

Killing melanoma cells with ROS provides immuno-protection against tumor growth in vivo

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Purpose/Objectives: Immunogenic cancer cell death (ICD) delivers inflammatory stimuli to elicit anti-tumor immune responses. Release of adjuvant find-me (HMGB1, ATP) and eat-me (calreticulin; CRT) signals enables DC maturation and cross presentation of tumor antigen to T cells. Effective ICD-inducing therapies are drugs such as anthracyclines, ionizing irradiation, or photodynamic therapies. Intriguingly, these antitumor strategies show concomitant generation of reactive oxygen species (ROS) that can drive cell death and immunogenicity signaling responses through redox relays. In cancer cells, the importance of ROS are underappreciated in the onset of ICD.

Materials/methods: A novel technology, cold physical plasma, was used to generate various ROS that can be effectively delivered to B16F10 melanoma cells. The oxidation and ATP levels as well as expression levels of MHC class I and CRT were measured. Plasma-treated tumor cells were injected into syngeneic mice with a subsequent re-challenge with live cells. Mitomycin C (MMC) and mitoxantrone (MTX) served as negative and positive control, respectively. Lymph node cells of sacrificed mice were co-cultured with melanoma cells, and T cell activation was assessed.

Results: Cold physical plasma oxidized melanoma cells and led to an increase of ATP release as well as MHC class I and CRT expression. Mice “vaccinated” with plasma-treated melanoma cells showed less tumor growth compared to mice receiving MMC-treated cells but more tumor growth compared to positive control MTX. Activation of lymph node-derived T cells ex vivo with melanoma cells was best in MTX mice, followed by the cells from the plasma group, and was lowest in cells from the MMC group.

Conclusion: Not only the event of cell death but also its auxiliary signals are important in the formation of anti-tumor immune responses. ROS play a significant role in this process. Deep phenotyping of ROS-treated melanoma cells will decipher the molecular machinery important in eliciting the responses observed.

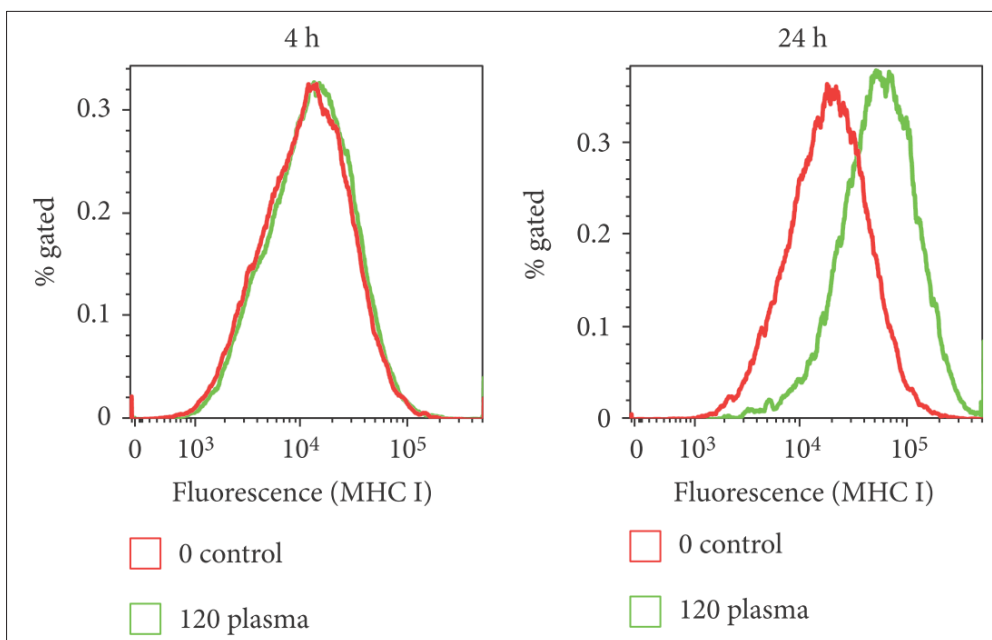


Figure 1: MHC class I expression assayed with flow cytometry of control and plasma-treated B16F10 melanoma cells at 4h and 24h post treatment.

Reference

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