NXT22-005 - Lipid metabolism in granulomatous diseases

Abstract

Sarcoidosis is a chronic multi-organ granulomatous disease of unknown origin that can lead to organ damage. The mechanistic target of rapamycin (mTOR) pathway is a key regulator of immune cell metabolism and highly upregulated in granuloma-associated cells. In our WWTF-funded project, we treated cutaneous sarcoidosis patients with the mTOR inhibitor sirolimus in an investigator-initiated trial with a response rate of 70%. In addition, we defined macrophages, T cells and fibroblasts as granuloma-driving cell populations and found that the lipid metabolism is important for granuloma formation in patient-derived macrophages and in a sarcoidosis mouse model. In this transfer project, we now want to assess the clinical importance of our findings with the following two aims: i) evaluation of the lipid profile in a new patient cohort of granulomatous diseases (sarcoidosis affecting various organs, granuloma annulare) and communication with patient groups and physicians from different disciplines and ii) analysis of metabolic signatures in our available single-cell RNAseq dataset of sarcoidosis skin and blood cells in responders and non-responders to mTOR inhibition from the WWTF-funded clinical study. Our findings will provide new insights into the modulation of the lipid metabolism in granulomatous diseases and form the basis of a large multi-centre clinical trial. The results on the lipid profile of patients will be communicated with patient groups and physicians of various disciplines to emphasize lipid-lowering medications and lifestyle changes.

Keywords:
granulomatous diseases, lipid metabolism, sarcoidosis, granuloma annulare

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Further links to the persons involved and to the project can be found under
https://www.gmbh.wwtf.at/funding/programmes/ei/NXT22-005/