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HEMATOLOGY/ONCOLOGY

CASE STUDY

Fractionated radiation therapy stimulates anti-tumor immunity mediated by both resident and infiltrating polyclonal T-cell populations when combined with PD1 blockade

Dovedi SJ, et al. *Clinical Cancer Research*. 23(18):5514-5526. 2017.
SEPTEMBER 2017

WHY IMMUNOSEQ?

Mouse TCRB assay allows translational and pre-clinical work

Allows comparison of repertoires and clones, as well as comparison of overlap between multiple samples

Can help determine source of tumor infiltrating lymphocytes (TILs) and mechanism of action of various therapies

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CASE STUDY: Fractionated radiation therapy stimulates anti-tumor immunity mediated by both resident and infiltrating polyclonal T-cell populations when combined with PD1 blockade—*Dovedi SJ, et al. Clinical Cancer Research. 23(18):5514-5526. 2017.*

BACKGROUND

Approximately half of all cancer patients receive radiation therapy (RT), and while local results are good, systemic or abscopal effects on tumors outside of the field of radiation are rare. In addition, recurrence following radiation is common. It has been shown that signaling through the PD-1/PD-L1 pathway in the tumor can limit the effect of RT, but the effect of combination RT and PD-1 therapy is still under investigation. In this paper, the authors use mouse models to investigate local and abscopal effects of RT combined with PD-1 blockade.

AIM

- Compare the efficacy of radiation and PD-1 treatment alone and in combination, in dual-tumor mouse models.
- Evaluate and compare TCRB repertoires in blood, treated tumors, and distant tumors, in the different treatment groups.
- Determine ratio of T cells present in tumor pre-treatment and those infiltrating in response to treatment.

METHODS

BALB/c and C57Bl/6 mice were used and treatment was started 7-10 days post-tumor inoculation, when subcutaneously implanted tumors reached at least 100mm^3. Each group contained at least 5 mice and represent at least two independent experiments.

1. Inoculate mice with tumor cells at two distinct sites.
2. Treatment groups: No treatment, radiation to single tumor while shielding second tumor, anti-PD-1 alone, radiation and anti-PD-1 together.
3. Collect both tumors and blood following treatment → gDNA → **immunoSEQ (mmTCRB)**

RESULTS

- Radiation alone leads to increased TIL density and transient local tumor control, but not systemic control.
- The addition of PD-1 in combination with RT, leads to a local and distant TIL density increase and distant tumor control in over 70% of mice.
- Radiation alone resulted in an increased TCRB overlap between blood and treated tumor, and this was further increased and extended to the distant, untreated tumor with the addition of PD-1.

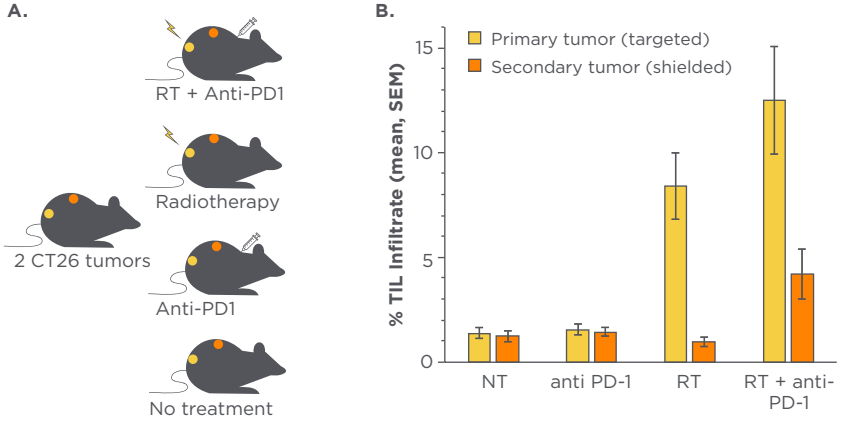

Figure 1. A) overview of treatment groups. B) TIL density of targeted tumor (yellow) and shielded tumor (orange) post treatment. Radiation in combination with anti-PD-1 treatment results in increased TIL density in both the targeted and shielded tumors.

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CONCLUSIONS

- Radiation alone can result in T-cell expansion and infiltration at the treated site.
- Concurrent addition of anti-PD-1 enhances this effect and leads to similar increases in T-cell infiltration at distant sites suggesting a systemic response.
- Both resident TILs and T cells infiltrating from blood contribute to anti-tumor effects.

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