Abstract

Peroxisome proliferator-activated receptors (PPARs) are nuclear transcription factors. For each of the PPAR subtypes (alpha, beta/delta, and gamma), agonists and antagonists are available. PPARα and γ are mostly antineoplastic while PPARβ/δ seems to promote tumor growth. We showed that pharmacological activation of PPARβ/δ in vivo promotes lung cancer growth and metastasis formation in mice, which implicates activation of tumor angiogenesis. The aim of the current project is to test the therapeutic potential of PPARβ/δ antagonists to reduce cancer growth and metastasis formation. We will induce different tumor types, treat the animals with PPARβ/δ antagonists and measure tumor growth and metastasis formation. To gain insights into the cell types involved in the response, we will isolate the tumor stroma and the tumor to define alterations in the different cell types of the tumor stroma (endothelial, immune, hematopoietic cells, and fibroblasts) as well as in the tumor cells (proliferation analysis) upon treatment with the PPARβ/δ antagonist. Ongoing from the results obtained, we will then genetically dissect the contribution of the different PPARβ/δ expressing tumor stroma cell types by employing conditional PPARβ/δ knockout mice crossed with different cell-type specific inducible Cre lines. In
these animals, we will perform a comparable tumor growth and metastasis analysis as mentioned above. The project will clarify whether PPARβ/δ antagonists might become a novel approach for tumor therapy and identify involved cell types and mechanisms therein.

Key words

Cell biology
Animal Pathophysiologie
Genetics
Cancer
Peroxisome proliferator-activated receptors
Angiogenesis

Related Publications

Vascular PPARβ/δ Promotes Tumor Angiogenesis and Progression.
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