Abstract

FFA1, FFA4 and GPR84 are all receptors sensing free fatty acids. FFA1 and FFA4 are implicated in release of gut hormones such as GIP, GLP-1 and ghrelin. Therefore, the receptors are interesting in relation to obesity and type 2 diabetes, where modulating the above hormones might provide a tool to fight or alleviate symptoms of obesity and type 2 diabetes. FFA4 and GPR84 are both implicated in inflammation. By sensing fatty acids, the receptors may prove a link between metabolism and inflammation.

In chapter 2, an optimized synthesis of two congeners of the newly discovered lipid class fatty acid esters of hydroxy fatty acids is described. This class of lipids have been linked to anti-inflammatory and antidiabetic effects. The two synthesized compounds, **5-** and **9-PAHSA**, have previously been reported to be active on FFA1 and FFA4. We found both to be inactive on FFA1 and FFA4, but heir constitutive hydroxyfatty acids, 5- and 9-hydroxystearic acid, to show activity on one or both receptors. This sets the stage for further research.

Chapter 3 describes and discusses our studies towards an iterative synthesis of polyunsaturated fatty acids. Some methods for such an iterative synthesis already exist, but they suffer from various drawbacks, i.e. poor functional group tolerance or less than ideal control of double bond configuration. Our vision was to develop a building block for the skipped 1,3-diene present in polyunsaturated fatty acids. The chapter explores two methodologies: one based on MIDA-boronates and the Suzuki reaction and one based on organozinc compounds and the Negishi reaction.

Chapter 4 contains the synthesis of a range of GPR84 agonists based on the previously reported **cmp 51**. A new method for their synthesis is explored. Additionally, in collaboration with PhD student Lukas Ieremias, a strategy for converting a GPR84 agonist to an antagonist is explored.

Chapter 5 and publication 1 outlines our work on a general synthesis of hydroxyfatty acids, as well as the activity of hydroxyfatty acids, exemplified by hydroxylauric acids, on FFA1, FFA4 and GPR84. The fatty acids showed some activity on both FFA1 and GPR84, but no activity was observed on FFA4.

Chapter 6 discusses the development of a dietary supplement based on hydrolyzed pine nut oil. It was shown that ionic strength of the solution as well as stirring rate had a dramatic impact on the hydrolysis.

In chapter 8, the identification of [Cu(IPr)(pyridine]OTf, an *N*-heterocyclic carbene-Cu complex, as a catalyst for the aerobic oxidation of alcohols is shown and partially optimized. The reaction takes place both in dimethyl sulfoxide and acetonitrile with several different bases and nitroxyl radicals.