

# Combining radiotherapy with immunoadjuvant gold nanoparticles to enhance the abscopal effect in pancreatic cancer model.

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## INTRODUCTION

Pancreatic cancer is one of the leading causes of cancer deaths in the United States. So far, only 7% of pancreatic cancer patients have a survival rate of 5 years due to metastasis. It has been stated that using radiotherapy (RT) to treat a primary tumor can lead to rare metastatic regression of untreated secondary tumors, the so called **"abscopal effect"**.

Studies on the role of systematic administration of immune adjuvants (IA) in the enhancement of the abscopal effect have begun to pave the way, but more work is required to find the appropriate dose of radiation and immunoadjuvants to make this phenomenon a reliable treatment option for cancer patients.

Cluster of differentiation 40 (CD40) is a TNF protein receptor expressed on antigen presenting cells (APCs) such as dendritic cells and macrophages that stimulate inflammatory and immune responses. The interaction of CD40 with CD40Ligand enables the activation of T- cells as well as the activation of an adaptive immune response. Gold Nanoparticles (GNPs) are radio sensitizing agents used to amplify radiation dose by increasing the dose deposited locally around the GNPs via the photoelectric effect.

## AIM

The purpose of this study is to examine the combination effect of GNP, IA, and RT on a pancreatic tumor mouse model to enhance the abscopal effect.

## METHOD

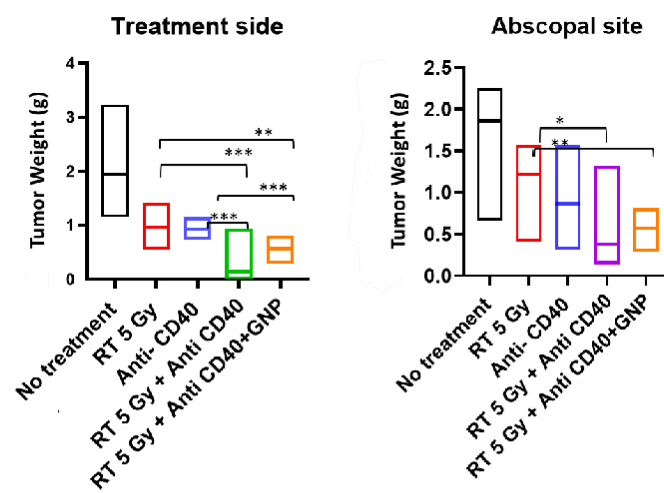
- The mice in this study were C57/BL6 injected with pancreatic cancer in syngeneic murine models from Taconic.
- Both flanks were injected with Panc-02 cell line and one was treated after 2 weeks once tumors were treatable size.
- GNP (0.5mg/kg), IA (20µg, Anti-CD 40 antibody) and RT (5 Gy) was used to treat one tumor.
- The second tumor was monitored for the abscopal effect.
- Cohorts were treated two weeks after tumor inoculation with a single fractionated dose of 5Gy (image guided RT-IGRT), 20ug of Anti-CD40 and 1mg/ml of GNP.
- A Small Animal Radiation and Research Platform (SARRP) was used on the initial date of treatment.
- Mice were euthanized 6 weeks post treatment for tumor collection



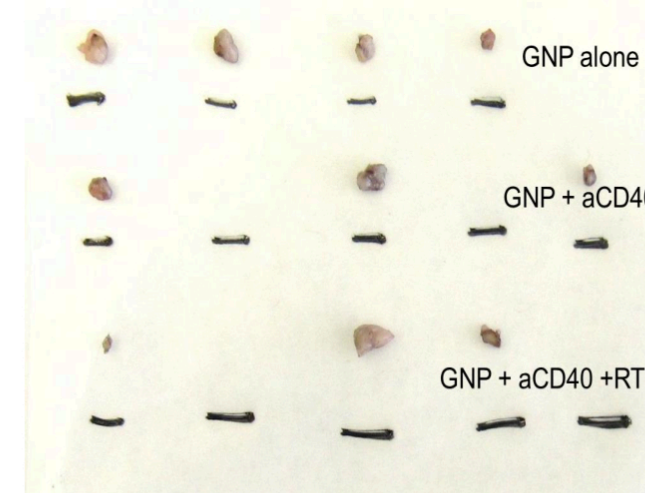
**Figure 1:** Graph of 5 Gy radiation dose administered to left tumor and surrounding tumor tissue area.

## RESULTS

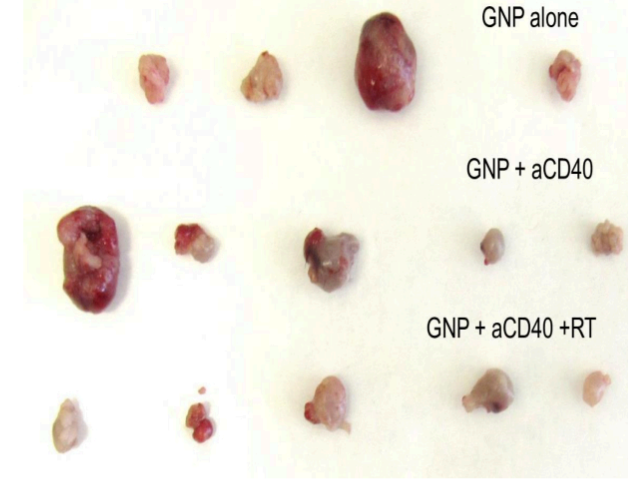
- There is a significant difference between each cohort to control.
- The tumor weight for 5Gy alone was less than the control and Anti-CD-40 alone was slightly smaller than 5Gy radiation.
- Adding anti-CD40 showed the tumor weight decreased at a higher rate compared to the 5Gy radiation alone and Anti-CD40 alone.
- A combination of GNP + 5Gy RT + Anti-CD40 showed the largest decrease in tumor weight compared to the other treatments



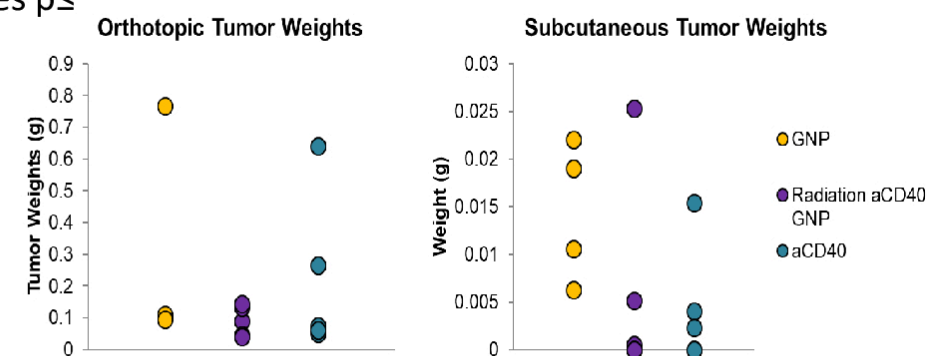
**Figure 2:**Box plot of tumor weight: Indication of tumor weight in grams for each cohorts for the treated left side and untreated (abscopal) right side. \* indicates  $p \leq 0.05$ , \*\* indicates  $p \leq 0.01$ , \*\*\* indicates  $p \leq 0.001$



**Figure 3:** Tumor sizes of subcutaneous tumors (Intertumoral injection).

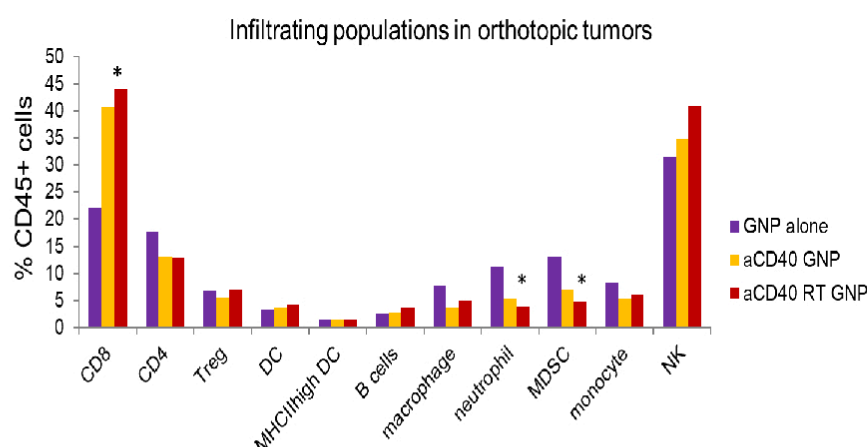


**Figure 4:** Tumor sizes of orthotopic (untreated) tumors



**Figure 5:**Tumor weight of orthotopic (untreated) tumor volume

**Figure 6:** Tumor weight of subcutaneous(treated) tumor



Increase in CD8+ T cells, decrease in most myeloid cell types, particularly neutrophils and MDSCs. No apparent phenotypic change in DC populations (MHCII, CD11b, CD8) either in tumor or in draining LN from irradiated site. CD40 and CD40+RT groups appear similar.

## CONCLUSIONS

- The combination of 5Gy radiation + Anti-CD40 and GNP is an effective treatment.

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