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Generation and Control of Plasma Induced Reactive Oxygen/Nitrogen Species in Liquids: a Route Toward Selective Cell Responses

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Oxidative stress, caused by the intracellular imbalance between the excessive formation of reactive oxygen/ nitrogen species (RONS) and antioxidant defenses, is connected to many pathologies ranging from age-related disorders to cardiovascular and neurodegenerative diseases. Plasma treated water solutions (PTWS) are well known as possible sources of RONS for triggering specific biological responses. Recently it has been shown that cancer therapy, based on PTWS, includes not only the ability to selectively kill cancer cells but also to promote immunogenic cancer cell death, ICD. [1] . The mechanism of the effect of PTWS to kill malignant cells is either via augmenting ROS (i.e. O_2^-, H_2O_2, $^1O_2$) generation through exogenous agents or by the inhibition of the antioxidant system. Currently, the mechanism of PTWS is mainly linked to the presence of H_2O_2, but very recently researches have demonstrated that a synergistic effect of H_2O_2 and NO_2^- can be on the base of the RONS-based apoptosis induction in tumor cells, including a clear involvement of cellular produced secondary singlet oxygen in this mechanism [2]. The role of the species containing nitrogen, like NO, is only hypothesized but not fully explored. The main reason of the scarce investigation of NO is due to the complexity of chemical reactions that occur in buffered liquids, mostly in plasma treated cell culture media, and the difficulty of NO detection. The chemical interferences, due to presence of other oxidant species, is often underestimated during the detection of single components of the PTWS. This talk will provide a comprehensive picture of what is currently known about the redox interplay among active species produced in PTWS and cells. A critical review and discussion about the intricate redox sensitive relationship and cooperation of active species in cell fate decisions will be provided. Our hypothesis is that stable plasma-derived RONS directly interact with cells and tissues but, after a preliminary trigger, secondary molecules, derived from primary RONS, can play a pivotal role. During the talk the need of a multi-diagnostic approach to assess the presence of specific redox pathways will be illustrated. Finally, it will be shown how an enrichment of selected reactive species as well as a correct detection in complex media, without “artifact”, is necessary to assess the specific role each of them on the response of primary and immortal cell lines. In particular, results of *in vitro* biological effects of chemically different PTWS will be shown.

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References

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