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The Role of Neurotrophic Factors in Dental Pulp Stem Cell

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Abstract

Neurotrophic factors are growth factors that can nourish neurons and promote neuron survival and regeneration. They have been studied as potential drug candidates for treating neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease. Since their identification, there are new evidences to indicate that neurotrophic factors are also expressed in non-neuronal tissues and promote the regeneration of tissue-specific adult stem cells.
Dental pulp stem cells (DPSCs) are multipotent mesenchymal cells that can differentiate into different cells originally derived from ectoderm, mesoderm and endoderm. Researches indicate that human DPSCs are able to differentiate into neuron, blood vessel, dentin, bone and adipose tissue under appropriate conditions. These properties make DPSCs a promising resource for stem cell therapy.
This study aims to investigate the role of neurotrophic factors in the DPSCs. The hypothesis is that neurotrophic factors promotes the DPSCs proliferation, and may also be involved in DPSCs migration and differentiation. Using Quantitative PCR, the expression of the neurotrophic family members and receptors in the DPSC were determined. Preliminary data indicated that neurotrophic factor PSPN has a dose dependent effect on the DPSCs migration. The future direction is to investigate the effect of different neurotrophic factors on DPSCs behavior, and the downstream signaling pathways involved in the process. This work will be important to understand the molecular mechanism of the dental pulp regeneration post trauma and pulpectomy, and will also shed light on the potential application of neurotrophic factors and DPSCs in other adult tissue regeneration.

Background

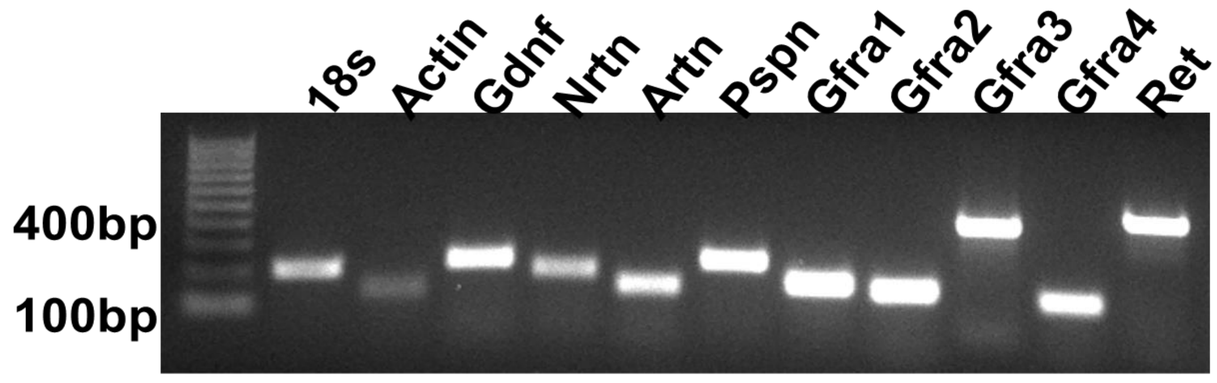
Neurotrophic factors include NGF, BDNF, NTs and the glial cell derived neurotrophic factors (GDNF) family. Besides GDNF, the family also includes neurturin (NRTN), artemin (ARTN) and persephin (PSPN). The GDNF family neurotrophic factors are also considered members of the transforming growth factor-beta (TGF-beta) family. By activating the GDNF family receptors (GFR) and the co-receptor tyrosine kinase RET, GDNF family is reported to improve neuron survival, proliferation and migration. GDNF is also reported enriched in salivary gland stem cells, and increases post radiation salivary gland regeneration.

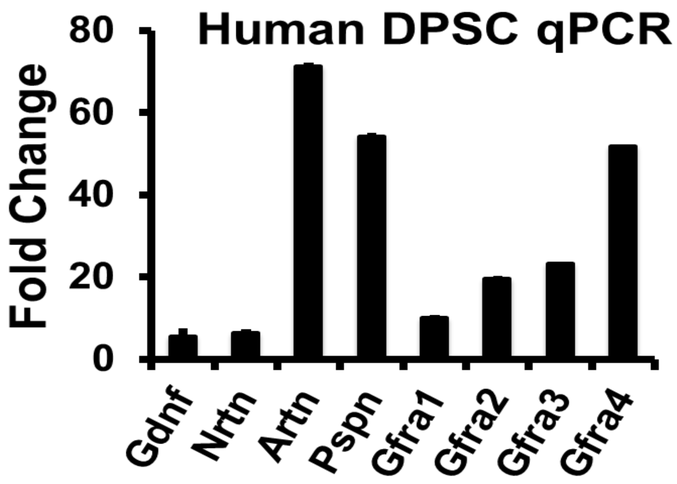
Materials & Methods

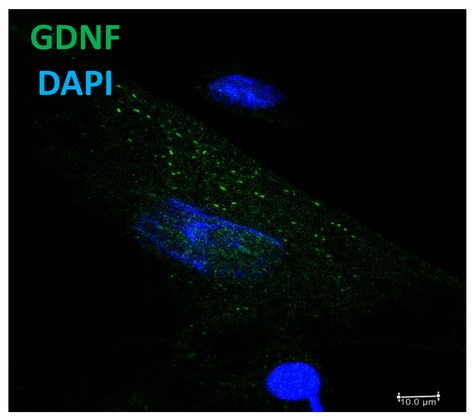
Human DPSCs cells were gift from Dr. Songtao Shi, Chair and Professor Department of Anatomy & Cell Biology, University of Pennsylvania School of Dental Medicine
DPSCs mRNA was extracted from samples of five different patients, and reverse transcripted into cDNA. Primer sequences were designed with Primer3web online software. Quantitative PCR was performed on the cDNA samples using a 7900HT detection system (Applied Biosystems). All PCR reactions were carried out in triplicate. Quantification of the samples was calculated with the threshold cycle by ΔΔCt method.
Immunofluorescent staining images were acquired using a Leica TCS SPE confocal microscope. Scratch assay images were acquired using a Leica DMiL inverted microscope.

Results

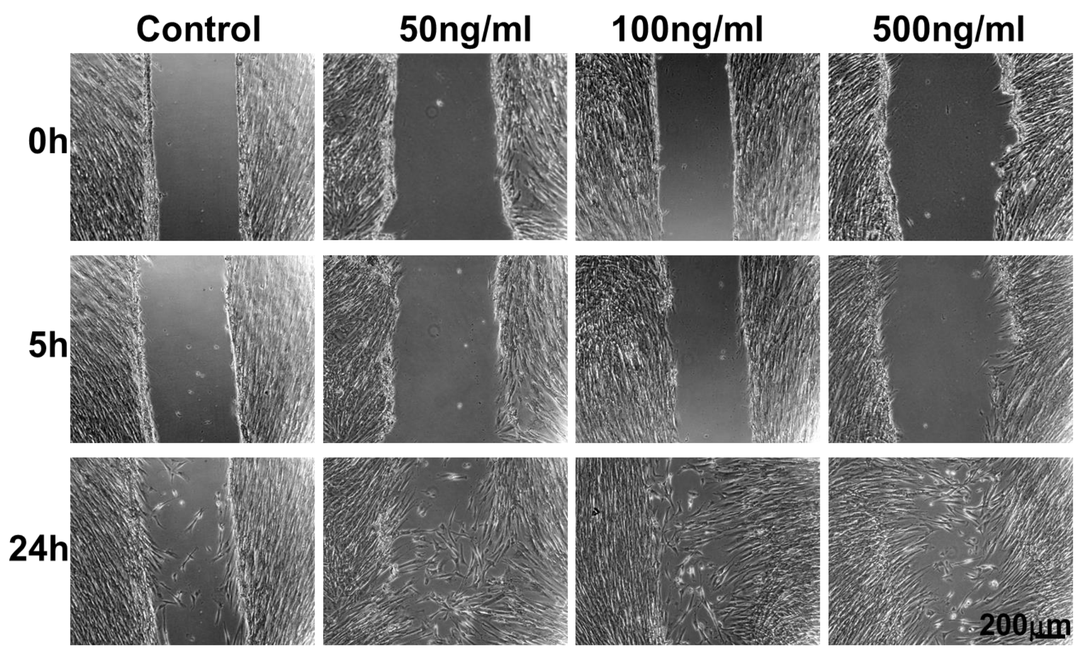
GDNF family Neurotrophic Factors and Receptors are expressed in DPSCs.

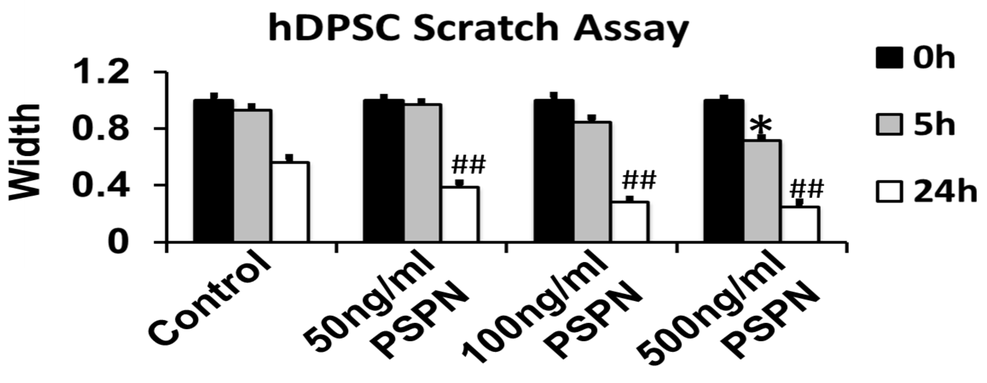






Recombinant hPSPN increases DPSC migration.





Future Directions

The effects of different Neurotrophic factors on DPSCs proliferation and differentiation under normal condition and inflammatory condition.
The molecular pathways downstream of the neurotrophic factors in regulating DPSCs behavior.

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