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Title of the project

Dynamic covalent split aptamers and DNA-based machines

MSCA-PF Research Panel

☒ Chemistry (CHE)

☐ Social Sciences and Humanities (SOC)

☐ Economic Sciences (ECO)

☐ Information Science and Engineering (ENG)

☐ Environment and Geosciences (ENV)

☒ Life Sciences (LIF)

☐ Mathematics (MAT)

☐ Physics (PHY)

Description of the project

Bioorganic group/Utu (https://bioorganic.utu.fi/) has extensively studied dynamic pH-responsive reactions on a DNA template. The hybridization-driven proximity effect leads to a huge rate acceleration and increased equilibrium constant of the reactions, which without the DNA-template show only modest reactivity in aqueous media. The advantage of the pH-responsive reactions is their adjustability, which can be utilized for dynamic recognition processes or DNA-based molecular machines. Encouraged by the preliminary experiments, Bioorganic group has recently utilized this concept e.g. for a reversible assembly of a cocaine-binding split aptamer. This was the first description of a dynamic covalent ligation between split aptamer fragments utilizing a small-molecule substrate as a template. The next step and fellow's task is to expand the scope of this concept to a set of different aptamers, hybridization-based machines and dynamic drug delivery vehicles.

Research objectives or research questions of the project

1. The role of the dynamic covalent bridges of the split aptamers for the substrate detection should be studied in detail. Set of different aptamers with different substrates will be studied. Splitting sites will be varied and their role for the detection (affinity and specificity) will be studied in detail.

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2. The same idea will be expanded to DNA-based machines, in which the substrate-binding leads to a further process. The further process can be enzymatic or resembling activities.
3. The pH-responsive ligation will be utilized for the drug delivery. The drug substrate should be bound to the DNA-construct in the blood stream (pH above 7), but once the construct enters the cell and further to acidic endosomal conditions or cytoplasm of some cancer cells, the construct should undergo degradation, leading to the drug's release.