Design and synthesis of novel ligands and receptors through covalent and non-covalent conformational restriction of biomolecules

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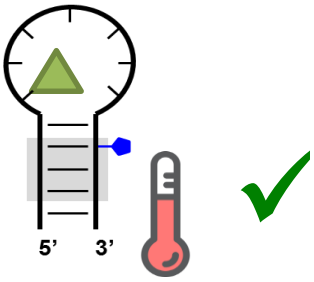
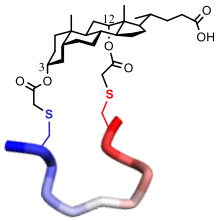
The talk will give an overview of our most recent achievements in the field of ligand and receptor design where conformational stabilization is key to success.

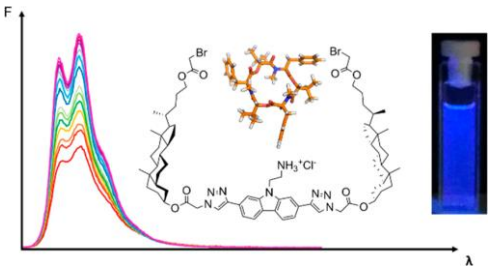
As a first example, the design and synthesis of so-called 'frozen' aptamers as small molecule receptors will be discussed. Introduction of imidazole modified nucleotide building blocks in a particular sequence context, allows for stabilization of the aptamer fold through non-covalent interstrand interactions. [1] Furthermore, efforts towards exploitation of our furan-oxidation induced covalent interstrand crosslinking technology[2] for aptamer stabilisation will be discussed.





A second part of the talk will focus on our newly developed technology for the covalent restriction of peptide loop conformations onto non-peptide scaffolds. Several applications of the technology for the design of biologically active stabilized peptides will be discussed.[3]

Finally, the bottom-up design of an artificial receptor for medium-sized cyclodepsipeptides will be highlighted. Through a combination of careful design and modelling with experimental validation of binding affinity, we have developed a series of receptors for the food toxins Beauvericin and Cereulide.[4] Applications in solid phase extraction of the toxins out of complex food matrices as well as the potential use of the artificial receptors as anti-dotes for Cereulide poisoning will be illustrated.



[1] a) Buyst & Madder, *Nucleic Acids Research,* ***2014,*** 43(1), 51; b) Op de Beeck & Madder, *JACS,* **2011**, 133, 796; c) Verdonck, Madder & Martins, *Nucleic Acids Research,* ***2018,*** 46(22), 11671.
[2] a) Stevens, K.; Madder, A. *Nucleic Acids Research,* **2009**, 1555; b) Op de Beeck, M. Madder A. *JACS* **2011**, *133* (4), 796-807; c) Op de Beeck, M. Madder A. *JACS*, **2012**, 10737.
[3] Van Lysebetten & Madder, *to be submitted*.[4] Ornelis & Madder, *Organic Letters,* **2018**, 20, 6368.