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Study on the diagnostic and prognostic aspects of bone marrow microenvironment components in Non-Hodgkin's lymphoma before and after therapy

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Objectives: The main goal of the study is the evaluation of the stromal cells of bone marrow microenvironment (BMM) in bone marrow trephine biopsy (BMTB) and fibronectin, tumor necrosis factor- alpha (TNF-α), L-selectin of bone marrow (BM) plasma in Non-Hodgkin's Lymphoma (NHL) patients, before and after therapy.

Material & Methods: A total of 80 de novo NHL patients which were divided as B-cell lymphoma 64/80 (80%), comprising follicular cell lymphoma (FCL) 32/80 (40%) patients, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) 12/80 (15%) patients, and diffuse large cell lymphoma 20/80 (25%) patients and T-cell lymphoma, which constituted 16/80 (20%) of patients, all diagnosed as T-Lymphoblastic lymphoma. Patients were evaluated before and after therapy, and compared to 25 BM donors as control group. BMTB and BM aspirate were taken for morphological assessment of stromal cell. Plasma of BM samples was examined for TNFα, L-selectin, which were tested by ELISA technique, and Fibronectin by Radial immunodiffusion (RID).

Results: BM stromal cells comprising reticular macrophages and fibroblasts were increased in 53.3% of NHL at diagnosis. BM Fibronectin levels were decreased, while BM TNFα and L-selectin were higher at diagnosis in comparison to CR ($p<0.05$) and control ($p<0.05$). In NHL, elevated values of BM TNFα and BM L-selectin were associated with signs of aggressive disease, including, extra nodal sites were increased (>1), detectable B cell-symptoms, high grade NHL, signs of BM and CNS invasion, high International prognostic index (IPI) ($p<0.05$).

Conclusion: BMM components, TNFα, L-selectin and fibronectin in NHL can be useful in evaluating disease activity, extent and response to treatment and as prognostic markers according to (IPI).

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Crosstalk signals between transplanted neural stem cells, the host niche and dopaminergic neurons via. astrocytes trigger dopaminergic nigrostriatal neurorestoration in Parkinsonian mice

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Within their specialized germinal niches, populations of local astrocytes instruct neural stem/progenitor cells (NSCs) via. complex cell-cell interactions and signaling cascades, which include the activation of the Wnt/β-catenin pathway, a signalling system required for specification and neurogenesis of midbrain dopaminergic (mDA) neurons, the pivotal neuronal population that degenerates in Parkinson's disease (PD) and in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) mouse model of PD. Recently, we uncovered that the midbrain aqueduct (Aq)-periventricular regions (PVRs) SVZ act as a natural niche for mDA progenitors. Accordingly, mDA neuron death induced by the neurotoxin MPTP, promotes an early astrocyte-dependent activation of these Aq-PVR-DA progenitors, but a lack of appropriate niche environmental signals restrict their neurogenic potential and compromise neuronal survival/rescue. Given that transplanted NSCs possess intrinsic capacity to ameliorate the injured microenvironment and to rescue dysfunctional neurons, here we used adult green fluorescent protein $(GFP)^+$ NSCs as a graft source for unilateral transplantation above the subtantia nigra (SN) of MPTP mice. Remarkably, grafted GFP-NSC survived within the SN, in situ. Spatio-temporal analyses showed a significant protection/restoration of SN-TH^+ cell bodies. Additionally, GFP^+-NSCs were seen to accumulate at the Aq-SVZ niche, where they induced a profound remodelling of host $GFAP^+$ astrocytes and β-catenin over-expression thus suggesting activation of astrocyte-dependent Wnt signaling. Increased β-catenin expression was also observed in SN-repairing neurons together with a robust striatal reinnervation, thereby uncovering a critical role of NPC crosstalk with the host niche and DA neurons via astrocytes for DA neuroprotection and neurorestoration, with implications for cell-based therapies for PD.

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