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Effect of mesenchymal stromal cells on T cells in a septic context: Immunosuppression or immunostimulation?

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Sepsis is a complex process, including a first wave of damage partially due to the body's response to pathogens, followed by a phase of immune cell dysfunction. The efficacy of a pharmacological approach facing a rapidly evolving system implies a perfect timing of administration, this difficulty could explain the recent failure of clinical trials. Mesenchymal stromal cells (MSCs) are usually defined as immunosuppressive and their beneficial effects in preclinical models of acute sepsis have been shown to rely partly on such ability. If nonregulated, this phenotype could be harmful in the immunosuppressed context arising hours after sepsis onset. However, MSCs being environment sensitive, we hypothesized that they could reverse their immunosuppressive properties when confronted with suffering immune cells. Our objective was to evaluate the effect of human MSCs on activated human lymphocytes in an in vitro endotoxemia model. Peripheral blood mononuclear cells (PBMCs) underwent a 24-h lipopolysaccharide (LPS) intoxication and were stimulated with phytohemagglutinin (PHA) in contact with MSCs. MSCs induced a differential effect on lymphocytes depending on PBMC intoxication with LPS. Unintoxicated lymphocytes were highly proliferative with PHA and were inhibited by MSCs, whereas LPS-intoxicated lymphocytes showed a low proliferation rate, but were supported by MSCs, even when monocytes were depleted. These data, highlighting MSC plasticity in their immunomodulatory activity, pave the way for further studies investigating the mechanisms of mutual interactions between MSCs and immune cells in sepsis. Thus, MSCs might be able to fight against both early sepsis-induced hyper-inflammatory response and later time points of immune dysfunction.

Biography

Juliette Peltzer research aims to understand the coordinated relationships between metabolic and contractile pathways occurring during the differentiation of muscle satellite cells. In 2008, she joined Prof. Lataillade's laboratory specialized in cell therapy using mesenchymal stromal cells in different contexts and especially in humans in the case of radiation burns. She was first in charge of the characterization of perinatal MSCs, which we believe to be a good candidate for allogeneic cell therapy. Then they started to work on septic shock requiring extremely short processing times and therefore the use of immediately available cells from allogenic banking.

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