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## Regulation of reactive species in gas plasma and the application in tumor therapy

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In recent years, with the rapid development of atmospheric pressure cold plasma technology, the application of plasma in biomedicine is increasing day by day. In particular, the potential application of plasma in tumor therapy has drawn wide attention. Plasma produce many active particles, such as oxygen and nitrogen-containing active particles (ROS and RNS) that are highly reactive and could interact with tumor cells and kill tumor cells efficiently. Which species play the most important role in tumor cell inactivation? What is the molecular mechanism of plasma induced tumor cell apoptosis? How about the safety of plasma treatment in tumor therapy? All these questions should be well addressed before the clinical trials of gas plasma. By computer simulation and biomedical experiments, we demonstrated that H<sub>2</sub>O<sub>2</sub> and O<sub>2</sub>- are the two most important particles that can interact with cells. Both of them are capable of generating hyperactive OH in situ under the catalysis of ferritin on cells, thereby inducing tumor cell death. Further screening by protein microarray revealed that increased plasma ROS led to a significant increase in the expression of death receptor CD95 and subsequent caspase activation and cell death. It was found by ChIP that p53 could bind to the CD95 promoter and increasing the mRNA and protein expression of CD95. CD95 was found to be less expressed in normal cells and more in tumor cells from cell lines and clinical samples, which could be used as a good target for selective inactivation of cancer cells by plasma. In addition, we showed that plasma activated water treatment can be used to treat immuno-deficient nude mice without significant safety problems. In a whole, our results showed that plasma treatment could be used as a

potential tool for cancer treatment in the future.

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