Immune regulation and immuno-monitoring in human diseases: auto-immunity, cancer, and COVID-19

Although we have learned a great deal about human immune response in health and disease, and how to interrogate human blood samples to get insights into lymphocyte activation state, and immune regulation, many questions remain unsolved.

We set-up a new flow cytometry method for analysis of immune-phenotype and cell cycle, and we discovered the presence of T cells in S-phase of cell cycle in human peripheral blood, named T_DS cells. CD8 T_DS cells were abundant in Infectious Mononucleosis (the clinical manifestation of acute Epstein-Barr virus (EBV)-infection) but not in healthy EBV-carriers. In Type 1 Diabetes, high levels of CD8 T_DS cells reactive to islet antigens was associated with an aggressive effector phenotype (1). That alterations of T_DS cells represent a key trait of immunopathology was confirmed in severe COVID-19 patients, showing a roughly ten-fold increase in T cells in G1 or S-G2/M in the blood (2). Collectively, our results point to a clinical relevance of T_DS cells, with potential translational use in humans.

Immunotherapy has revolutionized cancer treatment and it is now well established that the immune cells continuously operate immunosurveillance against stressed, damaged and malignant cells. Nevertheless, there is an urgent need for refined immuno-monitoring in the field of cancer immunotherapy, particularly in respect to response to immune check point inhibitors (ICI) and possibly other forms of innovative therapies (3).

Senescence is a cellular state of stress response that has great potential as immunomodulatory tool for its intimate connection with the immune system. We demonstrated that drug-induced senescent tumor cells are recognized and cleared by lymphocytes of the innate immunity, namely Natural Killer cells, providing the proof of concept that pro-senescence therapy can be considered as a new type of immunotherapy (4). The disclosure of the crosstalk between senescent cells and the components of the immune system is of great relevance for fighting cancer and age-related diseases.

References:


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