



**Title:** Humoral response to autologous hematopoietic lineage-negative cells administration in patients with neurodegenerative diseases – novel view on the paracrine effect consolidation

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**Abstract:**

Neurodegenerative diseases constitute a group of incurable disorders characterized by a gradual loss of neural cells or their function. Therefore, any form of trophic support provision for the degenerating neurons may bring beneficial effects or at least slow the progression of the disease. In multidirectional research conducted by our team over the previous years we have focused on different approaches towards neurotrophins delivery in patients with amyotrophic lateral sclerosis and degenerative diseases of the retina. Our studies have shown that the utilization of autologous lineage negative hematopoietic cells derived from bone marrow which are characterized by increased expression of neurotrophic factors is a safe and feasible route of trophic support delivery. Moreover, this therapy approach in ALS patients may exert beneficial effects on articular functions and regulate selected pathways related to immune response which is also one of the proposed factors involved in ALS pathogenesis. In retinitis pigmentosa cells injection is correlated with improved bioelectrical function of the retina and contributes to better visual acuity. Our search for potent routes of trophic support provision has also led us towards the use of novel biocompatible nanoparticles which can act as protein delivery systems. In vivo studies in mice have shown that PAMAM cores coated in neurotrophins when administered intravitreally improve the function of the retina. Their further modifications including the encapsulation in PEG polymer molecules stabilizes their structure and prolongs the protein release period what could increase their future therapeutic potential. Better understanding of their interactions with living cells which depend on their physicochemical properties is needed to fully and consciously harness them as neurotrophic support providers in human research. In the future the conjoined efforts utilizing both – cellular and nanoparticle based therapy approaches could contribute to development of sustained neurotrophins delivery systems in neurodegenerative diseases.