Characterization of zebrafish tumors using MR imaging and MR spectroscopy.

Clinical relevance

Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumors. Currently, there is no effective treatment for patients with PPGLs other than removal of a tumor when operable. There is an urgent clinical need for development of therapeutics against this disease, which requires a better understanding of the etiology of PPGL and therefore generation of relevant animal models. Our zebrafish model is the first viable vertebrate animal model for PPGLs and thereby will yield urgently needed insights in the etiology of this cancer type.

Background

A mutation in one of these PPGL-related genes, the *succinate dehydrogenase B* (*SDHB*), is the strongest indicator of malignancy of this cancer type. The SDHB protein is part of a four subunit (A-D) protein complex, the succinate dehydrogenase (SDH) complex. The SDH complex converts succinate to fumarate, one of the steps of the TCA cycle. When this complex is dysfunctional there is a build-up of the oncometabolite succinate in the cell. Succinate stabilizes hypoxia-inducible transcription factors (HIFs). HIF-targets are subsequently transcribed and in turn boost proliferation and angiogenesis, two essential processes of tumor formation. Tumor formation can be detected and followed over time by using magnetic resonance imaging (MRI). Furthermore, the characteristic hallmark of *SDHB*-associated PPGLs is the accumulation of succinate, which can be measured with magnetic resonance spectroscopy (MRS). We already have experience with MRI and MRS experiments of zebrafish.

Goal

The goal of this project is to generate a tool-box to detect and follow tumor growth in zebrafish. One important goal is to further optimize MRI and MRS imaging in zebrafish. We are open to discuss other techniques and goals of interest within the context of this project.

We offer:

The possibility to perform and present exciting high-quality research in a professional, multi-cultural and highly-motivating work environment in a well-equipped department. You will have the opportunity to learn a broad range of techniques and skills, such as MRI and MRS measurements, genotyping and phenotyping of KO zebrafish via fin clipping, PCR, DNA gels, histology, handling and breeding zebrafish and planning, scientific writing and presenting.

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