DEVELOPMENT AND OPTIMIZATION OF A CELL SURFACE-MIMICKING MODEL SYSTEM BY INTEGRATING ARTIFICIAL MEMBRANES, DNA-BASED NANOSTRUCTURES AND MICROFABRICATION TECHNIQUES, TO STUDY MOLECULAR SIGNATURES THAT ENHANCE DISEASE DIAGNOSTICS AND TARGETED THERAPIES

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The goal of the project is to develop a DNA nanotechnology-based platform to analyze the nanoenvironments of membrane receptors within lipid rafts, ordered microdomains involved in several cellular functions. The aim is to understand how spatial molecular interactions influence different cellular phenotypes, drug responses, and the emergence of resistance. This approach will enable more accurate prediction of the functional state of membrane receptors, guide personalized therapeutic choices, and contribute to the development of new targeted treatments.

The method will rely on an innovative technology (RepliSeq), which employs polygonal DNA nanostructures to read the spatial organization of proteins through sequencing, with nanometer resolution. These nanostructures will interact with artificial membranes (SLBs) that mimic the cell membrane while preserving the mobility and functionality of incorporated proteins. The SLBs will be enriched with lipid rafts and used to reconstitute target proteins of interest.

The project will focus on the membrane receptor Her2, a key protein in breast cancer, as a proof of concept to demonstrate the platform feasibility. Recent evidence suggests that mere overexpression of Her2 is not sufficient to explain therapeutic responses; the composition and spatial organization of proteins surrounding Her2, particularly within rafts, play a critical role. The project therefore aims to investigate the influence of lipid rafts on Her2 activation and oligomerization.

Functionalized surfaces will be designed to immobilize the DNA nanostructures, which will be placed on micropatterned substrates for artificial membrane formation. These nanostructures will allow controlled positioning of individual proteins, modulation of lipid domains, and simultaneous analysis of their spatial organization.

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