

Therapeutic Approaches Based on Plasmas and Nanoparticles

Abstract

Plasma medicine is a new multi-disciplinary field embracing physics, chemistry, engineering and biology. Unique highly non-equilibrium chemistry and plasma composition makes plasma potential in medicine unmatched by other approaches. Nanomedicine is more mature field that utilizes unique properties and features of nanoparticles. This editorial outlines existing and potential synergies between these two fields.

Keywords: Cold atmospheric plasma; Nanoparticles; Non-equilibrium plasma chemistry

Editorial

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Abbreviations: CAP: Cold Atmospheric Plasma, ROS: Reactive Oxygen Species, RNS: Reactive Nitrogen Species; AuNPs: Gold Nanoparticles

Editorial

Plasma medicine is a new, largely unexplored, multi-disciplinary scientific field, which involves physics, chemistry, engineering and biology. This field emerged as results of intense research effort over last few decades in low-temperature (or cold) atmospheric plasma application in bioengineering [1-3]. The unique chemical and physical properties of cold atmospheric plasma (CAP) have enabled recent biomedical applications including sterilization, bacteria deactivation, wound healing, tissue or cellular removal, dentistry [4-6]. More recently potential of CAP application in cancer therapy has been explored [7-10]. CAP treatment leads to selective eradication of cancer cells in vitro and reduction of tumor size in vivo.

CAP provides a unique, rich environment of reactive oxygen species (ROS), reactive nitrogen species (RNS), charged particles, photons, and electric field. Some chemical components of the CAP are highly selective, such as oxygen, which might promote a "plasma killing effect," while others such as nitric oxide could produce a "plasma healing" effect. It should be pointed out that CAP produces a level of reaction chemistry and unique chemical composition similar to endogenous ROS/RNS cell chemistry. Combining these species in various controlled blends provides an unprecedented possibility to activate specific signaling pathways in cells and tissue. This is critical in fields such as cancer therapeutics in which introduction and delivery of these potentially selective highly reactive species into tumors would enable selective removal of cancer cells, while sparing healthy tissue [11,12].

Synergy between nanotechnology and CAP technology can provide an additional strong benefit in biomedical applications [13]. In one of the first reports in this arena it was shown that a special antibody-conjugated gold nanoparticle could selectively target cancer cells [14]. In fact in that study a five-fold increase in melanoma cell death over the case of the CAP alone by using air plasma with gold nanoparticles was achieved. Additional recent result indicated that strong synergy exists between gold nanoparticles and cold atmospheric plasma in cancer therapy [15]. Gold nanoparticles (AuNPs) in combination with CAP can significantly promote glioblastoma cell death. In fact, cancer cells viability decreased by 30% in comparison with control group having the same plasma dosage but no AuNPs applied. Results of that study correlates well with the theory that intracellular ROS accumulation results in oxidative stress, which further changes the intracellular pathways, causing damage to the proteins, lipids and DNA. In addition, CAP can promote nanoparticle uptake by cells [16]. In fact it was shown that gold nanoparticles were endocytosed at an accelerated rate in the U87 cell membrane due to the plasma treatment while no significant difference in gold nanoparticle penetration into normal cells was observed. Thus, combining CAP advantage with nanoparticles opens up multiple benefits such as enhancing plasma action and nanoparticle uptake outlined above. In addition, using this strategy can lead to reduction of overall toxicity.

As a future possible direction one can imagine use of nanoparticles as a carrier of uniquely prepared plasma species. To this end plasma-stimulated media [17] can be used. Plasma generated ROS/RNS can be trapped by nanoparticles through chemical or physical sorption. Nanoparticles enriched with ROS/RNS can be then directed towards to diseased tissue. Overall synergy between CAP and nanoparticles goes beyond simple combination but can potentially open new opportunity by

utilizing unique advantages of both technologies. As such hybrid technologies can have enormous importance in future medicine.

Result of outlined synergetic approach might be fully adaptive system based on plasma and system based on plasma and nanoparticles. Schematically a possible approach is shown in Figure 1. This approach is based on ability to change plasma composition and key plasma parameters (such as density and temperature) on demand dependent on specific application and

needs. Accuracy and localization of the plasma action can be achieved by utilizing nanoparticles. Nanoparticles, in particular, gold nanoparticle can enhance plasma-mediated effect while at the same time plasma can enhance nanoparticle-based drug delivery. Biological response of living tissue will be recording using variety of imaging tools as well as chemical and biological reporters. Such feedback mechanism will enable adaptive feature of the plasma-based therapeutic system.

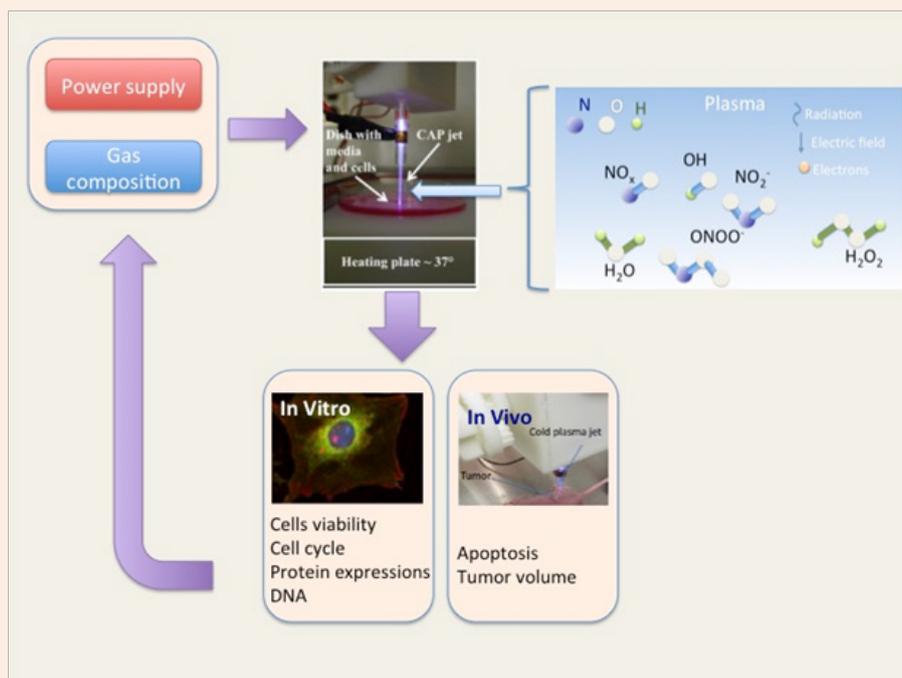


Figure 1: Schematics of adaptive plasma therapeutic approach.

This approach is based on ability to change plasma composition on demand via feedback mechanism dependent on specific application and needs.

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