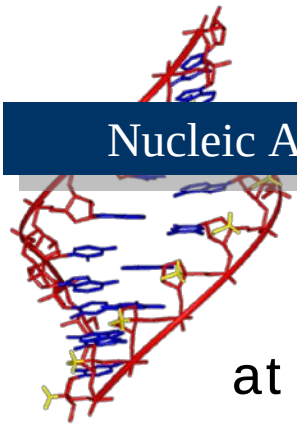

University of Southern Denmark

Nucleic Acid Center **Seminar** no. 68

Friday 20 February 2015
at 11:00 in the FKF Colloquium-room

Prof. Annemieke Madder

Organic and Biomimetic Chemistry Research Group (OBCR)
Department of Organic and Macromolecular Chemistry
Ghent University, Gent, Belgium

"Modified oligonucleotides for applications in nucleic acid crosslinking and catalysis"

Web: http://www.orgchem.ugent.be/?q=node/24

Abstract: One of the core interests at OBCR is the precise and controlled introduction of non-natural functionalities into oligonucleotide duplexes for various purposes including catalysis and crosslinking. During the talk two examples will be discussed in which the introduction of a small heterocyclic moiety has been achieved for the construction of reactive oligonucleotide probes.

In a first example the construction of imidazole modified DNA for the generation of catalytic duplexes will be illustrated. We have explored the use of a 14mer DNA duplex as a scaffold for the precise and predictable positioning of catalytic functionalities. Given the ubiquitous participation of the histidine-based imidazole group in protein recognition and catalysis events, histidine-like modified duplexes were investigated.
The motif contributes to a stabilization against thermal melting of 6°C and is key in modulating the pKaH of the imidazolium group.

In a second example a new method for DNA interstrand crosslinking, recently developed in our laboratory, will be discussed which relies on the incorporation of a furan moiety as a caged reactive entity into oligodeoxynucleotides. These furan-modified nucleic acids form cross-links with their hybridized complements upon selective furan oxidation.

A series of applications of the developed furan modified probes, from nucleic acid duplex and triplex cross-linking to DNA-protein cross-linking will be discussed. Whereas a duplex cross-linking approach finds applications in the antisense strategy, cross-linking with triplex forming oligonucleotides that bind in the major groove of dsDNA has potential applications in gene expression modulation and in gene targeting technologies. The methodology has also been further extended for its bidirectional use in protein – nucleic acid cross-linking (DPC), modifying protein or nucleic acid respectively to react with the unmodified counterpart as target.