



FORSCHUNGSARBEIT

„IL-21 modulates memory and exhaustion phenotype of T-cells in a fatty acid oxidation-dependent manner.“

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IL-21 modulates memory and exhaustion phenotype of T-cells in a fatty acid oxidation-dependent manner.

Romy Loschinsky has been a doctoral student within the International Doctorate Program “i-Target: Immunotargeting of cancer” in the laboratory for translational tumor- and transplantation immunology at the Universitätsklinikum of Erlangen. Here the research group of Prof. Dr. Andreas Mackensen and Prof. Dr. Dimitrios Mouggiakakos studies the immune system in cancer and following stem cell transplantation. Tumors can impact immune responses and thereby escape from immune surveillance. A better understanding of the underlying mechanisms shall help us to develop innovative immune-based therapies against cancer.

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T-cell-based therapies represent a promising strategy for cancer treatment. In this context, cytokines are discussed as a bona fide instrument for fine-tuning T-cell biology. One promising candidate is the pleiotropic interleukin-21 (IL-21) with only little being known regarding its direct effects on human T-cells. Thus, we sought out to characterize the impact of IL-21 on T-cell metabolism, fitness, and differentiation. Culturing T-cells in presence of IL-21 elicited a metabolic skewing away from aerobic glycolysis towards fatty acid oxidation (FAO). These changes of the metabolic framework were paralleled by increased mitochondrial fitness and biogenesis. However, oxidative stress levels were not increased but rather decreased. Furthermore, elevated FAO and mitochondrial biomass together with enhanced antioxidative properties are linked to formation of longer lasting memory responses and less PD-1 expression. We similarly observed an IL-21-triggered induction of central memory-like T-cells and reduced levels of PD-1 on the cell surface. Taken together, IL-21 shifts T-cells towards an immunometabolic phenotype that has been associated with increased survivability and enhanced anti-tumor efficacy. In addition, our data reveals a novel interconnection between fatty acid metabolism and immune function regulated by IL 21.

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International Doctorate Program “i-Target”:

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