"Immunological aspects of Malignant Melanoma and Soft Tissue Sarcoma-correlation to prognosis and treatment"

**Background:**
The tumor microenvironment (TME) consists of interactions between malignant and non-malignant cells, and play a crucial part in all steps of tumorigenesis. Soft tissue sarcomas (STS) are rare, heterogenous tumors where oncological treatment has modest effect, and with a great need for new treatment strategies. Until recently, malignant melanoma (MM), much like STS, had very dismal prognosis when metastasized. The development of new treatment strategies ie tyrosine kinase inhibitors (BRAFi and MEKi) and immunotherapy have dramatically improved the prognosis even at advanced stage. Increased knowledge on the interplay between malignant cells and TME poses one of the great challenges in oncology today. This project aims to investigate the role of the tumor immune microenvironment in STS and MM, and will also contain a retrospective clinical study on MM based on 2-year experience of the use of Next Generation Sequencing (NGS) in a real clinical setting.

**Method/Results:**
I. In this project, prognostic value of stroma factors in STS, immunohistochemical (IHC) stainings were performed for evaluation of CD163, colony-stimulating factor (CSF)-1, CD16, CD31 (for microvessel density) and hypoxia-inducible factor 1 (HIF-1α) in 73 high-grade STS. Expression of HIF-1α was associated with presence of necrosis, and independently predicted shorter metastasis-free survival (HR 3.2, CI 1.4-7.0, p=0.004), whereas neither expression of the stromal markers CD163, CD16 and CSF-1 nor microvessel density was prognostically relevant.

II. 2-year experience of NGS in real clinical setting of melanoma patients was analyzed. Mutation patterns from 165 patients with stage 3 and 4 MM are described with special focus on BRAF-mutation status. This study confirms previously reported mutational profile of MM analyzed by NGS.

Three more projects are planned with focus on immune microenvironment in MM and STS (project III and V) and circulating immunosuppressive cells in MM (project IV).

**Relevance:**
The project will contribute to new knowledge in the area of TME and its relation to prognosis and treatment outcome in STS and MM. Results from paper I suggest HIF-1α as a possible prognostic biomarker in STS.

**Published paper**
I. Nyström H, Jönsson M, Werner-Hartman L, et al Hypoxia-inducible factor 1α predicts recurrence in high-grade soft tissue sarcoma of extremities and trunk wall
*Journal of Clinical Pathology* 2017;70:879-885