

ABSTRACT**Porous Nanoparticle-Supported Lipid Bilayers (Protocells) for Targeted Delivery Including Transdermal Delivery of Cargo and Methods Thereof**

The present invention is directed to protocells for specific targeting of hepatocellular and other cancer cells which comprise a nanoporous silica core with a supported lipid bilayer; at least one agent which facilitates cancer cell death (such as a traditional small molecule, a macromolecular cargo (e.g. siRNA or a protein toxin such as ricin toxin A-chain or diphtheria toxin A-chain) and/or a histone-packaged plasmid DNA disposed within the nanoporous silica core (preferably supercoiled in order to more efficiently package the DNA into protocells) which is optionally modified with a nuclear localization sequence to assist in localizing protocells within the nucleus of the cancer cell and the ability to express peptides involved in therapy (apoptosis/cell death) of the cancer cell or as a reporter, a targeting peptide which targets cancer cells in tissue to be treated such that binding of the protocell to the targeted cells is specific and enhanced and a fusogenic peptide that promotes endosomal escape of protocells and encapsulated DNA. Protocells according to the present invention may be used to treat cancer, especially including hepatocellular (liver) cancer using novel binding peptides (c-MET peptides) which selectively bind to hepatocellular tissue or to function in diagnosis of cancer, including cancer treatment and drug discovery.

FIGURE 1