DNA electrotransfer mechanisms: *in vitro* and *in vivo* studies

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Abstract

Gene electrotransfer into cells and tissues is a complex process involving multiple steps that lead to plasmid DNA passage from the extracellular region to the cell nucleus crossing the barriers of the plasma membrane, cytoplasm and nucleus membrane. It is well documented that plasmid DNA, during application of electric pulses first forms aggregates in the electroporated membrane, which then are translocated into the cytoplasm. Electrical parameters of pulses used for gene electrotransfer affect the initial steps of DNA-membrane interactions. At later stages, translocation of the aggregates across the membrane is related with some endocytotic pathways. Several studies employing various endocytosis inhibitors has shown that that these inhibitors decreased transfection efficiency both *in vitro* and *in vivo*. Whatever the mechanism of the DNA uptake, our studies show that translocation of DNA through the membrane leads to increase in membrane permeability for small molecules. When considering gene electrotransfer into tissues it becomes clear that other nonelectrical conditions are also of primary importance.