

ORAL PRESENTATION

Open Access

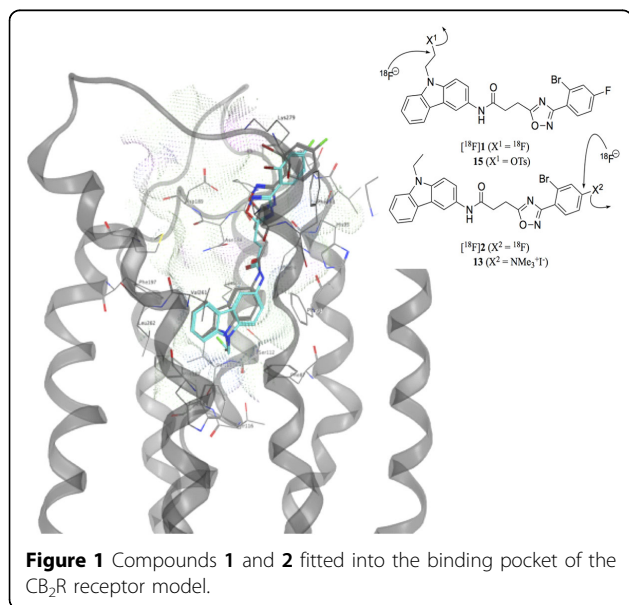
Development of cannabinoid receptor (CB₂R) ligands for application in PET studies - where to attach the radiolabel?

Robert Günther^{1*}, Rareş Moldovan¹, Corinna Lueg², Winnie Deuther-Conrad¹, Bernhard Wunsch², Peter Brust¹

From 9th German Conference on Chemoinformatics
Fulda, Germany. 10-12 November 2013

The cannabinoid receptors type 2 (CB₂R) are involved in many physiological processes but their expression level in healthy and diseased brain has not been unravelled. With positron emission tomography (PET) it is possible to monitor quantitatively very low amounts of compounds labelled with positron emitting isotopes like ¹⁸F in living organisms at high spatial resolution. For application in clinical research, such radiotracers have to show high selectivity and affinity to the target protein.

A series of fluorinated *N*-carbazolyl-oxadiazolyl-propionamides [1] was synthesised and the affinity towards the human CB₂R was measured in receptor binding studies. Here, we combine our CB₂R receptor model with 3D-QSAR data [2] to support molecular docking studies employing the MOE software (Version 2012.12 Chemical Computing Group Inc. Montreal. <http://www.chemcomp.com>). The studies revealed that both the primarily investigated compound **2** and the 2-fluoroethyl substituted carbazole derivative **1** ($K_i = 3.6$ nM) fits well into the binding pocket. Attachment of the fluorine at different positions of the structure does not lead to significantly different poses in accordance with the experimental data. Organ distribution studies on CD1-mice verified our prediction, [3] that [¹⁸F]**1** and [¹⁸F]**2** can cross the blood-brain barrier.



Authors' details

¹Department of Neuroradiopharmaceuticals, Institute of Radiopharmaceutical Cancer Research, Helmholtz-Zentrum Dresden-Rossendorf, Research Site Leipzig, Leipzig, 04368, Germany. ²Department of Pharmaceutical and Medicinal Chemistry, University of Münster, Münster, 48149, Germany.

Published: 11 March 2014

References

1. Rühl T, Deuther-Conrad W, Fischer S, Günther R, Hennig L, Krautscheid L, Brust P: **Cannabinoid Receptor Type 2 (CB₂)-Selective *N*-Aryl-Oxadiazolyl-Propionamides: Synthesis, Radiolabelling, Molecular Modelling and Biological Evaluation.** *Org Med Chem Lett* 2012, **2**:32.
2. Günther R, Brust P: **Synergistic approach of structure- based and ligand-based drug design for the development of selective cannabinoid receptor ligands.** *J Cheminform* 2012, **4**(Suppl 1):P11.
3. Gerebtzoff G, Seelig A: **In Silico Prediction of Blood-Brain Barrier Permeation Using the Calculated Molecular Cross-Sectional Area as Main Parameter.** *J Chem Inf Model* 2006, **6**:2638-2650.

doi:10.1186/1758-2946-6-S1-O9

Cite this article as: Günther et al.: Development of cannabinoid receptor (CB₂R) ligands for application in PET studies - where to attach the radiolabel? *Journal of Cheminformatics* 2014 **6**(Suppl 1):O9.

* Correspondence: r.guenther@hzdr.de

¹Department of Neuroradiopharmaceuticals, Institute of Radiopharmaceutical Cancer Research, Helmholtz-Zentrum Dresden-Rossendorf, Research Site Leipzig, Leipzig, 04368, Germany

Full list of author information is available at the end of the article