ImmunoTools *special* Award 2018

Jana Palmowski, PhD-student

Supervisor: Prof. Dr. Karsten Krüger

Leibniz University Hannover, Institute of Sports Science, Department of Sports and Health, Am Moritzwinkel 6, 30167 Hannover, Germany

Immunometabolism of T-cells: Higher Capacity in Endurance-Trained Athletes?

Chronic endurance exercise, classified as a long duration and low-frequency activity, induces well-known cardiovascular benefits. Beyond, exercise is an acute metabolic stressor enhancing metabolic functionality in muscle cells. Cardiovascular adaptations result from shear forces and adrenergic stimulation leading to an improved vascularization. Additionally, an increase in important metabolic enzymes, and mitochondrial mass is evident. Human lymphocytes also express adrenergic receptors on their cell surface. Their stimulation leads to a biphasic exercise response. An initial lymphocytosis is followed by lymphopenia, 1-2 until 24 hours after exercise. Scientists still argue whether endurance exercise enhances immune surveillance in the periphery termed “exercise immune enhancement hypothesis” or leads to an “open window” putting the athlete on a high risk for infection the hours after practice. For instance, the incidence of upper respiratory tract illness is higher after intense prolonged endurance events, although redeployment of T-cells to the gut and lungs may cause local immune surveillance.

It may end the ongoing discussion to identify the role of T-cell metabolism in this scenario. Recently, lymphocyte metabolism as a modulator for the cells immune function receives a high reputation. In the state of quiescence, T-cells rely on the more effective and high yield –oxidative pathway, using fatty acids as their main substrate. In contrast, at T-cell stimulation, a so-called “metabolic-switch” sets on and the cells' metabolism turns to the high flux pathway of energy production –the glycolytic pathway. After the “switch”, need of glucose augments to maintain a higher glycolytic flux to meet the energy and biomaterial demand of the cell. This, so-called metabolic plasticity, the flexibility of metabolism to adapt to the need of the cell, is essential to cause proliferation and differentiation of naïve T-cells. Knowing about metabolic adaptations to chronic endurance exercise, we propose the metabolic plasticity and capacity of T-cell immune metabolism in endurance athletes is higher than in their controls.

To test whether this hypothesis is true, we will conduct cell culture experiments. Therefore, whole blood of 10 endurance-trained male athletes and age-matched controls is collected. Subsequent $CD4^+$ and $CD8^+$ T-cells from human PMBCs are isolated by fluorescence-activated cell sorting with ImmunoTools antibodies. Subsequently, we activate the isolated cells with anti-CD3/anti-CD28 and culture them in media supplied with IL-2. After activation, we measure respiration, levels of important substrates and intermediates, metabolic key enzymes, and membrane transporters, being crucial for the glycolytic and oxidative pathway. For the immune analysis part, we use flow cytometry to identify naïve, effector und memory T-cell subsets with ImmunoTools antibodies (CD45RO, CD45RA, and CD62L). In addition, in order to connect exercise effects on cell metabolism, we will also measure lymphocyte capacity to produce cytokines such as TNF-α, IL-10, and IFN-γ by ELISA and cellular sensitivity to apoptosis by using Annexin-V and flow cytometry. Finally, we correlate our findings of metabolism with immune cell functions.

Our results may elucidate a missing link between the immune system and exercise. If exercise promotes function of T-cell immune metabolism, the attitude “exercise instead of a pill” will receive more attention in near future. Immune adaptations of T-cells may be vital for an improved overall adaptive immune health or more rapid cure of diseases.

ImmunoTools *special* AWARD for **Jana Palmowski** includes 25 reagents

FITC - conjugated anti-human CD3, CD4, CD8, Annexin V-FITC, CD62L

PE - conjugated anti-human CD3, CD45RO, Annexin-PE

PerCP - conjugated anti-human CD3, CD4, CD8, CD45RA

human ELISA-set (for one 96 plate) TNF-α, IFN-γ, IL-10

recombinant human cytokines: rh IL-2

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