

Immune profiling of a cisplatin-eluting polymer with radiation

Alice C. Yu, MD¹; Yazeed Alhiyari, PhD²; Lauran Evans, MD, MPH¹; Yang Liu, PhD³; Supriya Atta, PhD³; Tuan Vo-Dinh, PhD³; Maie St. John, MD²

¹ Department of Otolaryngology–Head and Neck Surgery, UCLA • ² Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins • ³ Department of Biomedical Engineering, Duke University

BACKGROUND

- Systemic toxicity of chemotherapy is a limiting factor in treatment of locally advanced or recurrent HNSCC.
 - Prior studies of a cisplatin-eluting polymer demonstrated efficacy at halting tumor growth and radiosensitization.
 - Gold nanostars (GNS) have been demonstrated to concentrate the effects of radiation.
- Study question**
- Does addition of GNS to the cisplatin-eluting polymer potentiate radiosensitization and modify the local tumor immune microenvironment?

STUDY AIMS

Specific Aim 1

Assess efficacy of the GNS-loaded, cisplatin-eluting polymer with radiation therapy in an in vivo mouse model.

Specific Aim 2

Describe effects of the cisplatin-eluting polymer on the tumor immune microenvironment (TIME) via immunofluorescence of harvested tumors.

METHODS

In vivo model

- Mouse SCC line SCCVII/SF injected at 600K cells/0.05 mL into flanks of C3H/HeJ mice.
- Tumors grown to ~1 × 1 × 1 cm, then debulked to ~0.5 × 0.5 × 0.5 cm.
- Radiation delivered on POD1–4; tumors measured daily.
- Animals sacrificed for humane endpoints or at 6 weeks (ongoing).

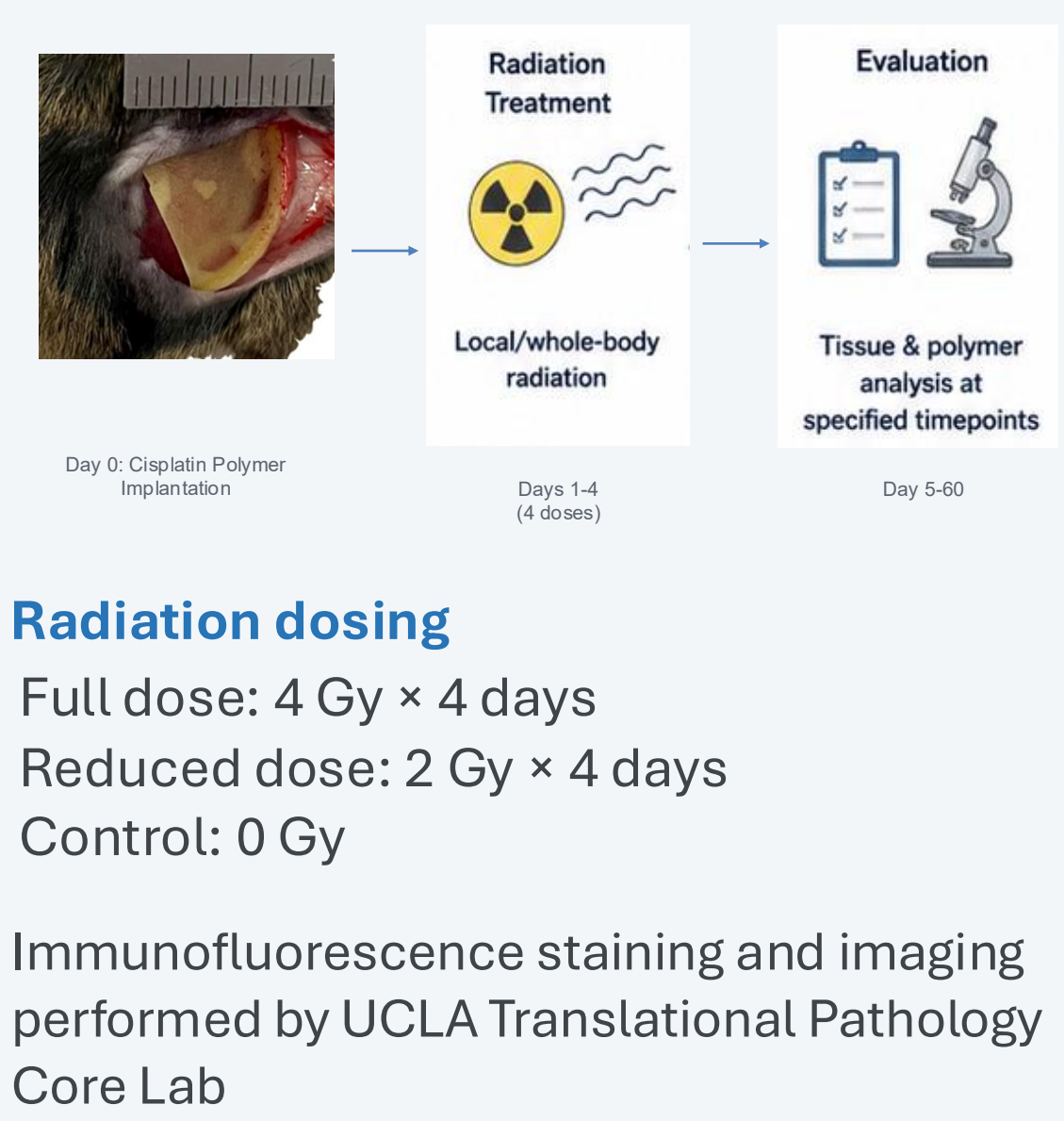
Treatment groups

XRT Doses:	4Gy	2Gy	0Gy
ctrl	2	4	5
GNS	2	3	2
cis	4	8	2
GNS/cis	6	8	3
			49

Immune profiling

- Control and GNS/cisplatin samples with and without 4 Gy radiation were collected.
- Tumor adjacent to the polymer and tumor not in contact with the polymer were analyzed.
- CD4, CD8, and PD-L1 immunofluorescence; integrated density quantified in ImageJ.

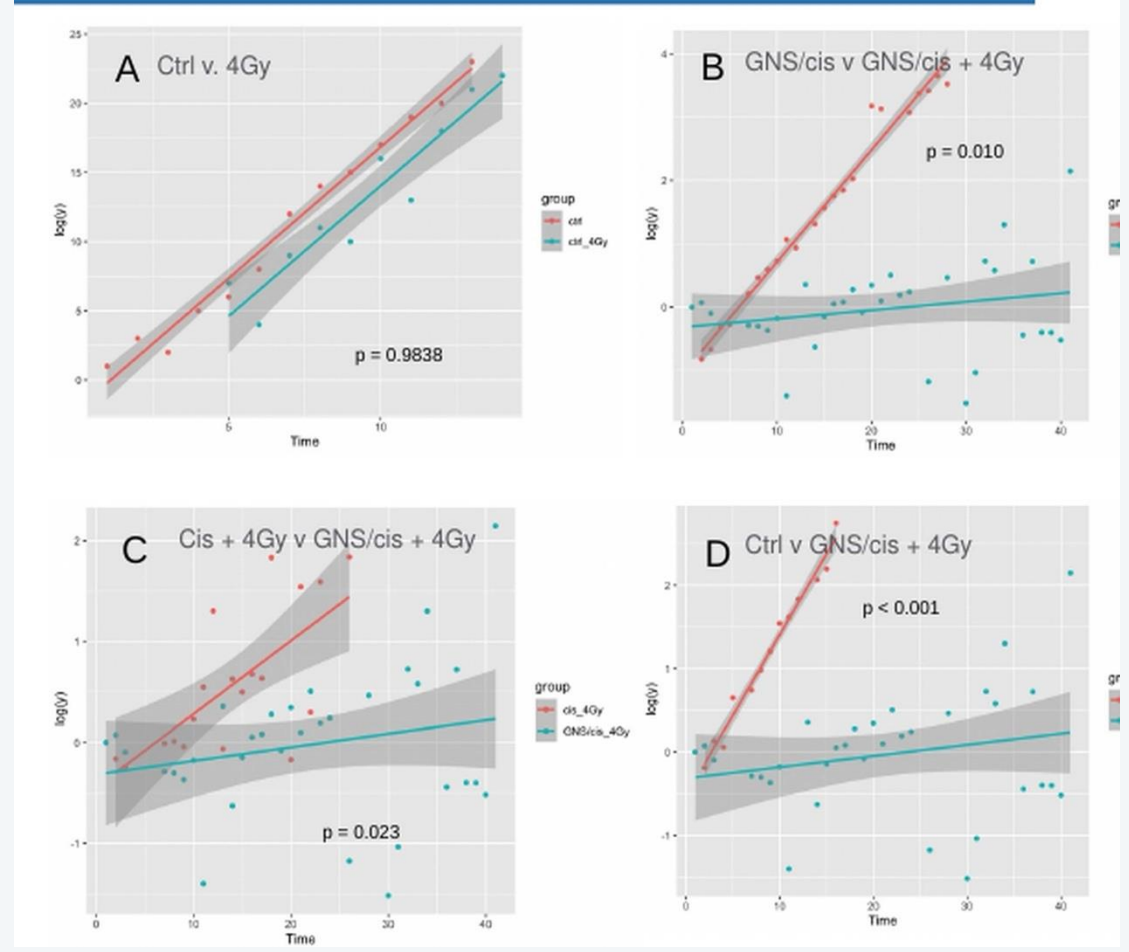
EXPERIMENTAL WORKFLOW



RESULTS: RADIOSENSITIZATION

Full-dose radiation

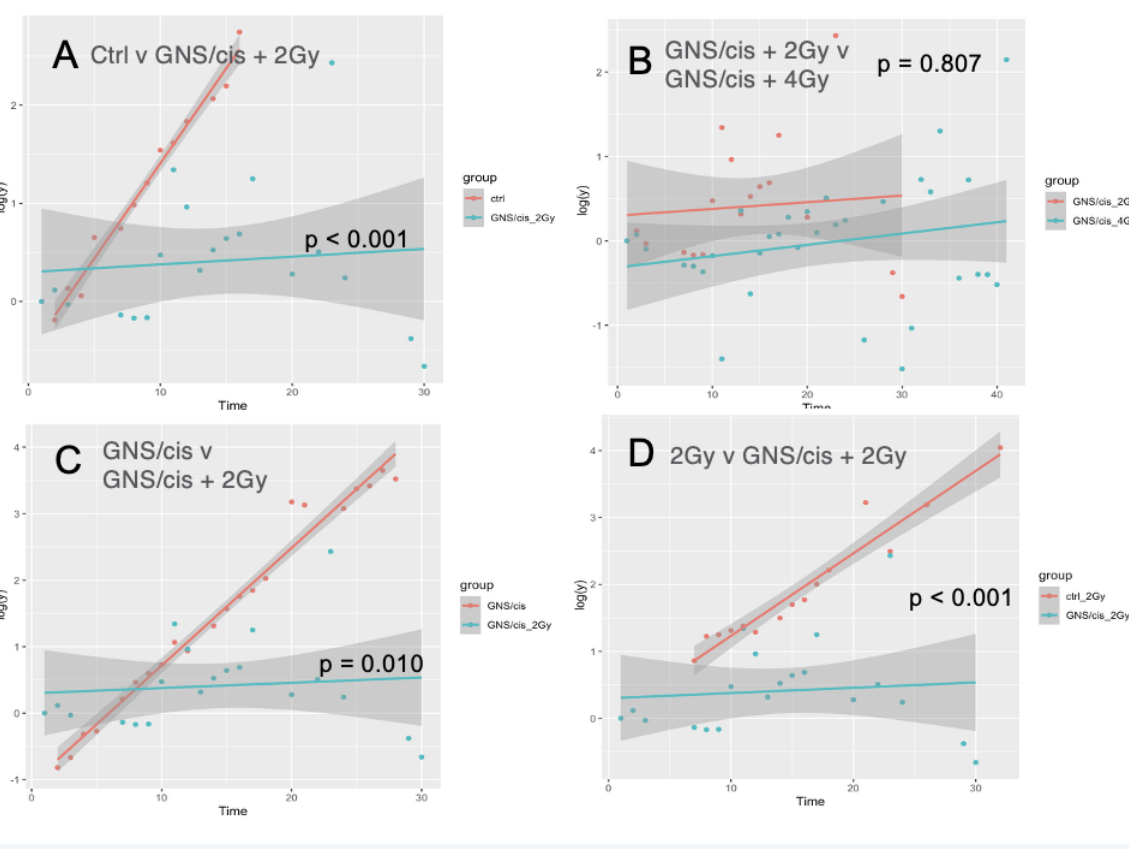
- 4 Gy alone was ineffective.
- Adding 4 Gy to GNS/cisplatin improved survival.
- GNS improved performance of cisplatin/4 Gy.



A–D: growth-curve comparisons; p = 0.9838, 0.010, 0.023, and <0.001.

RESULTS: REDUCED-DOSE RADIATION

- GNS/cisplatin with reduced radiation was better than control.
- Outcomes were comparable to GNS/cisplatin with full-dose radiation.
- Adding 2 Gy to GNS/cisplatin improved outcomes.

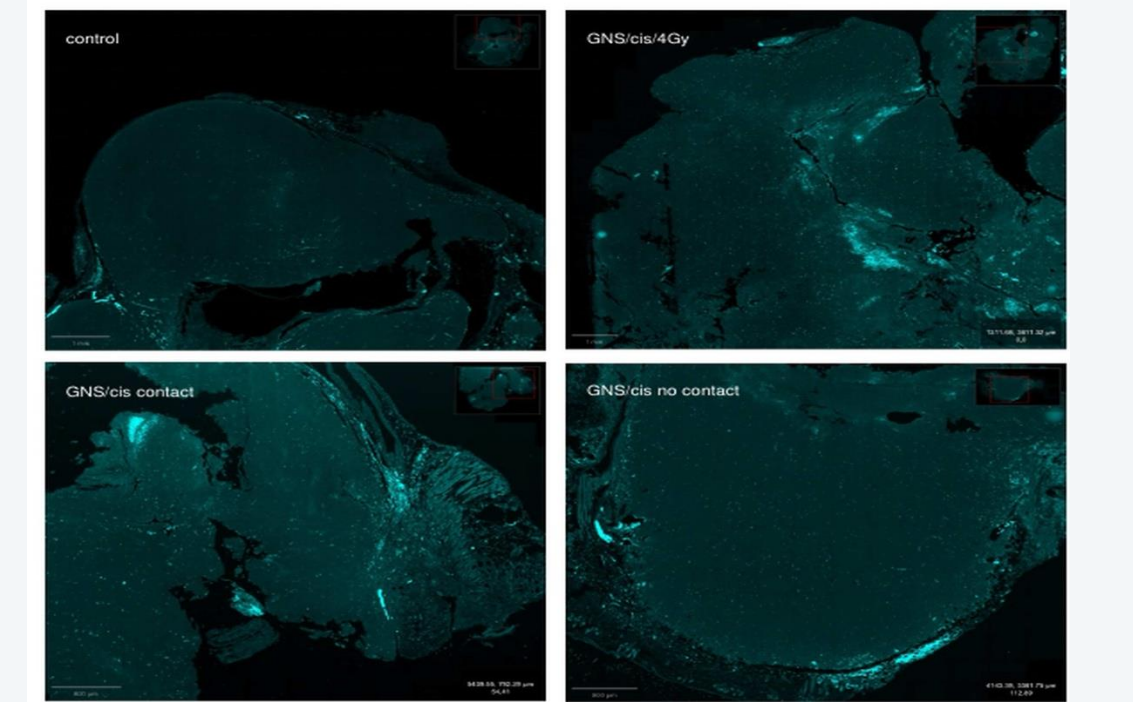


A–D: p <0.001, 0.807, 0.010, and <0.001.

RESULTS: IMMUNE PROFILING

CD4 immunofluorescence

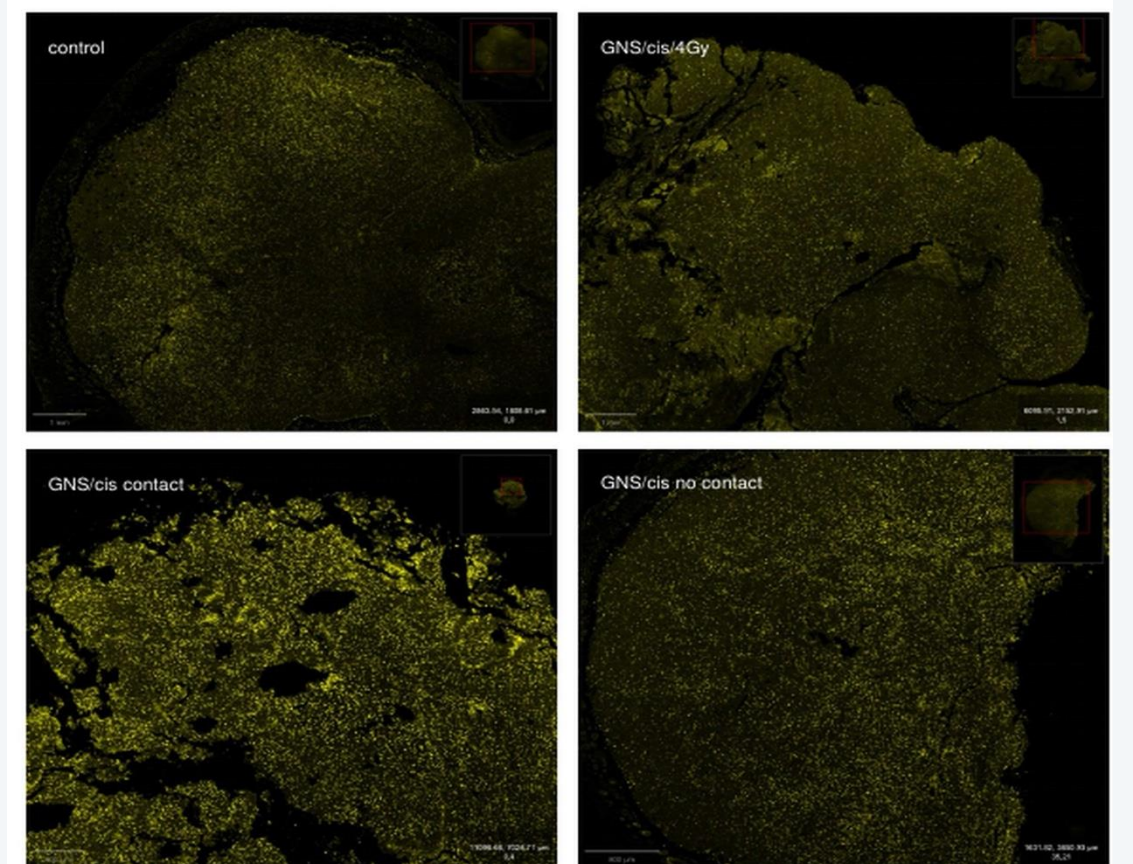
Treatment with GNS/cisplatin induced increased CD4 penetration of the tumor; areas without polymer contact appeared similar to control.



Direct polymer contact appeared important to induce the local immune upregulatory effect.

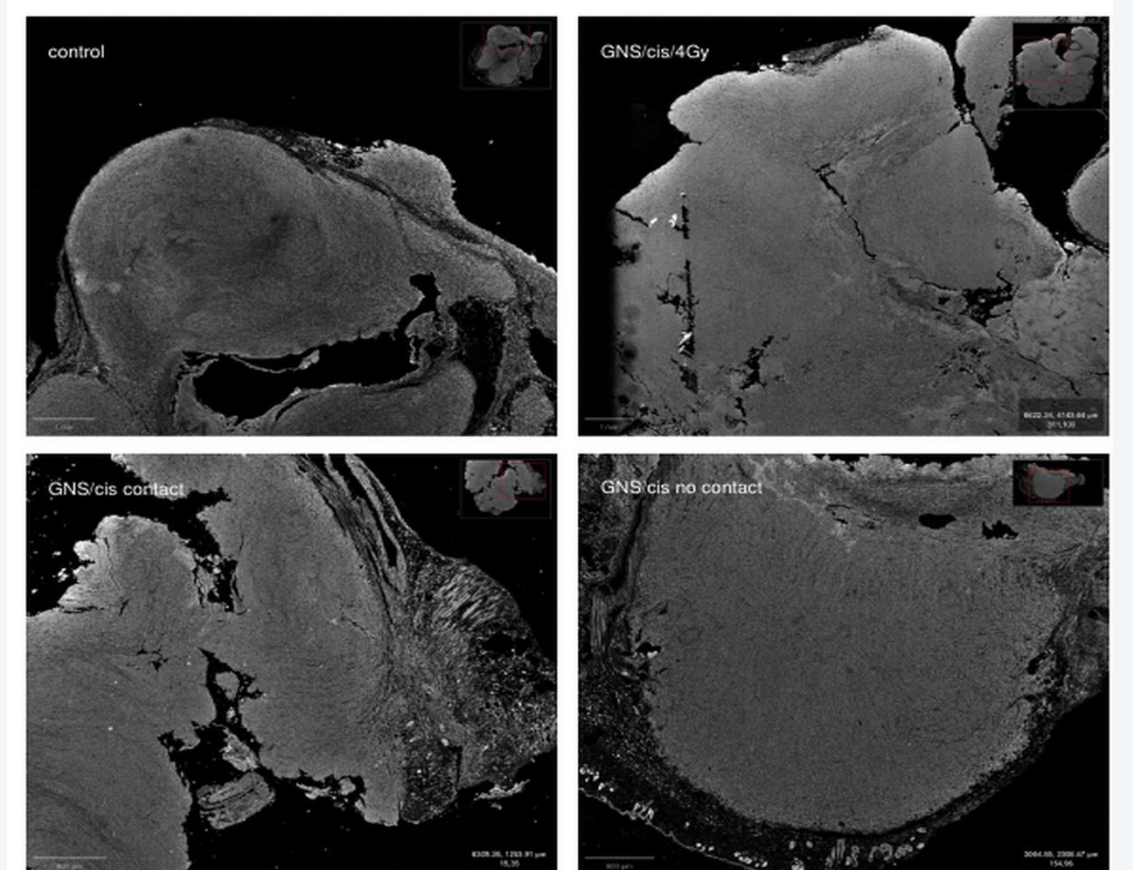
RESULTS: CD8 IF

CD8 expression increased in tumor samples in contact with the polymer, with gross differences between contact and non-contact regions.

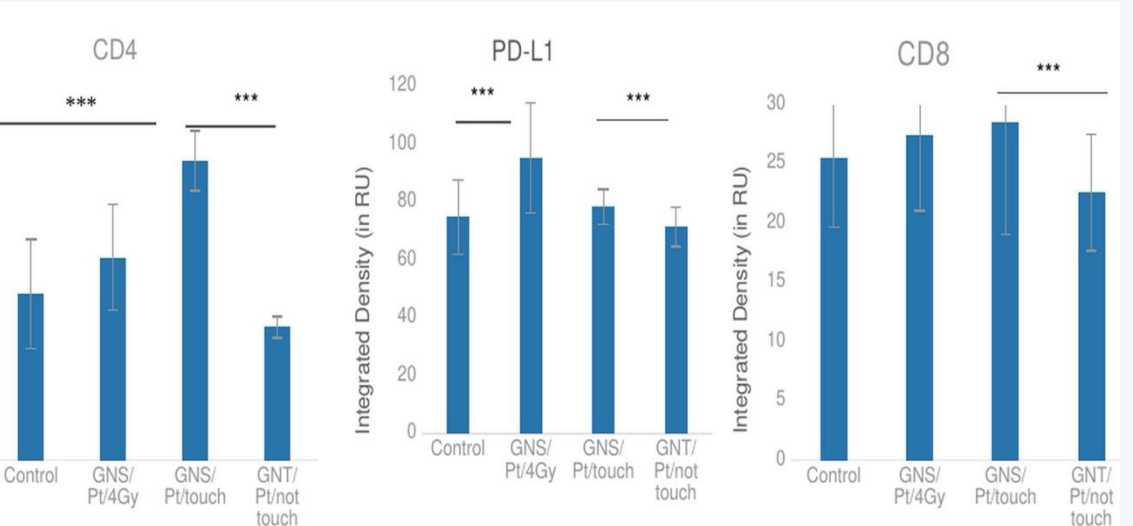


RESULTS: PD-L1 IF

PD-L1 expression differed significantly in treated cells versus control; uncontacted tumor appeared more similar to control.



RESULTS: IHC QUANTIFICATION



Direct contact with the polymer resulted in increased CD4, PD-L1, and CD8 expression.

CONCLUSIONS & NEXT STEPS

- Topical therapies may upregulate immune function in the tumor immune microenvironment and sensitize the local tumor bed to radiation.
- GNS/cisplatin showed similar responses with reduced-dose versus full-dose radiation
- Next steps: trial checkpoint inhibition in combination with the polymer to see whether sensitivity to checkpoint inhibitors can be induced

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