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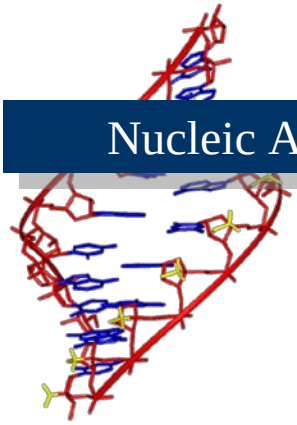

Nucleic Acid Center **Seminar** no. 73

Monday 20 June 2016
at 11:15 in the FKF Meeting-room

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"*Invader probes: Exploiting the energy of intercalation to facilitate recognition of chromosomal DNA*"

Web: http://www.webpages.uidaho.edu/~hrdlicka/index.htm

Abstract:

The development of molecular strategies that enable recognition of specific double-stranded DNA (dsDNA) regions has been a longstanding goal as they can be developed into tools that enable modulation of gene expression at the transcriptional level, gene editing, and detection of specific genetic signatures. Major advances have been made with triplex-forming oligonucleotides, peptide nucleic acids (PNAs), minor groove binding polyamides, and – more recently – engineered proteins such as CRISPR/Cas9. Despite these advances, an unmet need remains for easily deliverable hybridization-based probes that recognize specific mixed-sequence dsDNA regions under physiological conditions. Over the past ten years, my laboratory has been exploring *Invader probes* towards this end, i.e., double-stranded oligonucleotide probes that are activated for dsDNA-recognition through modification with interstrand zipper arrangements of intercalator-functionalized monomers based on 2'-amino-α-L-LNA, 2'-*N*-methyl-2'-amino-DNA or RNA scaffolds. We have shown that the stability difference between Invader probes and probe-target complexes can be used to drive mixed-sequence recognition of linear dsDNA targets, DNA hairpins, and chromosomal DNA. In the course of this presentation, I will outline the Invader concept, discuss structure-property relationships, and disclose results from biological dsDNA-recognition experiments. Collectively, the results suggest that the hitherto elusive goal of mixed-sequence DNA recognition is within grasp, which has exciting implications for karyotyping, in vivo imaging, and gene regulation.