Project 7.1 Dissecting immunological responses to neoadjuvant radiotherapy and immunotherapy in soft tissue sarcoma

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Background:

Preclinical studies and translational data from clinical trials suggest that most soft tissue sarcomas have very low levels of immune infiltrates, and their microenvironment is highly immunosuppressive. Thus, they can be classified as "cold-tumors". This can potentially explain negative results of recent clinical trials with immunotherapy in sarcoma. New strategies targeting tumor microenvironment or interactions between tumor and immune cells, e.g. activators of antigen-presenting cells (APC) are tested in other cancer with promising signals of efficacy. We are currently conducting a clinical trial (EFTISARC-NEO) with immunotherapy with eftilagimod alfa (soluble LAG-3 protein and APC activator), pembrolizumab (anti-PD-1 antibody) and radiotherapy in neoadjuvant setting. We hypothesize that combined treatment with radiotherapy, an anti-PD-1 antibody and an APC activator can have a synergistic effect in patients with localized soft tissue sarcoma, leading to changes in the tumor microenvironment, conversion of "cold-tumors" to "hot-tumors" and activation of immune responses. The neoadjuvant approach provides a unique opportunity to derive biological information related to tumor response.

Aim:

The main aim of the project is to evaluate local and systemic immunologic responses to neoadjuvant immunotherapy combined with radiotherapy in patients with soft tissue sarcomas. The project will be conducted on tumor and blood samples obtained in EFTISARC-NEO trial. The project includes the following research tasks: 1) To analyze the composition of tumor microenvironment with special interest in immune infiltrates, before and after the treatment; 2) To evaluate effects of neoadjuvant treatment on activation of APC and effector cells (T cells, NK cells); 3) To assess changes in diversity of T-cells receptors upon treatment. All results will be additionally correlated with clinical outcomes – rate of pathological response, disease-free and overall survival. The following techniques will be used in the project (among others): NGS (WES and RNA-Seq), IF/IHC, flow cytometry, protein expression analyses.

Requirements:

- MD or MSc in biology, biotechnology, chemistry, or related life science fields,
- laboratory experience with working knowledge of molecular biology,
- previous experience with flow cytometry, NGS technology, and immunofluorescence/immunohistochemistry will be an advantage,
- interest in bioinformatics is foreseen but not required,
- strong motivation to learn and to make scientific discoveries,
- ability to work as a team member in a multidisciplinary team
- very good knowledge of English language