Humoral immunity following neural precursor cell administration in naive rodents

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Background: In multifactorial diseases, such as Multiple Sclerosis (MS), cell therapies with Neural Precursor Cells (NPCs) of Central Nervous System (CNS) may be candidates for transplantation. Despite indisputable positive results in the animal model of MS, Experimental Autoimmune Encephalomyelitis (EAE), many issues remain unclarified.

Goals: The potential immune response(s) after NPCs administration in naive mice.

Methods: NPCs cultured from C57BL/6 newborns were inoculated in naive C57BL/6 adult mice. MOG_{35-55}-EAE mice and NAIVE mice were used as positive and negative control. On day-17-Acute phase blood sampling was performed and antisera (NPCs-AS, EAE-AS, NAIVE-AS) were collected. Humoral immunity was evaluated by Western Blot (WB). On days 17 and 50-Chronic phase post EAE induction, CNS tissues were examined by immunohistochemistry (IHC) for inflammatory markers and by Real-time PCR (qPCR) for inflammation-related genes expression.

Results: WB showed dominant immunoreactivity on NPCs substrate indicating specific bands (100kDa, 60kDa, 50kDa, ~40kDa, 30kDa, 25kDa), when using NPCs-AS. On spinal cord (SC) substrate 25kDa band was yielded, suggesting a mere presence of immunoreactivity against CNS. IHC on brain sections of NPCs, EAE and NAIVE animals, with anti-CD3, anti-Mac-3 and anti-B220 revealed elevated expression (cells/mm^2) of all markers in NPCs- and EAE-group during acute and chronic phase respectively; NPCs:CD3: 111.0±18.84 and 18.73±7.90, Mac-3: 83.69±15.36 and 416.1±73.90, B220: 9.82±5.12. EAE:CD3: 91.66±18.96 and 82.40±32.43, Mac-3: 213.0±39.31 and 221.7±38.27, B220: 4.42±2.05. qPCR showed CCL2 and CCL20 mRNA overexpression mainly in the brain of NPCs- versus EAE-group; CCL2-Acute:15.55- vs 57.69-fold,$p<0.001$, CCL2-Chronic:28.48- vs 8.46-fold,$p<0.01$; CCL20-Acute:5.59- vs 1.13-fold, $p<0.01$; CCL20-Chronic phase:19.94- vs 1.82-fold, $p<0.001$. IL-17RA-mRNA was upregulated in SC in acute phase (NPCs:23.21-, EAE:35.17-fold) and remained increased only in NPCs-group in chronic phase (38.19-fold).

Conclusions: Cellular and humoral immune responses after naive mice immunization with NPCs provide evidence of their potential involvement in autoimmunity. Cross-talk between NPCs and CNS immune mechanisms warrants further investigation.