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Особливості міграції в культурі нейральних клітин плодів та новонароджених щурів

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Characteristic of Migration in Culture of Newborn and Fetal Rat Neural Cells

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The use of neural stem/progenitor cells (NSPCs) holds great promise for the treatment of central nervous system disorders. At the same time, for effective recovery and regeneration, NSPCs must be capable of targeted migration to diseased or damaged tissues. There is currently limited understanding of the ways and mechanisms underlying migration of both transplanted and endogenous NSPCs.

The aim of the work was to study the features of migration in the culture of newborn and fetal rat neural cells (NCs).

Cells were isolated from newborn and fetal (E15-16) rat brains. Neural cells were seeded at the concentration of 2×10^6 cells/well in 24-well plates and cultured in a CO_2 incubator in DMEM/F12 in the presence and absence of serum. The formation of NCs aggregates was stimulated by pipetting. The formed aggregates were reseeded.

Most of the cell aggregates (fetal and newborn) of both initial cultures and after reseeding attached to the substrate. After that, their cells proliferated, differentiated and migrated in all directions. Two days after the replacement of the medium with serum-free medium, in the initial NCs cultures of both fetal and newborn rats, the formation of cell chains was observed, which is typical for migrating NSPCs and neuroblasts of the neurogenic zones of the postnatal brain of mammals. The chains consisted of neuroblast-like (with two short processes), or round, undifferentiated cells. There were no guiding structures along which the cells lined up. During cultivation, the length of chains and their number increased. Chains were observed in cultures for 2 months after formation, after which they disintegrated. The shape of the chains was rectilinear, arcuate, sinusoidal. The chains could cross. A parallel arrangement of several chains was observed.

After cryopreservation, the ability of NCs cultures to form chains was preserved. However, unlike the initial cells, the formation of chains by cryopreserved cells occurred 5 days after the medium was replaced with serum-free medium.

The studies performed have shown that heterogeneous suspensions of fetal and newborn rat brain NCs contain a significant amount of cryoresistant stem/progenitor cells capable of proliferating, differentiating, and migrating. The ability of newborn and fetal rat NSPCs to a chain migration indicates their ability during transplantation to colonize damaged areas of brain tissue, crossing the intact tissue. This gives grounds to assume a high therapeutic efficiency of the studied cells.

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Індукована паклітакселом периферична нейропатія *in vitro*

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Paclitaxel Induced Peripheral Neuropathy *in Vitro*

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Paclitaxel induced peripheral neuropathy (PIPN) is a severe adverse effect observed in most cancer patients receiving paclitaxel for the treatment of breast, ovarian or lung cancer. Recent studies have aimed at defining the underlying mechanisms of PIPN. *In vitro* models using dorsal root ganglion (DRG) neurons have revealed a number of molecular pathways affected by paclitaxel within axons of sensory neurons, such as altered calcium signaling, neuropeptide and growth factor release, mitochondrial damage, reactive oxygen species formation, activated ion channels that mediate responses to extracellular cues and role for the matrix-metalloproteinase 13 in mediating neuropathy. In this study, DRG derived sensory neuron culture system obtained from adult rats as a useful *in vitro* model, has been used as a neurotoxicity-screening model to evaluate the effect of paclitaxel on the neurite elongation. To preserve neuronal health, DRG were kept as cold as possible throughout the dissection. Once dissected and cleaned, DRG were then collected in a pre-cooled medium to allow good nerve tissue survival. The neurotoxic effect of this drug was analyzed by measuring the neurite length of post-mitotic, non-dividing cells, such as neurons. Paclitaxel-induced tubulin polymerization in these cells is thought to interfere with axonal transport, causing peripheral neuropathy. The neurotoxic effect of paclitaxel is dose and time dependent. Moreover, in DRG dissociated post-mitotic neurons, the morphological features of paclitaxel-induced cellular death were studied and the DRG neurons were observed to die by necrosis. DRG derived sensory neurons, as well as DRG explants are a good, simple and well-accepted model for studying peripheral neuropathy induced by various antineoplastic agents. Currently, there are no therapeutic options available for the prevention or successful therapy of PIPN and only a few drugs are recommended for the treatment of existing neuropathies because the mechanisms of PIPN remain unclear. Our findings demonstrate a previously known neurotoxic effect of paclitaxel in DRG derived sensory neuron culture system and suggest advantages of this *in vitro* model, as high efficiency and reproducibility of cell culture studies in the field of toxic neuropathy induced by paclitaxel.

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