Conférence co-organisée ISMO-IGPS

Amphithéâtre Hervé Daniel - 18 décembre à 10H00

Bâtiment Henri Moissan (HM2) – 17 avenue des Sciences - Orsay

Modulating cells function with RNA

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Accumulating work points out relevant genes and signaling pathways hampered in human disorders as potential candidates for therapeutics**.** Developing nucleic acid-based tools to manipulate gene expression, such as siRNAs, mRNA and genome editing strategies, open up opportunities for personalized medicine. Yet, although major progress was achieved in developing RNA targeted delivery carriers, mainly by utilizing monoclonal antibodies (mAbs) for targeting, their clinical translation has not occurred. In part because of massive development and production requirements and high batch-to-batch variability of current technologies, which relies on chemical conjugation. Here we present a self-assembled modular platform that enables to construct theoretically unlimited repertoire of RNA targeted carriers. The platform self-assembly is based on a membrane-anchored lipoprotein, incorporated into RNA-loaded novel, unique lipid nanoparticles that interact with the antibody Fc domain. We show that a simple switch of 8 different mAbs, redirects specific uptake of siRNAs by diverse leukocyte subsets *in vivo*. The platform therapeutic potential is demonstrated in an inflammatory bowel disease model, by targeting colon macrophages to reduce inflammatory symptoms, and in Mantle Cell Lymphoma xenograft model, by targeting cancer cells to induce cell death and improve survival. In addition, I will discuss novel approach for delivering modified mRNA to specific cell types *in vivo* utilizing this platform. I will also share some data on the first mRNA vaccine for extracellular bacterial infection. Finally, I will share new data showing very high efficiency genome editing in glioma, metastatic ovarian cancer and mantle cell lymphoma. This modular delivery platform can serve as a milestone in turning precision medicine feasible.

Dan Peer is a Professor and the Director of the Laboratory of Precision NanoMedicine at Tel Aviv University (TAU). He is also the Vice President for Research and Development at Tel Aviv University. From 2017 - Present, he is the Founding and Managing Director of the SPARK program of Translational Medicine at TAU. **Prof. Peer**'s work was among the first to demonstrate systemic delivery of RNA molecules using targeted nanocarriers to the immune system and he pioneered the use of RNA interference (RNAi) in immune cells. His lab was the first to show systemic, cell specific delivery of mRNA in an animal to induce therapeutic gene expression of desired proteins. This has enormous implications in cancer, inflammation and infection diseases (e.g. COVID 19 mRNA vaccines). In addition, his lab was the first to show systemic high efficiency, cell specific therapeutic genome editing in cancer. Prof. Peer has more than 130 pending and granted patents. Some of them have been licensed to several pharmaceutical companies and one is currently under registration (as a new biological drug in Inflammatory Bowel Disease). In addition, based on his work, four spin-off companies were generated aiming to bring innovative personalized medicine into clinical practice. Prof. Peer received more than 30 awards and honors and he serves on the scientific advisory board and as Board Member of more than 15 companies, and on the editorial board of more than 20 journals. In 2014, he was elected to the Israel Young Academy and in 2023 he was elected to the US National Academy of Engineers (NAE).