**BI-FUNCTIONAL NANOPARTICLES AS NEW IMMUNOTHERAPEUTIC APPROACH TO RE-ESTABLISH COMMUNICATION BETWEEN CANCER AND IMMUNE CELLS**

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Cytotoxic T cells (CTL) play a pivotal role in recognizing and eliminating tumor cells. However, their effectiveness can be compromised by immune escape mechanisms, leading to cancer progression. Here, we present a nanoplatform able to restore compromised immunological synapses. The nanodevice consists of a Janus mesoporous silica-Au nanoparticle functionalized with specific binding sites in opposite faces (J-pHLIP-PD1) for cancer cells (targeted through the membrane-intercalating peptide pHLIP) and for CTL (targeted through the PD1 receptor).

J-pHLIP-PD1 nanoparticles effectively bind the surface of tumor cells (Sk-Mel-103 cells). Using a transwell co-culture system, we confirmed the ability of J-pHLIP-PD1 to facilitate binding between T-lymphocytes (Jurkat T-cells) and tumor cells. Furthermore, *in vitro* evaluation of human primary CTL cytotoxicity against Sk-Mel-103 demonstrated increased efficacy with the complete J-pHLIP-PD1 nanodevice compared to control groups (J-PHLIP, J-PD1, and free PD1). Finally, therapeutic potential of J-pHLIP-PD1 is demonstrated in a metastatic melanoma cancer model. The treatment with J-pHLIP-PD1 produces a significant decrease in metastatic burden accompanied by an increased presence of cytotoxic T cells. These findings underscore the potential of J-pHLIP-PD1 as a promising strategy for enhancing immunotherapeutic approaches.

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