ImmunoTools *special* Award 2025

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Do adipocytes shape the tumor microenvironment of Lymphoma?

Haematological neoplasia's account for 9% of all cancers and are the fourth most frequently diagnosed malignancy in developed countries. In 2018, Hodgkin's lymphoma (HL) accounted for 79,990 new cases (0.4% of all new tumours) and 26,167 deaths worldwide. Recent evidence underscores the critical role of the tumor microenvironment (TME) in HL development, particularly within primary lymph nodes (LNs) and during metastatic progression to the bone marrow (BM) (Matos A, *Tumour Biol*. 2016). Despite significant advancements in HL therapy, a considerable number of patients develop aggressive, metastatic forms of the disease that exhibit poor responses to treatment, culminating in relapse or progression and ultimately leading to mortality.

The cellular heterogeneity of HL is a key contributor to its clinical outcomes. Among non-immune cellular populations within the TME, adipocytes are emerging as pivotal players. Obesity, in particular, is known to exacerbate immunoinflammatory responses and trigger a cytokine/adipokine storm. A large cohort study involving 5.8 million individuals revealed that each 5 kg/m² increase in body mass index (BMI) was associated with a 10% increased risk of developing HL.

Our project seeks to investigate the role of adipocytes in shaping the TME in HL and to identify novel targets for immunomodulatory therapies. Specifically, we aim to establish and characterize a biomimetic, patient-derived system that mimics the HL microenvironment. This system integrates perilymphonodal adipose tissue (PLAT) and LNs from HL patients, enabling us to explore the influence of adipocytes within a multi-cellular TME. Patient samples will be collected from both obese and non-obese individuals at the Instituto Português de Oncologia do Porto and Centro Hospitalar de São João in Porto, Portugal. The *in vitro* model will include macrophages, T cells, and malignant cells derived from patient samples. PLAT and LN tissues will be

dissociated to create multi-cellular cultures, to which adipocytes will be added to assess their impact. Flow cytometry will be used to immunophenotype cancer cells (CD15, CD30, PAX5, CD56, CD45, PD-L1, CD47, HLA-ABC), macrophages (CD14, CD86, HLA-DR, CD163, CD206, CD40), and T cells (CD3, CD4, CD8, CD25, CD69, CTLA-4, CD279, IFN-γ). Additionally, the cytokine and adipokine profiles in the culture supernatants will be analyzed using multiplex assays to elucidate intercellular interactions within the TME.

This project aims to provide a deeper understanding of how adipocytes and obesity influence HL outcomes by modulating the immune landscape of the TME. Insights from this research will guide interventions for obesity management in cancer patients while also unveiling potential therapeutic targets to modulate the immune system in HL.

The selected ImmunoTools collection of flow cytometry antibodies lits will be fundamental to dissect the impact of perilymphonodal adipose tissue on the TME. The role of local adipocytes and obesity will be dissected to unveil its interaction with immune and cancer cells, paving the way to identify novel targets for therapeutic regulation, narrow the relapse and contribute for better options for target immunotherapy.

ImmunoTools *special* AWARD for **Andreia Matos** includes 10 reagents

FITC - conjugated anti-human CD3, CD45, CD86

PE - conjugated anti-human CD25, CD40, CD56

PerCP - conjugated anti-human CD8, CD14

APC - conjugated anti-human CD15, CD69

DETAILS more AWARDS