

## Dissecting the role of IL8 in cancer using a new humanized mouse model

Master project (30 hp)  
Department of Medicine  
Karolinska Institutet  
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### Background

IL8 (interleukin 8) plays a complex role in tumor progression. In addition to directly feeding tumor growth in a paracrine and autocrine manner, IL8 also induces the recruitment of tumor-associated neutrophils and myeloid derived suppressor cells, promotes angiogenesis, activates epithelial-mesenchymal transition, and increases the drug resistance of tumor cells. In addition, elevated IL8 levels are strongly associated with poor outcome of immunotherapy in several cancer forms. Phase I clinical trials in patients with solid tumors demonstrate that IL8-blockade is well tolerated and leads to reduced IL8 levels in serum. However, due to the lack of relevant preclinical models, the mechanistic role of IL8 in tumor progression, and in resistance to immunotherapy, is poorly understood. We have therefore generated IL8-humanized mice with physiological expression of human IL8 and its receptors CXCR1 and CXCR2.

### Aims and purpose:

The principal aim of this project is to use our new IL8-humanized mouse model to increase the understanding of how IL8 contributes to tumor progression. The purpose is to elucidate how IL8 blockade could be harnessed for more efficient cancer immunotherapy. The specific aims are:

- Determining the role of IL8 in tumor growth and metastasis in vivo.
- Determining the role of IL8 in checkpoint blockade.

### Methods:

The student will characterize immune cells from IL8-humanized mice using flow cytometry and will use syngeneic tumors cells to study tumor progression in vivo. The student will genetically modify existing cancer cell lines using CRISPR/Cas and BAC (bacterial artificial chromosome) transfection. The student will also use immunotherapy and IL8 blockade to elucidate the role of IL8 in anti-tumor immune responses in vivo.

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