THE NEW ERA OF 3D (DRUG DISCOVERY & DELIVERY)

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Our research focuses on a comprehensive drug discovery process, encompassing target protein selection and characterization, as well as the design and optimization of drugs and the development of advanced tailor-made drug-delivery systems and novel biogenic nanomaterial. By leveraging the multidisciplinary expertise of researchers from different IBF sections (Milano, Pisa, Palermo) and from the CellTech-Hub (a joint IBF-IRIB lab), we aim to establish a wide platform for drug design and delivery, able to foster collaborations and service agreements with international academic institutions (e.g. ETH Zurich; Max Planck Inst., Erlangen), IRCSS (e.g. Mario Negri, Istituto Tumori, San Raffaele) and companies (e.g. Dompé, Linari Nanotech S.r.l.). The platform is already integrated in the PNRR infrastructure EBRAINS-Italy and its approach is successfully implemented in European projects (FET-Proactive BOW project), in other PNRR projects (extended partnerships: PE13 - INFACT, national centers: CN3-RNA, regional ecosystems: Samothrace) and in national funding programs (e.g. PRIN MUR, CNR grants).

Specifically, we conduct structural and functional studies of therapeutic targets by combining experimental characterization of recombinant proteins with *in silico* analysis, supported by artificial intelligence and machine learning methods. Such an approach aims to elucidate protein functions and to identify promising therapeutic targets. Subsequently, molecular docking and dynamic simulations are employed to validate novel hotspots, followed by dynamic docking to identify small molecules capable of modulating, inhibiting, or restoring protein function[1a,b,c]. In collaboration with Mario Negri Institute, we plan to design and characterize, through diffusion models, new artificial proteins able to bind specific targets to be developed as novel therapeutic and/or diagnostic tools.

To enhance the precision and effectiveness of drug delivery, we are also developing systems based on nanobodies of PLGA [poly(lactic-co-glycolic acid)], liposomes and electrospun nanofibers designed for the controlled release of therapeutic compounds directly to target organs[2].

Further, we aim to develop smart drug delivery systems based on extracellular vesicles (EV), nanoparticles designed by nature to actuate cell-to-cell communication with exceptional bioavailability, biocompatibility, stability and capability of organotropic targeting. We implemented a pilot-scale production plant of graded extracellular vesicles from Microalgae, including upstream and downstream production, EV characterization and a portfolio of methods for EV engineering and loading of different drugs[3]. The effort for the technological transfer to industrial product and processes has originated a CNR spin-off company, EVE-biofactory (www.evebiofactory.com).

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