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Plasma Processes and Polymers Special Issue on: Plasma and Cancer

Guest Editors:

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Michael Keidar, George Washington University

During the last two decades, research efforts on the application of low temperature plasmas in biology and medicine have positioned nonequilibrium low temperature plasmas as a technology that has the potential of revolutionizing healthcare.^[1,2] Low temperature plasmas can be applied in direct contact with living tissues to inactivate bacteria,^[3] to disinfect wounds and accelerate wound healing,^[4] and to induce damage in some cancer cells.^[5–11] The research work on all the above mentioned applications constitutes a new scientific field today known as "Plasma Medicine." This fascinating multidisciplinary field, which involves physics, chemistry, engineering, and biology is rather young and has been around for only two decades. It is not to be confused with the old (and rather controversial) fields of electrotherapy or carbon arc lamps therapies where plasma (even if present) does not play a direct or central biological role in the therapy. Plasma medicine as we know it today had its beginnings about two decades ago under a US Air Force Office of Scientific Research (AFOSR) funded program that sought to use nonequilibrium atmospheric pressure plasmas (including air plasma) to inactivate pathogens in order to decontaminate/sterilize both abiotic and biotic materials. This program aimed at developing and optimizing a plasma-based technology that can be used in forward deployed military theaters to decontaminate gear (abiotic) and to disinfect soldiers' wounds (biotic) and speed up the wound

healing process. Subsequently, and by the turn of the century, plasma medicine as a field of research developed quite rapidly and today involves the study of both fundamental scientific investigations as well as the applied aspects of the interaction of low temperature, atmospheric pressure plasma with biological cells and biological systems. By low temperature plasma it is meant plasma with biologically tolerable gas temperatures. This usually means temperatures less than $40\,^\circ C$ (or about 313 K). In plasma medicine, the plasma is not treated as a "black box" that has magical effects on biological systems. To the contrary, the plasma itself is carefully investigated and characterized in details using advanced diagnostics methods. This is done so that each plasma-generated agent that may have biological implication is identified and quantitatively measured. This is one of the key roles played by the plasma physicists working in the field. The role of the biologists/biochemists is to determine the effect of each of these agents, alone or in synergy with others, on the cellular and sub-cellular levels. This includes physical effects, chemical effects, and cell signaling. With this collaboration between physicists, engineers, and biologists/biochemists the scientific inquiry into the interaction of plasma with biological cells has quickly progressed from its humble beginning of the mid 1990's to more complex lines of research involving both healthy and cancerous mammalian cells, with major research milestones and advances occurring almost every two years. As more medicaloriented plasma applications/therapies are proposed, the collaboration has also recently expanded to include

medical researchers and personnel. This is justifying more and more the inclusion of the word "medicine" in the name of this new field of application of plasma.

Low temperature plasmas are known to exhibit enhanced gas phase chemistry without the need for elevated temperatures. It is this remarkable characteristic that allows the use of these plasmas in biological and medical applications. It has been found that the plasma-generated reactive oxygen species (ROS) and reactive nitrogen species (RNS) play a major role in the interaction of low temperature plasmas with biological cells.^[1,2] These chemical species which include O, O²⁻, OH NO, and NO₂ exhibit strong oxidative properties and/or trigger signaling pathways in biological cells. The fact that these biochemical mechanisms and pathways can be activated with plasmas that are generated at atmospheric pressure and that remain at temperatures close to room temperature makes plasma an attractive medium upon which new medical therapies can be established.

One of the relatively recent findings is the realization that low doses of plasma can induce apoptosis, or programmed cell death. This opened up the possibility to use plasma technology to kill cancerous cells in vitro and in vivo.^[5–11] Of all the possible applications of low temperature plasma in biology and medicine, the killing of cancer cells could lead to a paradigm shift in the way cancer tumors and lesions can be treated without serious side effects to the patient. However, this exciting prospect can only be achieved after extensive fundamental scientific work is done to understand the complex interaction of plasma with cells in general and with cancer cells in particular. This highly interdisciplinary work requires a close collaboration between plasma physicists/engineers and biology/microbiology/biochemistry experts. Research efforts, being now conducted in various labs around the world, are aiming at elucidating the intricate physical and biochemical processes that play a role when cancer cells are exposed to plasma.

With the already achieved advances in the understanding of how plasma interacts with cancer cells, the guest editors and the editorial board of Plasma Processes and Polymers (PPaP) felt that time has arrived to publish quality papers from the leading experts in a consolidated special issue. This initiative resulted in an excellent collection of papers that greatly enriches the literature related to plasma medicine in general and the application of low temperature plasma to cancer in particular. The topics covered by the papers included in this special issue range from molecular dynamics simulations of the interaction between plasma and biomolecules and tissues, to the chemistry involved when plasma is applied to biological systems, and to the destruction of various cancer cells by plasma. The prospects of plasma technology

as a new possible player in cancer therapy of the 21st century are also discussed. Many of the topics discussed in this issue were presented at the inaugural First Workshop on Plasma for cancer Treatment (IWPCT-1) which took place at the George Washington University Convention Center in Washington DC, USA, March 25-26, 2014. At this meeting, which was organized by the guest editors of this special issue, world experts from eleven countries (4 continents) gathered to discuss the stateof-the-art of plasma application in cancer.

The guest editors would like to thank the editorial board of PPaP for supporting the idea of publishing a special issue on "plasma and cancer." We are very grateful to Renate Forch for expertly coordinating the special issue with great care and enthusiasm. In addition, a big thank you goes to the reviewers who invested time and effort in ensuring that the contents of the papers are free of mistakes and are of the best quality possible. Last but not least we would like to thank the authors for their excellent contributions to this special issue which is truly special as it is the first such journal issue, mainly dedicated to the topic of the effects of low temperature plasmas on cancer cells and to the prospects of plasma technology as a possible future cancer treatment modality.

Mounir Laroussi and Michael Keidar Guest Editors

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