

THE PERIPHERAL IMMUNE SYSTEM AS BIOMARKER OF THE DISEASE SEVERITY AND TISSUE DAMAGE EXTENT IN MULTIPLE SCLEROSIS

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Myeloid-derived suppressor cells (MDSCs) are immature regulatory cells present in several immune-related disorders, including multiple sclerosis (MS). In the context of the experimental autoimmune encephalomyelitis (EAE), MDSCs contribute to the acceleration of T cell suppression within the spinal cord. Their *in vivo* inactivation worsens the clinical affectation of the EAE mice whereas their potentiation is parallel to clinical course amelioration. All these data suggest that MDSC abundance might be indicative of a more or less severe disease course in EAE and MS.

In this work, we carried out a longitudinal prospective study in the EAE model between the peripheral blood level of MDSCs and the future severity of the clinical course together with the histopathological affectation of immunized mice (demyelination, axonal damage, NG2 recruitment to the demyelinated area). Our data indicate that the higher level of MDSCs is related to a less severe disease course, a lower CNS affectation and a higher density of NG2 cells around the demyelinated area.

In MS patients, the level of MDSCs in the peripheral blood at the very first relapse of the disease was higher than in both controls and MS patients in remission. Interestingly, the abundance of MDSCs in MS patients inversely correlated with their EDSS at the moment of the relapse. In addition, we have identified MDSCs in the CNS of MS patients associated to demyelinated plaques with a spontaneous capacity of remyelination. Moreover, the abundance of MDSCs in highly inflammatory lesions from MS patients showed a direct correlation with the previous disease length.

In sum, our data point to MDSCs as a putative biomarker not only of a milder severity of the future clinical course but also of a less damaged CNS prone to spontaneous remyelination.

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