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Plasma Immunotherapy

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Immune checkpoint blockade (ICB) therapy is promising cancer therapy that have greatly transformed the landscape of human cancer therapeutics. Although ICB has been approved for specific-featured cancers, the limitations associated with ICB treatment such as low objective response rate and unbiased immune attack on normal organs and tissues still exist [1]. Combination with therapies and targeted/local delivery have been suggested to overcome these limitations. However, some combined therapies currently show variable efficacy and often impose increased toxicities, since they either require administration of additional toxic substances (e.g., chemotherapeutics, radioactive and photothermal drugs) or can damage surrounding healthy tissues (e.g., radiotherapy). Hence, there is an urgent need to develop effective and safe combined therapies and delivery approaches for ICB, with a goal to improve the impact of current and future cancer therapies.

Plasma is an ionized gas composed of positively/negatively charged species (e.g., reactive oxygen and nitrogen species, RONS), neutral species, radicals, and photons. Cold atmospheric plasma (CAP), operating at atmospheric pressure and non-thermal temperature, has shown great potential for many biomedical applications. Recent studies suggest that high levels of RONS induced by CAP can effectively induce DNA damage in cancer cells or induce cancer immunogenic cell death (ICD) and activate T-cell mediated anti-tumor immunity [2].

We reported a cold atmospheric plasma (CAP)-mediated ICB therapy integrated with microneedles (MN) for the transdermal delivery of ICB and an injectable Pluronic hydrogel was employed for intratumoral administration [3]. We found that the hollow-structured MN (hMN) patch and injectable hydrogel facilitates the transportation of CAP through the skin for enhanced ICB therapy causing tumor cell death and releasing tumor-associated antigens in situ and evoking both strong innate and adaptive, local and systemic anti-tumor immune responses, therefore, can synergistically augment the efficacy of immune checkpoint inhibitors. Moreover, we described an injectable hydrogel-mediated approach that can further enhance CAP-induced ICD by elevating the phosphorylation of eIF2α (Fig. 1) [4, 5], CAP/trehalose therapy promoted dendritic cell (DC) maturation, initiating tumor-specific T-cell mediated anti-tumor immune responses. Overall, those treatment strategies with CAP can not only potentially minimize ICB-related systemic side effects. But also, can be extended to treat different cancer types and various diseases on cancer treatment.

References
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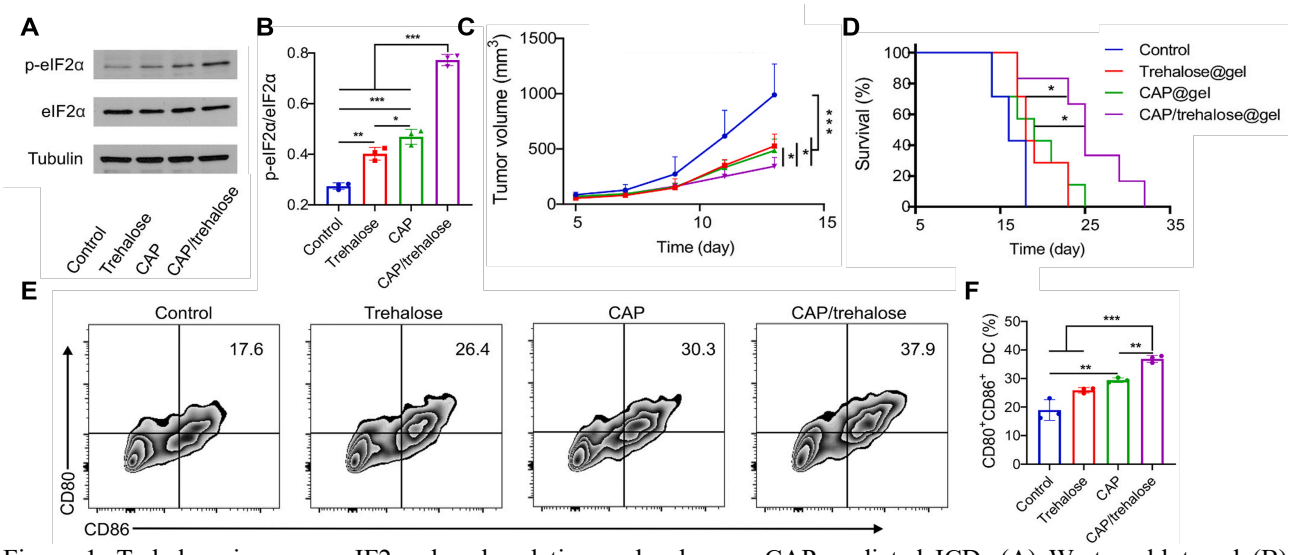

Figure 1. Trehalose increases eIF2α phosphorylation and enhances CAP-mediated ICD. (A) Western blot and (B) quantification of eIF2α and p-eIF2α levels in CT26 cells. (C) Average tumor growth kinetics and (D) Survival of mice after different treatments. (E) Representative flow cytometric plots and (F) quantification results of DC maturation (CD86+CD80+) after bone-marrow-derived DCs were cocultured with treated CT26 cells.