

## **Immune response induced by atmospheric pressure low-temperature plasma for bladder cancer**

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Recently the efficacy of robotic surgery and PD-1 inhibitors such as pembrolizumab has been reported in clinical trials for the treatment of muscle-invasive bladder cancer. For bladder cancer, the increase of PD-1 expression and tumor mutation burden correlate with therapeutic efficacy of immune checkpoint inhibitors. This indicates the possibility of freeing bladder cancer patients from the limitations of antitumor immunity. Actually, many clinical trials for bladder cancer have demonstrated the high efficacy of immune checkpoint inhibitors such as anti-PD-1 and PD-L1 antibodies. This confirms that anti-tumor immunity has a significant impact on bladder cancer patients. Plasma is unique as it enables concomitant treatment from a complex mix of molecules such as ROS and reactive nitrogen species (RNS) as well as other physical components. Plasma can efficiently generate local ROS at the irradiated area and induce cancer cell death. In our analysis using mouse model, we observed migration of CD4 T cells and CD8 T cells in tumor lesions irradiated with low-temperature atmospheric pressure plasma compared to the untreated group. In contrast, Foxp3 cells showed decreased migration compared to the no-treatment group. Western blot analysis showed increased expression of PD-1 and PD-L1 by irradiation of low-temperature atmospheric pressure plasma. The generation of ROS by plasma causes immune modulation and enhances antitumor immunity, resulting in a high antitumor effect. We investigated and presented the results of the anticancer immunity induced by plasma for bladder cancer in vivo.