# Ian de Bus

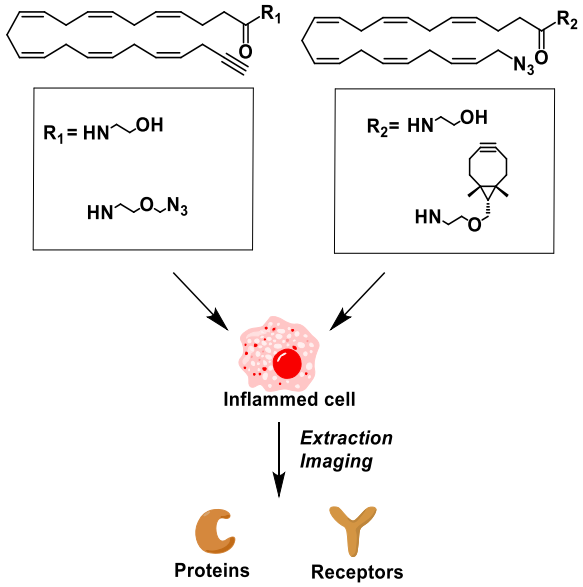
| | |
|---|---|
| **Supervisor(s)** | Dr. Bauke Albada, Dr. Michiel Balvers, Prof. Dr. Han Zuilhof, Prof. Dr. Renger Witkamp |
| **Project** | Fishing for endogenous inflammation inhibitors derived from omega-3 fatty acids. |
| **Fields of interest** | Bio-orthogonal chemistry, Chemical Biology, PUFA synthesis, Biochemistry, Pathway analysis |
| **E-mail** | ian.debus@wur.nl |
| **Telephone** | +31 (0)317482369 |

## Introduction

Omega-3 Poly Unsaturated Fatty Acids (PUFA's) are present in fatty fish (like tuna, mackerel and salmon) and fish oil supplements, which is the primary source of these molecules for humans. In humans, PUFA's are easily transferred to endocannabinoids, which are amide derivatives of PUFA's. Endocannabinoids have potent anti-inflammatory behaviour and have shown to inhibit various chronic inflammatory diseases like arthritis, cardiovascular diseases and even cancer and obesity (*1, 2*). An important endocannabinoid that showed anti-inflammatory effects is docosahexaenoyl ethanolamide (DHEA) (*2, 3*). Important for the anti-inflammatory response of DHEA is the role cyclooxygenase-2 (COX-2). Nevertheless, it is uncertain what the exact role of DHEA on COX-2 is (*3*). Our final goal is **to elucidate the modulation of inflammation by DHEA.**

## Methodology

First, a HRMS based COX-2 assay will be designed to screen for novel COX-2 derived endocannabinoid products of the ω-3 PUFA's, with potential anti-inflammatory properties. Second, various DHEA derived probes will be synthesized to specifically 'fish' for new receptors and proteins that are involved in the endogenous anti-inflammatory response of inflamed cells. Various bio-orthogonal handles are being introduced in both the 'head' and 'tail' part of the endocannabinoid structure. These self-synthesized endocannabinoid probes are used to elucidate the role of this novel COX-2 metabolites *in-vitro* and *in-vivo*.




## References


1. Calder, P. C. (2013) Omega-3 polyunsaturated fatty acids and inflammatory processes: nutrition or pharmacology?, *British Journal of Clinical Pharmacology 75*, 645-662.
2. Meijerink, J., Balvers, M., and Witkamp, R. (2013) N-acyl amines of docosahexaenoic acid and other n–3 polyunsatured fatty acids – from fishy endocannabinoids to potential leads, *British Journal of Pharmacology 169*, 772-783.
3. Meijerink, J., Poland, M., Balvers, M. G. J., Plastina, P., Lute, C., Dwarkasing, J., van Norren, K., and Witkamp, R. F. (2015) Inhibition of COX-2-mediated eicosanoid production plays a major role in the anti-inflammatory effects of the endocannabinoid N-docosahexaenoylethanolamine (DHEA) in macrophages, *British Journal of Pharmacology 172*, 24-37.


## Acknowledgement


This research is supported and financed by the VLAG Graduate School.