови клетки в приматния мозък

Очакваните резултати от проекта
The team has already established the foundational prerequisites for the success of this project: tissue samples and histological sections from monkey brains, completed RNA sequencing, and the expertise to conduct RNA in situ hybridization stainings.

Within the framework of this project, the project team will be the first in the world to report on:
(1) Functional and phenotypic characteristics of genes with differential expression after ischemia in SVZi and SVZa in the format of Excel tables and diagrams;
(2) Genes that increase their expression in SVZa or SVZi after ischemia in the format of Excel tables and diagrams;
(3) In situ expression in SVZi and SVZa of at least 10 genes in the form of micrographs and statistical data on the expression level in control and ischemic sections. Images will be uploaded to the online MONKEY-NICHE atlas (http://monkey-niche.org);
(4) Phenotypic analysis of one selected gene in the form of micrographs and statistical data on the percentage of co-expression with cell-specific markers;
(5) Identification of a new marker for stem cells in the primate brain.