Chemistry of Contrast Media

Biologicals

Aptamer imaging

Frederic Duconge
CEA, DSV, I²BM, Service Hospitalier Frédéric Joliot (SHFJ) – INSERM U1023 – Université Paris Sud, Orsay, France

Learning Objectives:

- Understand the properties of nucleic acid structures
- Recognize the methods to select aptamers
- Learn the methods to label or conjugate aptamers
- Understand biodistribution and specific targeting of aptamers

Sophisticated structures of nucleic acids play a key role in cells by interacting with proteins or other partners. Since 1990, several approaches of molecular evolution have been developed to study these natural properties of nucleic acid structures but also to develop non-natural ligands that bind to specific targets (amino acids, antibiotic, proteins…). The artificial ligands found by these techniques are named "aptamers", from the latin "aptus" meaning "to fit", and the method to identify them was popularized using the term "SELEX" for "Systematic Evolution of Ligands by Exponential enrichment". In vitro, it has been demonstrated that aptamers can rival antibodies as ligands, inhibitors or probes for several applications including sensors, biochips, chromatography, microscopy, flow cytometry. They present also several advantages for in vivo applications: 1- they have high specificity and affinity for their targets 2- they seem to lack immunogenicity 3- they can have an inhibitory activity on their targets, 4- they can be chemically modified in order to improve their stability against nucleases or to modify their pharmacokinetics, 5- straightforward modifications and functionalization of aptamers make them ideal targeting agents and 5- they can be selected against extracellular targets that are easier to access in vivo. Therefore, several aptamers have already been tested in vivo for therapeutic applications. Nine aptamers are already enrolled in clinical trials, and one is a commercially available treatment for age-related macular degeneration. A few experiments have been conducted in vivo to evaluate aptamers as targeting probes, mostly in small animal models of cancer. Radiolabelled aptamers have already been evaluated as radiotracers for SPECT imaging. Aptamers have also been tested as fluorescent probes including activatable probes or as targeting agent of nanoparticles for multimodal imaging or theranostic applications. These experiments provide some clues about the interest to use aptamers for molecular imaging.

Relevant Publications:

1. Pestourie C, Tavitian B and Ducongé F (2005) Aptamers against extracellular targets for in vivo applications. Biochimie 87 (9-10), 921-30
2. Tavitian B, Duconge F, Boisgard R and Dolle F (2009) In vivo imaging of oligonucleotidic aptamers. Methods Mol Biol, 535, 241-259.
3. Cibiel A Dupont DM and Ducongé F (2011) Methods To Identify Aptamers against Cell Surface Biomarkers. Pharmaceuticals. 2011; 4(9):1216-1235.

4. Cibiel A, Pestourie C and Ducongé F (2012) In vivo uses of aptamers selected against cell surface biomarkers for therapy and molecular imaging. biochimie, 94, 1595-1606.

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