

# Cannabinoid receptors in gastrointestinal inflammation and cancer

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## 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 01, 2018 00:00 and September 23, 2018 23:59 (CEST)

## Description

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**Background:** Cannabis has been traditionally used as a remedy against gastrointestinal (GI) diseases. Since the discovery of cannabinoid receptors and the endocannabinoid system, a modern pharmacological therapy of GI disorders 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 epithelial cells and/or leukocytes of the GI tract and play an important part in the pathophysiology of inflammatory bowel diseases and colon cancer. We recently identified GPR55 as a proinflammatory and procarcinogenic receptor that opposes the behavior of CB1 receptors<sup>1,2</sup>. The mechanisms how cannabinoid receptors and the endocannabinoid system regulate tumor growth are still elusive.

**Hypothesis and Objectives:** Depending on their localization, cannabinoid receptors are thought to regulate cell differentiation and regeneration. Using knockout mice of several cannabinoid receptors, we will investigate the role of CB1 and CB2 in models of colon carcinogenesis and intestinal inflammation. In vivo models will be complemented by primary cell culture techniques.

**Methodology:** In tissue obtained from the in vivo experiments, the content of infiltrated leukocytes and inflammation markers as well as the pathological status will be determined using flow cytometry, immunoassays and immunohistological techniques. Primary cells and organoids isolated from colon mucosa will be used to determine the role of the receptors in cell proliferation and differentiation. The PhD candidate will quantify receptor expression by real-time PCR, Western blot, fluorescence microscopy and flow cytometry. Functional responses of immunocytes will be investigated in assays of cell migration and adhesion, integrin up-regulation, and Ca<sup>2+</sup> signaling. Epithelial barrier integrity will be evaluated by cell impedance assays.

## 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 (2018) G protein-coupled receptor GPR55 promotes colorectal cancer and has opposing effects to cannabinoid receptor 1. *Int J Cancer*; 2018;142:121-132.

2. Stancic A, Jandl K, Hasenohrl C, Reichmann F, Marsche G, Schuligoi R, Heinemann A, Storr M, Schicho R: The GPR55 antagonist CID16020046 protects against intestinal inflammation. *Neurogastroenterol Motil* 2015;27:1432-1445.



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