

Brain delivery and intercellular crosstalk

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Nanomedicines (NMeds) are drug delivery systems used to encapsulate, protect, and deliver therapeutic molecules such as proteins, peptides, small molecules etc. NMeds can be also exploited via surface engineering for the targeting of specific and difficult-to-reach tissues or organs as the Central Nervous System. Nevertheless, once NMeds reach the desired target, their ultimate fate is often unknown because of intracellular trafficking or intercellular transposition via pathways such as Tunneling Nanotubes (TNTs), which should be properly investigated in order to fully describe the overall efficacy and safety of NMeds. TNTs have been demonstrated to transport various cargoes from prions, viruses, misfolded proteins, and even intracellular organelles. Previous data showed TNT mediated transport of poly lactic-co-glycolic acid (PLGA) NMeds from one cell to another. Better understanding how NMeds interact with TNTs and their formation dynamics can be crucial to understand their diffusion inside the target tissue; however, this topic is still poorly addressed in the literature. Therefore, fluorescently labelled PLGA based NMeds, either unmodified or surfaced modified with ligands for specific targeting (blood-brain barrier crossing or glioblastoma targeting) were obtained via nanoprecipitation and tested in neuronal (CAD) and GBM (U251) cell cultures. Preliminary data showed selective uptake of both targeted PLGA NMeds that remarkably were actively trafficked by TNTs. This data opens the hypothesis to further investigate on how engineered NMeds can tune the formation dynamics of TNTs to better control their final cellular fate, reaching towards a solution to one of the new challenges of nanomedicine.