Title: LNA/DNA Probes for Fluorescence Sensing of Nucleic Acids and Autoimmune Antibodies

Prof. Dr. Kira Astakhova

Nucleic Acid Center, Department of Physics, Chemistry and Pharmacy, University of Southern Denmark, DK-5230 Odense M, Denmark.

Several autoimmune disorders are characterized by production of antibodies against single- and double-stranded DNA. If not diagnosed and treated early, the autoimmune conditions can lead to serious health deterioration and even mortality. The sequence-specific autoimmune antibodies (autoantibodies) against single-stranded DNA have been thoroughly studied. In turn, non-sequence-specific autoantibodies against double-stranded DNA, a hallmark of autoimmune conditions such as antiphospholipide syndrome and systemic lupus erythematosus, have not been studied in detail. Generally, monitoring interactions of nucleic acids by fluorescence is a convenient method in modern bioanalysis and can be performed under native conditions without additional equipment or procedures. Currently, fluorescent oligonucleotides containing bright cyanine and xanthene dyes are often applied in bioanalysis of nucleic acids and proteins, including antibodies. Furthermore, affinity-enhancing locked nucleic acids containing 2′-amino-LNA monomers with fluorescent polyaromatic hydrocarbons (PAHs) attached at the 2′-amino group provide high target binding affinity and selectivity, remarkable fluorescence quantum yields and brightness values. Another appealing aspect of LNA/DNA probes is their high potential as aptamers in selective binding of diverse proteins. Herein I will describe novel fluorescent oligonucleotides for homogeneous (all-in-solution) detection of nucleic acids and autoimmune antibodies. The probes are prepared by efficient click chemistry between novel alkyne-modified locked nucleic acid (LNA) strands and a series of fluorescent azides. The multiply labeled fluorescent LNA/DNA probes prepared herein generally display high binding affinity to complementary DNA/RNA, high quantum yields and, hence, high fluorescence brightness values. With the novel fluorescent probes, specific sensing of the monoclonal human autoantibody is performed. It makes the novel "clickable" LNA/DNA probes a very promising tool in molecular diagnostics and in studies of nucleic acids and autoantibodies against DNA. The latter are produced under autoimmune conditions including antiphospholipide syndrome and systemic lupus erythematosus.

Biography

Kira Astakhova has completed her PhD at the age of 23 years from Institute of bioorganic chemistry of Moscow, Russia, and postdoctoral studies from the Nucleic Acid Center, University of Southern Denmark. She is currently an Associate Professor at the Nucleic Acid Center, Denmark, a premier research institution focusing on synthetic nucleic acids. She has published more than 25 papers in reputed journals and has been serving as an editorial board member of repute. Her main research interests include nucleic acid chemistry and synthetic biology (LNA, DNA and RNA), nanobioscience and diagnostics of human diseases.