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THE ROLE OF UROKINASE RECEPTOR AND ITS INTERACTION WITH α5β1 INTEGRINS IN NERVE REGENERATION

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Nerve regeneration depends on axon growth mediated by integrins interaction with extracellular matrix (ECM). Urokinase receptor (uPAR) is a GPI-anchored protein, which focuses uPA and promotes ECM proteolysis. uPAR-integrins interaction results in the change of integrin conformation and intracellular signaling. To evaluate the effect of uPA/uPAR system on nerve regeneration, we used traumatic injury model of n. Peroneus communis. The nerve recovery was assessed using nerve conduction velocity measurement in knockout mice lacking uPA (uPA-/-) or uPAR (uPAR-/-) and control mice (WT). No difference was found between uPA-/- and WT mice, suggesting an insignificant contribution of uPA. But the amplitude in uPAR-/- mice 14 days after trauma was reduced compared to WT and uPA-/- mice ($p < 0.05$) and the lengthening of the latent period was observed ($p < 0.05$) on the 7th day. This data indicate the important role of uPAR in nerve recovery. Immunofluorescent staining of crushed nerve cryosections demonstrated the increase in uPAR and α5β1 integrin expression and co-localization in uPA-/- mice compared to WT mice. Neuroblastoma cells (N2a) overexpressing uPAR (uPAR), uPAR-deficient cells (ΔuPAR) and control cells (WT), natively expressing uPAR, were used to prove that uPAR and α5β1 co-localization has a physiological relevance. Cells were platted on fibronectin or uncoated plastic and serum-deprived to stimulate neuritogenesis. Blocking peptide α325, which abrogates interaction of uPAR with α5β1 integrins but has no effect on their function, scrambled peptide s325 as a control were added to media. Administration of α325 reduced the number of neurite-bearing cells in WT cells compared to s325 ($p < 0.05$). ΔuPAR cells did not respond to the peptides. uPAR cells produced fewer neurites after α325 administration compared to s325 ($p<0.05$). This data indicate that uPAR-α5β1 integrin interaction is important for neuritogenesis.

Biography

Polina Klimovich is a PhD student of 3d year at the age of 26 from Faculty of Medicine, Lomonosov Moscow State University. Published 4 papers. She graduated with an honours degree in Pharmacy from Lomonosov Moscow State University, takes part in the scientific work devoted to the study the mechanisms of the directed vessels and nerves growth regulation by fibrinolytic system components and GPI-anchored navigation receptors. Participate of Pre-clinical evaluation of a drug based on gene-engineered construct bearing cDNA sequences of brain-derived neurotrophic factor and urokinase plasminogen activator to treat peripheral nerve injury. Received the award for the best poster presentation at the 4th Congress of Physiologists of the CIS in Sochi.

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