PUBLICATION REVIEW

Clinically translatable cytokine delivery platform for eradication of intraperitoneal tumors

Cytokines can activate the immune system to illicit an antitumor immune response, and many cytokines show promise for antitumor efficacy in clinical trials. The proinflammatory cytokine interleukin-2 (IL-2) is of particular interest for cancer immunotherapy, as it plays a critical role in the regulation of immune cells such as T cells. Although IL-2 has shown promise as a cancer immunotherapy, it suffers from a short blood half-life and the high-dose infusion regimens required result in off-target effects and toxicity in patients. Alternative approaches involving protein engineering and controlled release formulations aim to improve recombinant IL-2 safety and pharmacokinetics. While many of these alternative approaches show promise, they still suffer from the same shortfalls of traditional IL-2 therapy.

Evidence suggests that local delivery of IL-2 has the potential to circumvent the limitations of conventional intravenous and subcutaneous IL-2 administration. In the present study, the researchers developed living "cytokine factories" for the localized intraperitoneal (I.P.) delivery of cell-generated proinflammatory cytokines. Specifically, this cytokine delivery system consisted of human retinal pigmented epithelial (RPE) cells that were engineered to express cytokines of choice and encapsulated in alginate- based microparticle capsules. Non-invasive, longitudinal bioluminescence imaging was performed on Revvity's IVIS® Lumina Series optical imaging platform following I.P. injection of IVISbrite™ D-Luciferin bioluminescent substrate to assess the ability of this system to reduce tumor burden in ovarian I.P. cancer models.

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Publication highlights:

This study demonstrates that Revvity's IVIS imaging technology can be used for non-invasive, longitudinal monitoring of tumor responses to immunotherapy via bioluminescent imaging. Further, the IVIS platform can help to elucidate a mechanistic understanding of the tumor response to immunotherapy. Collectively, these results highlight the utility of IVIS imaging for preclinical immuno-oncology research applications.

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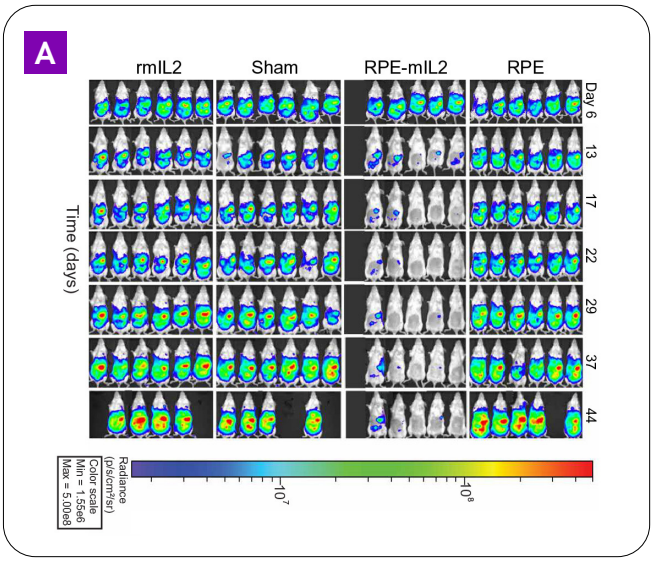
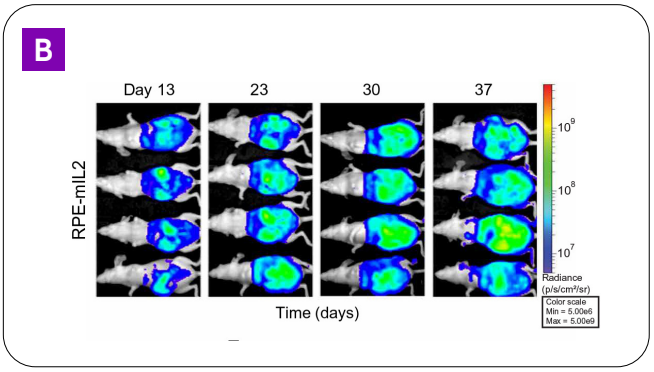
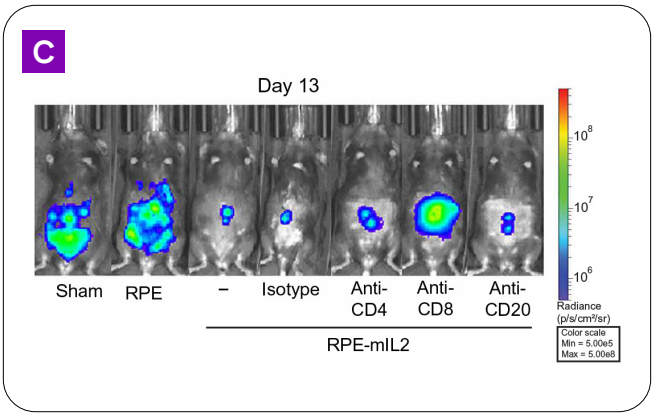


(A) C57BL/6 albino mice were I.P. injected with luciferase expressing ID8-Luc mouse ovarian cancer cells 1 week prior to treatment. Mice were then I.P. injected with RPE (200 capsules containing naïve RPE cells), RPE-mIL2 (200 capsules containing RPE cells that express mIL2), Sham (1mL saline) or rmIL2 (free recombinant IL2 injected at 250,000 IU/day for 3 days). Tumor burden was monitored longitudinally over the course of 44 days via IVIS bioluminescence imaging. Results demonstrate that the tumor burden in mice treated with RPE-mIL2 significantly decreased within 1 week of treatment and remained low for the duration of the study compared to the control groups.



(B) Nu/Nu mice (which lack functional T and B cells) were I.P. injected with ID8-Luc cells 1 week prior to treatment. Mice were then I.P. injected with RPE-mIL2 and assessed for tumor burden over the course of 37 days via IVIS bioluminescence imaging. Results demonstrate that RPE-mIL2 treatment did not result in a decrease in tumor burden and supports the role of the immune response for the antitumor efficacy of RPE-mIL2 treatment



(C) C57BL/6 mice were I.P. injected with ID8-Luc cells 1 week prior to treatment. Mice were then I.P. injected with Sham, RPE, RPE-mIL2, RPE-mIL2 + Isotype (100µg I.P. at day -2, 0, 2 after RPE-mIL2 implantation), RPE-mIL2 + Anti-CD4 (100µg I.P. at day -2, 0, 2 after RPE-mIL2 implantation to deplete helper T cells), RPE-mIL2 + Anti-CD8 (100µg I.P. at day -2, 0, 2 after RPE-mIL2 implantation to deplete cytotoxic T cells), or RPE-mIL2 + Anti-CD20 (250µg I.V. 2 days before RPE-mIL2 implantation to deplete B cells). Results demonstrate that mice treated with RPE-mIL2 that lack functional cytotoxic T cells have similar tumor burden compared to mice that did not receive RPE-mIL2, whereas mice that lack functional helper T cells or B cells exhibit a significant decrease in tumor burden. The results specifically implicate cytotoxic T cells as the main players in the antitumor immune response elicited by IL-2.

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