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Effect of plasma treatment on MDM2 and p53 expression in cancer cells

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For many years, researchers are focusing on the murine double minute 2 (MDM2)-p53 interactions. MDM2 proteins are produced by many cancer cells to inhibit the p53 transcriptional activity [1]. We recently reported that CAP treatment on cancer cells decreases NOX1 expression in A375 melanoma cells and oxidises the NADPH oxidase activator (Noxa 1) SH3 protein [2]. Decreased NOX1 expression might result in low production of superoxide which affects the generation of $^1O_2$. Hence, catalase enzymes remain in the active form and decompose the excess H_2O_2 in cancer cells, so there will be an alternative pathway for CAP-induced cancer cell death. The effect of plasma treatment on MDM2-p53 binding is still absent from the literature. In this study, we checked the expression of MDM2 and p53 in A549 and MRC-5 cell lines using Western blotting. A549 is lung cancer cells and fibroblasts MRC-5 cells developed from lung tissues. To understand the structural changes in MDM2 and p53 proteins after possible plasma treatment, we performed molecular dynamics simulation. We have divided them into 3 groups, like Plasma1, Plasma2 and Plasma3, as see in Figure 1. To determine the change in the binding free energies of MDM2-p53 before and after plasma oxidations, we used the molecular mechanics Poisson–Boltzmann surface area (MM-PBSA) method [3]. Plasma modifies the amino acids of proteins, affecting the protein structure and function, which results in changes in the secondary and/or tertiary structure of the proteins [4,5]. It was observed that the binding energy of MDM2 (oxidized)-p53 (not oxidized) was decreased as compared to the control -22 kJ/mol. However, the binding energy of MDM2 (not oxidized)-p53 (oxidized) was higher than the control. Although the oxidation of both MDM2 and p53 further increases the binding energies. We observed weak interactions between p53 and oxidized MDM2, which can provide more tumor suppressor protein (p53), results in cancer cell death. In contrast, the oxidized p53 strongly binds with MDM2 that increases tumor. Hence, this study provides insight into MDM2 and p53 that will help in further understanding of plasma oncology.

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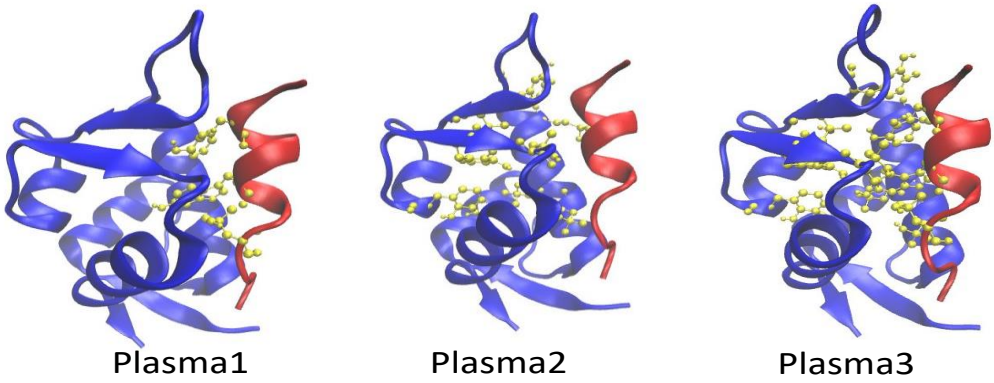

Figure 1. Schematic diagram of three plasma conditions. Plasma1, shows oxidized p53 and control Mdm2; Plasma2, displays oxidized Mdm2 and control p53 and Plasma3 shows both Mdm2 and p53 were oxidized. For p53, the Phe19, Trp23, and Leu26 amino acids were oxidized. For Mdm2, Leu54, Leu57, Met62, Tyr67, Val75, Val93, Phe86, and Phe91, amino acids where oxidized.