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Design of new Nano-tools to target mitochondria and study the metabolic plasticity of cancer cells

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Metabolic plasticity and mitochondrial function are crucial in tumorigenesis and cancer therapy response, making mitochondria a key target for novel treatments (1-2). Bioactive molecules, modulating mitochondrial activity, offer alternative therapies upon accumulation in mitochondria at effective doses (3). These molecules can be vectorized into mitochondria using nanovectors, improving their bioavailability and reducing off-target effects (4). Our team has focused on the mitochondrial import machinery, AIF/CHCHD4, essential for the control of mitochondrial bioenergetics, cell survival & response to stress conditions (5). Our team has also identified a peptide that inhibits AIF/CHCHD4 interaction, representing a promising anticancer therapeutic potential (6). Due to the peptide's fragility, two nanovectorization approaches were developed to protect and deliver it to mitochondria: Liposomes & Fluorescent nano diamonds (Fig.1). Nanocarriers were characterized for the peptide encapsulation efficiency, size, stability & cellular uptake. Nano formulations were functionalized by specific mitochondria targeting moieties and are now under investigation for mitochondrial localization and cancer cell survival

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Schematic representations of two nanovectorization

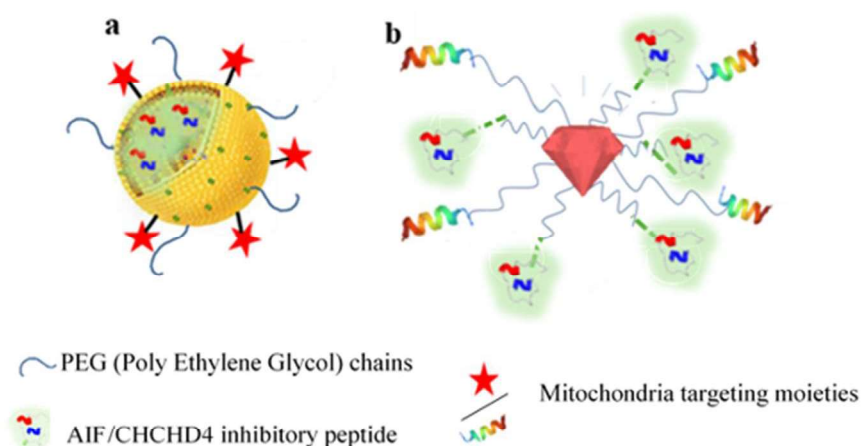


Figure1. Schematic representations of two nanovectorization approaches for mitochondria delivery of the inhibitory peptide. (a) Liposome (b) Fluorescent nanodiamond.