ImmunoTools *special* Award 2017

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Myeloid-derived suppressor cells and innate lymphoid cells in sepsis

Background

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. Both clinically and biochemically it is very difficult to distinguish sepsis from sterile inflammation. Sepsis requires antimicrobial chemotherapy immediately, while in patients with non-infectious inflammation antimicrobial therapy will not be beneficial and may even lead to an increase of resistant pathogens. Therefore, it is important to find tools that help discern infection from sterile inflammation. Current diagnostics are slow and/or are low in sensitivity and specifity. Hence, there is need for additional diagnostic tools to differentiate between sepsis and sterile inflammation.

Myeloid-derived suppressor cells (MDSCs) are a heterogeneous group of immature myeloid cells that egress the bone marrow to sites of inflammation during cancer, trauma or infection. MDSCs suppress the proliferation and function of T cells and NK cells through the expression of NOS2, ROS, arginase 1, TGFβ, IFN-y, IL-6 and IL-10 among many others. Their frequency increases during sepsis, but their function remains poorly understood. In some types of infection MDSCs seem to have a protective function while in others they aggravate infection. In surgical patients is shown that the MDSC level is related to adverse outcome. MDSCs may play a role in the development of the immunosuppressive phase of sepsis and favor the development of secondary, nosocomial infections.

Innate lymphoid cells (ILCs) are a recently identified lymphocyte group, who are shown to have multiple functions bridging the gap between the innate and the adaptive immune system. Those functions range from killing target cells (similar to conventional NK-cells) to T-helper like behaviour. On this moment three different subtypes are known, each with a different function and mechanism of action.

We hypothesized that monitoring blood MDSCs and blood ILCs could be useful for sepsis diagnosis and the follow-up of septic patients.

Project description

Instead of a defined subset of cells, MDSCs seem to be a group of phenoypically heterogeneous myeloid cells that have common biological activity. This makes phenotyping MDSCs for research difficult. To research MDSC in sepsis we will use a combination between flow cytometry, mass spectrometry (CyTOF) and Fluorescence-activated cell sorting. We will induce MDSC from human peripheral blood mononuclear cells using the GM-CSF and IL-6 from ImmunoTools. We will look at the activity of the induced MDSC using the ImmunoTools human ELISA-set. To create new panels for mass cytometry different surface markers will be tested using flow cytometry with the antibodies from ImmunoTools. Then, we will validate and titrate the antibodies in both inflamed patients and the induced MDSCs.

Contrary to MDSCs, ILCs are phenotyped quite well. The gap in knowledge about ILCs is their function and behaviour in sepsis and infection. We want to map the different subtypes of ILCs during sepsis and after recovery using the ImmunoTools antibodies in flow cytometry. Consequently, we want to determine the value of ILCs as a biomarker in sepsis.

We are going to set up a cohort of patients with an S. Pneumoniae pneumosepsis admitted to the ED or ICU and healthy controls are collected. Blood will be sampled on days 1, 3, 7, 28 and 90. Discharge and mortality will be monitored. The blood samples will be stimulated ex vivo. We will analyse the samples for both ILCs and MDSCs using the antibodies panels defined using the ImmunoTools antibodies.

Significance

MDSCs and ILCs could be a diagnostic tool to help distinguishing between sepsis and sterile inflammation and thus help clinicians within sepsis management. The ImmunoTools *special* award would help us to take the first steps in phenotyping MDSCs and ILCs within septic patients.

ImmunoTools *special* AWARD for **Irene Schrijver** includes 25 reagents

FITC – conjugated anti-human CD3, CD4, CD8, CD11c, CD13, CD14, CD15, CD16, CD19, CD20, CD31, CD33, CD38, CD80, CD86, IL-6

PE – conjugated anti-human CD10, CD57

APC – conjugated anti-human CD33

recombinant human cytokines: rh GM-CSF, rh IL-6

human ELISA-set (for one 96 plate): human IL-10 DETAILS more AWARDS