PI3K mediated electrotaxis of embryonic and adult neural progenitor cells in the presence of growth factors.

Journal: Exp Neurol

Publication Year: 2011

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PubMed link: 21092738

Funding Grants: Directing migration of human stem cells with electric fields

Public Summary:
We first tested the effect of electric fields in guiding migration of neural progenitor cells from rat. Using this model, we also tested the underlying mechanisms using genetic approaches. We found that application of electric fields guide migration of embryonic and adult neural stem cells. This electric field guided migration of neural stem cells requires epidermal growth factor and fibroblast growth factor. We also found that an important intracellular signaling pathway, PI3K/Akt pathway controls the response of the neural stem cells to applied electric fields. These results led us to successfully launch of experiments using human stem cells.

Scientific Abstract:
Correct guidance of the migration of neural progenitor cells (NPCs) is essential for the development and repair of the central nervous system (CNS). Electric field (EF)-guided migration, electrotaxis, has been observed in many cell types. We report here that, in applied EFs of physiological magnitude, embryonic and adult NPCs show marked electrotaxis, which is dependent on the PI3K/Akt pathway. The electrotaxis was also evidenced by ex vivo investigation that transplanted NPCs migrated directionally towards cathode in organotypic spinal cord slice model when treated with EFs. Genetic disruption or pharmacological inhibition of phosphoinositide 3-kinase (PI3K) impaired electrotaxis, whereas EF exposure increased Akt phosphorylation in a growth factor-dependent manner and increased phosphatidylinositol-3,4,5-trisphosphate (PIP3) levels. EF treatments also induced asymmetric redistribution of PIP3, growth factor receptors, and actin cytoskeleton. Electrotaxis in both embryonic and adult NPCs requires epidermal growth factor (EGF) and fibroblast growth factor (FGF). Our results demonstrate the importance of the PI3K/Akt pathway in directed migration of NPCs driven by EFs and growth factors and highlight the potential of EFs to enhance the guidance of various NPC populations in CNS repair therapies.

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