

Non thermal plasmas: newly-developed, multifaceted and complementary tool for cell permeabilization

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Non-thermal plasmas, produced from dielectric barrier discharges in air or from rare gas plasma jet devices, generate at room temperature, long and short lifetime reactive species (RS) in gaseous phase or in the liquid solution on which they impinge, ionic species, UV photons and intense transient electric fields (EF). In the last decade, the main focus was drawn on the RS to understand and optimize their action in the frame of the broad topic of "Plasma medicine". More recently, the characterization and implication of EF in biomedical applications is studied, considering the generation of ns to μ s duration, kV/cm amplitude features of plasma EF. Plasma have been shown to be a potential alternative to more "conventional technologies" for gene transfer, cell permeabilization, drug delivery in various applications including for cancer therapy. Quite recently, the concepts of reversible electroporation, especially the models of so called pore formation in cell membranes were broaden and detailed involving not only the key role of EF but also the oxidation of cell membrane associated with RS. Thus it appears we attend to a unique opportunity to reach more insights and achieve cell manipulation process optimization with considering the potential complementary or synergistic delivery of pulsed electric fields and plasma for in vitro and in vivo protocols.

Besides a quick overview of some significant works focused on the use of non-thermal plasmas in interaction with cell membranes, the lecture will document the results obtained so far with the Plasma Gun developed at GREMI for first, cancer cell permeabilization with various plasma delivery protocols, and second on the first demonstrations of the positive combined action of pulsed electric fields (PEF) and plasma for antitumor action. Cell permeabilization has been performed in vitro for different adherent cell lines, exposed to plasma jet delivered at various pulse repetition rates for short duration and followed with cell incubation in plasma treated solution. The combination of plasma and PEF is studied in vitro and with murine models considering the delivery of pulsed voltage and current pulses (electroporation) together with plasma treated solutions in contact with biological targets (suspended cancer cells in electroporation cuvettes or tumors) at different delays with respect to the electroporation step.

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