Medical University of Graz

Cannabinoid receptors in tumorigenesis

Summary

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Supervisor:	Prof. Dr. Rudolf Schicho
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 14, 2020 00:00 and October 10, 2020 23:59 (Europe/Zurich)

Description

Background:

Cannabis has been traditionally used as a remedy against many diseases, among them inflammatory diseases and cancer. Since the discovery of cannabinoid receptors and the endocannabinoid system, a modern pharmacological therapy with cannabinoids has become a potentially new option. Cannabinoids have been shown to activate or modulate a variety of receptors such as cannabinoid receptor 1 and 2 (CB1, CB2), GPR55, TRPV1 and PPARs. These receptors are present in tumor cells but are also found in many immune cells which are part of the tumor microenvironment. We recently identified GPR55 as a procarcinogenic receptor that opposes the behavior of CB1 receptors [1]. The mechanisms how cannabinoid receptors and the endocannabinoid system regulate tumor growth are still elusive.

Hypothesis and Objectives: Depending on their localization in tumor or immune cells, cannabinoid receptors are thought to regulate tumor growth by mechanisms such as apoptosis and differentiation. We will investigate the role of cannabinoid receptors in carcinogenesis and metastasis by use of in vivo models with wild type and knockout mice, complemented by primary cell culture experiments and immune cell assays.

Methodology: In tissue obtained from the in vivo experiments (e.g. syngrafts), the identity and amount of infiltrated leukocytes as well as the pathological status of tumors and inflammation markers will be determined using flow cytometry, immunoassays and immunohistochemistry/in situ hybridization[1,2]. The PhD candidate will quantify/localize receptor expression by real-time PCR, Western blot, and fluorescence microscopy. Functionality of immune cells will be investigated in assays of cell migration and adhesion, integrin up-regulation, Ca^{2+} signaling, apoptosis and differentiation.

References:

1. Hasenoehrl C, Feuersinger D, Sturm EM, Barnthaler T, Heitzer E, Graf R, Grill M, Pichler M, Beck S, Butcher L, Thomas D, Ferreiros N, Schuligoi R, Schweiger C, Haybaeck J, Schicho R. G protein-coupled receptor GPR55 promotes colorectal cancer and has opposing effects to cannabinoid receptor 1. Int J Cancer; 2018;142:121-132.

1. Kienzl M, Hasenoehrl C, Valadez-Cosmes P, Maitz K, Sarsembayeva A, Sturm E, Heinemann A, Kargl J, Schicho R. IL-33 reduces tumor growth in models of colorectal cancer with the help of eosinophils. OncoImmunology 2020; 9:1, DOI: 10.1080/2162402X.2020.1776059

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