O-28.5 Short talk

Characterization of nanoscale protein clusters at the cell membrane with DNA nanotechnology: an innovative tool to define a novel paradigm in oligomerization of membrane receptors

Elena Ambrosetti [1], Ana Teixeira [2], Giancarlo Ruocco [1]

[1] Istituto Italiano di Tecnologia Centre for Life Nano- and Neuro-Science - CLN2S@SAPIENZA, Roma, Italy

[2] Karolinska Institutet, Stockholm, Sweden

Super-resolution imaging has shown that most proteins at the plasma membrane are not uniformly distributed but rather localize within dynamic nanoscale domains. To explore their functional significance, methods enabling comprehensive analysis of the compositions and spatial organizations of membrane protein nanodomains in cell populations are needed. Despite recent advancements in super-resolution techniques, multiplexing analysis of cluster composition across entire cell populations remains challenging. In my work, I developed a non-microscopy-based approach for ensemble analysis of membrane protein nanodomains. This method, called NanoDeep, utilizes DNA nanoassemblies to translate membrane protein organization into a DNA sequencing readout and enables the identification of the protein inventory forming the nanoenvironment around any reference membrane protein in cell populations. Using NanoDeep, I characterized the protein nanoenvironments surrounding Her2, a receptor of critical relevance in cancer. Currently, I am advancing NanoDeep through the development of a new DNA nanotechnology-based multi-integrated platform, called DipRec, to analyze membrane receptor nanoenvironments at the cell surface within nanoscale-ordered membrane domains, known as lipid rafts, to further elucidate their role in the regulation of receptor clusterization and response to therapy.