

Remodeling Tumor Immune Microenvironment by Using Polymer-Lipid-Manganese Dioxide Nanoparticles with Radiation Therapy to Boost Immune Response of Castration-Resistant Prostate Cancer

Presented by: Abdulmottaleb Zetrini

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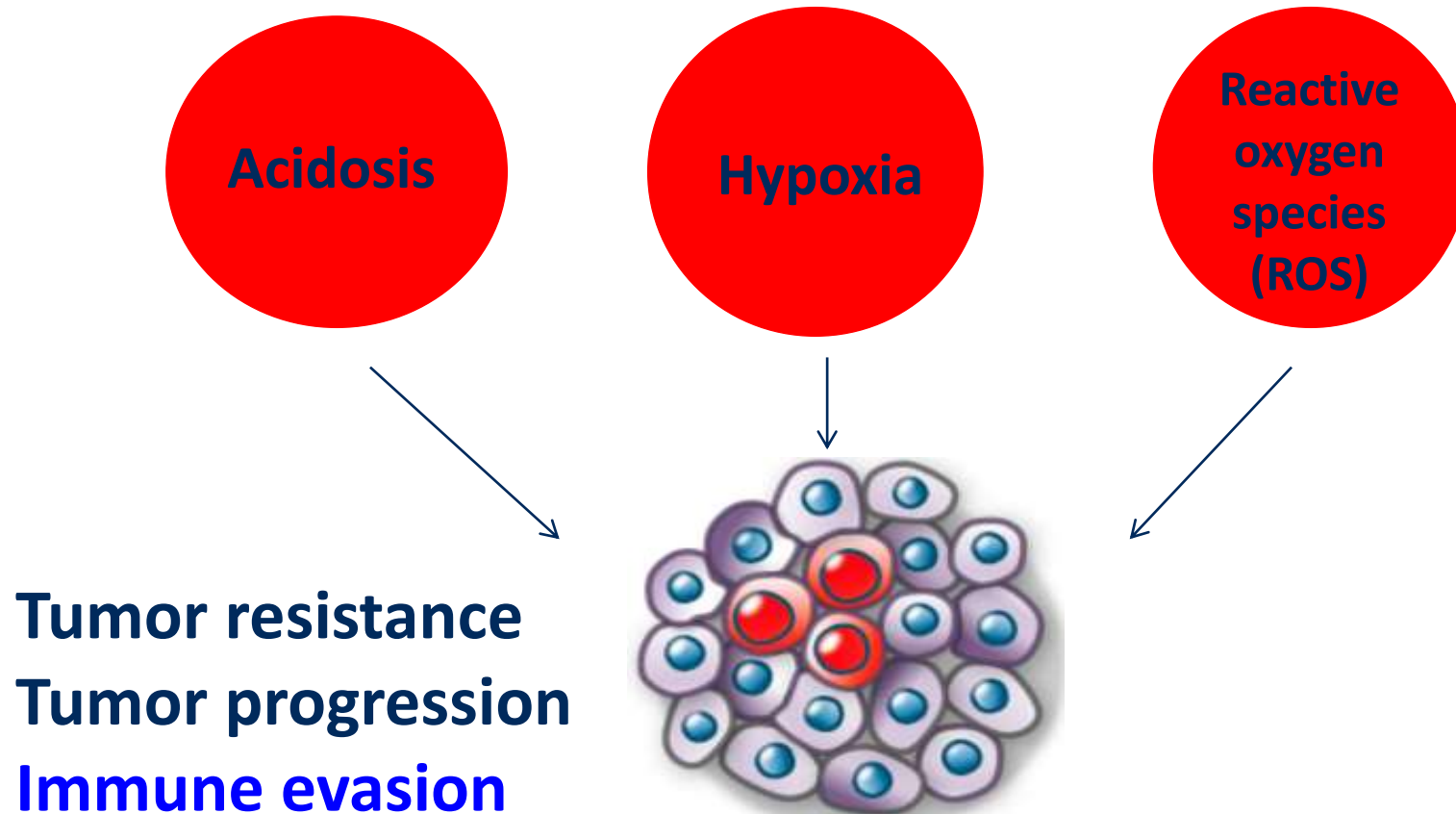
Prostate cancer statistics and treatment

- ◆ the second most commonly occurring cancer in men
- ◆ the fifth leading cause of death worldwide
- ◆ In 2022, 1.3 million new cases of prostate cancer worldwide

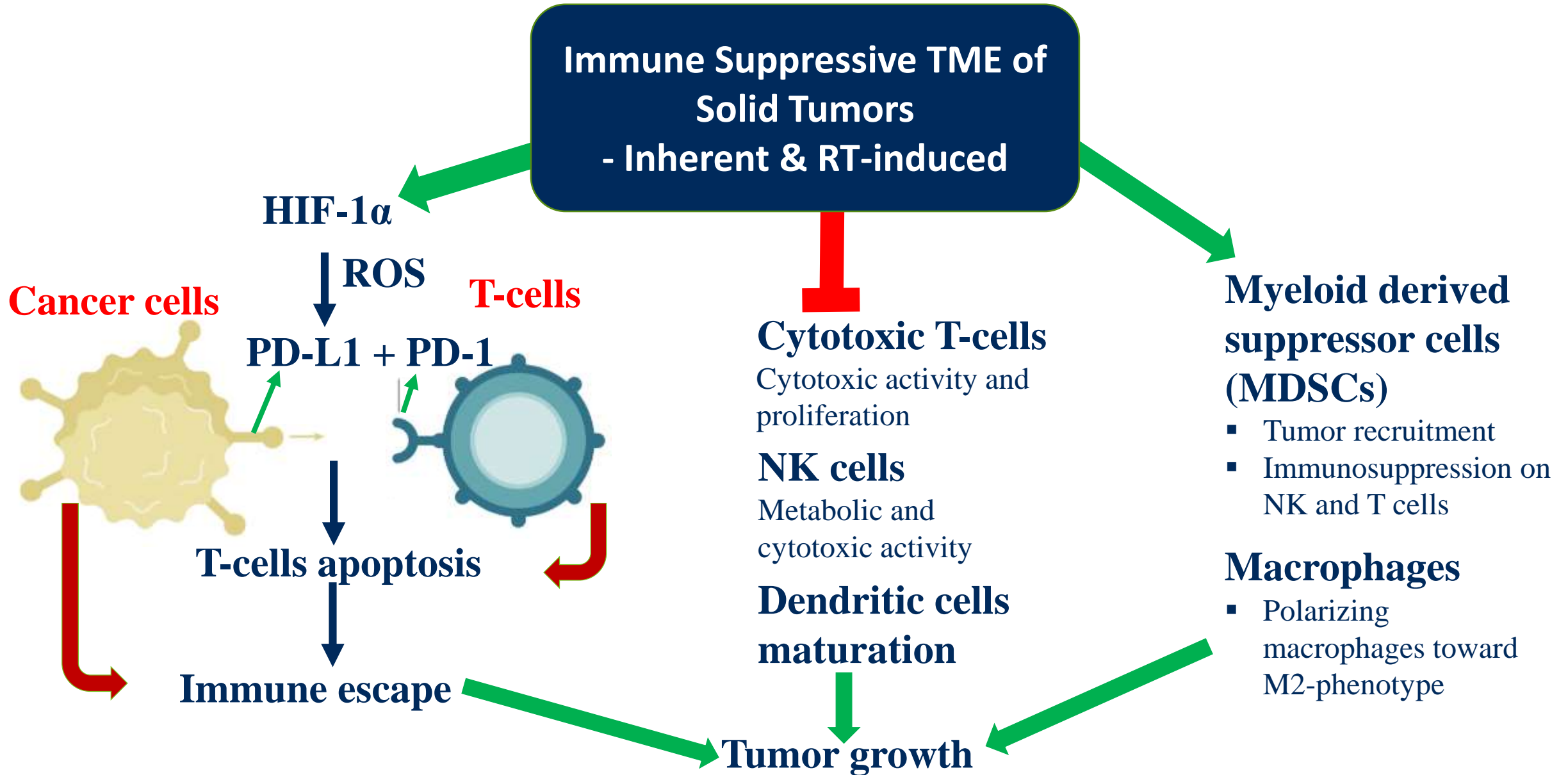


Rawla, P. (2023). Epidemiology of prostate cancer. World journal of oncology, 10(2), 63.

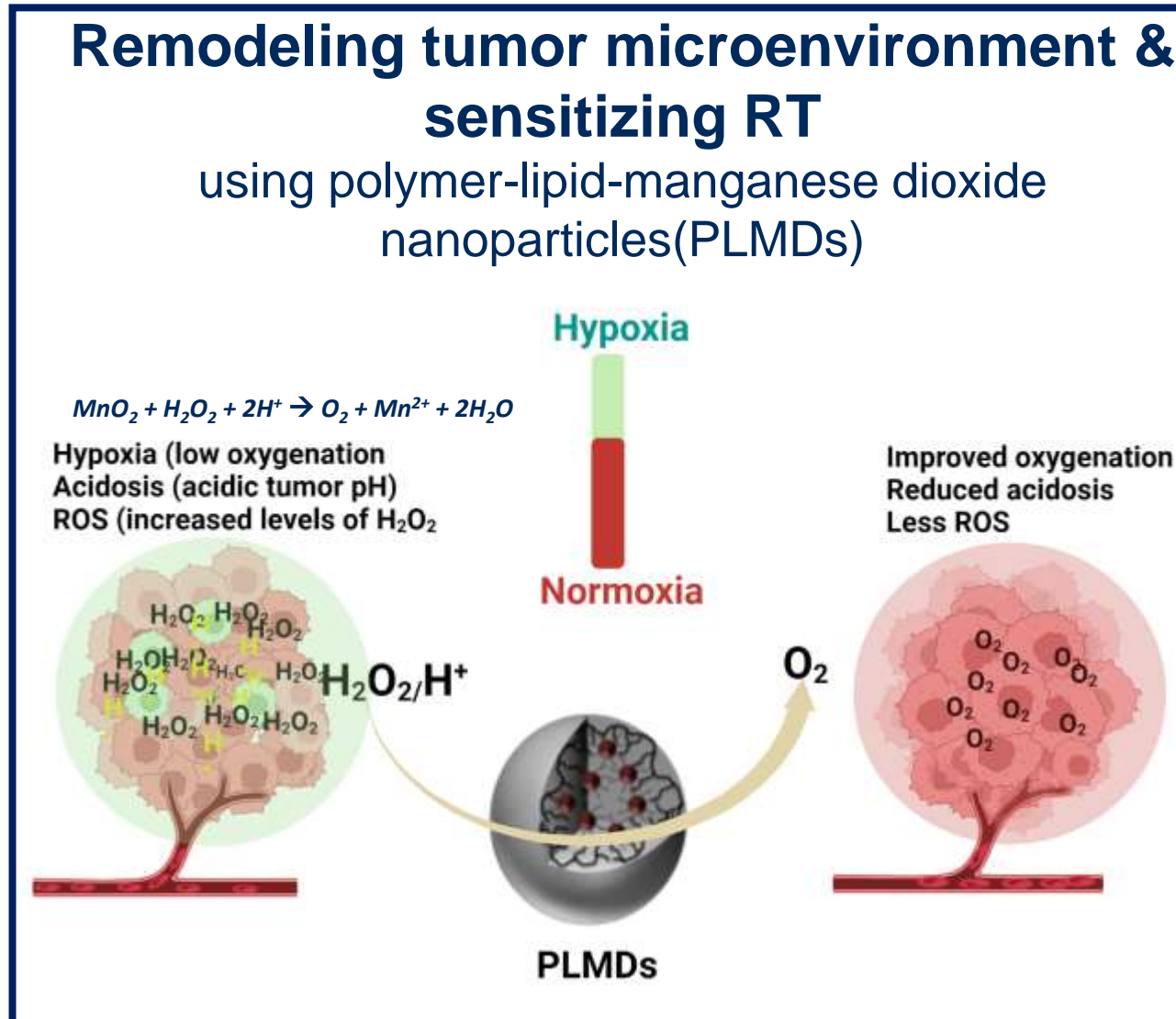
Main features of tumor microenvironment



Role of tumor microenvironment in tumor growth



Our approaches to enhancing RT efficacy in solid tumors



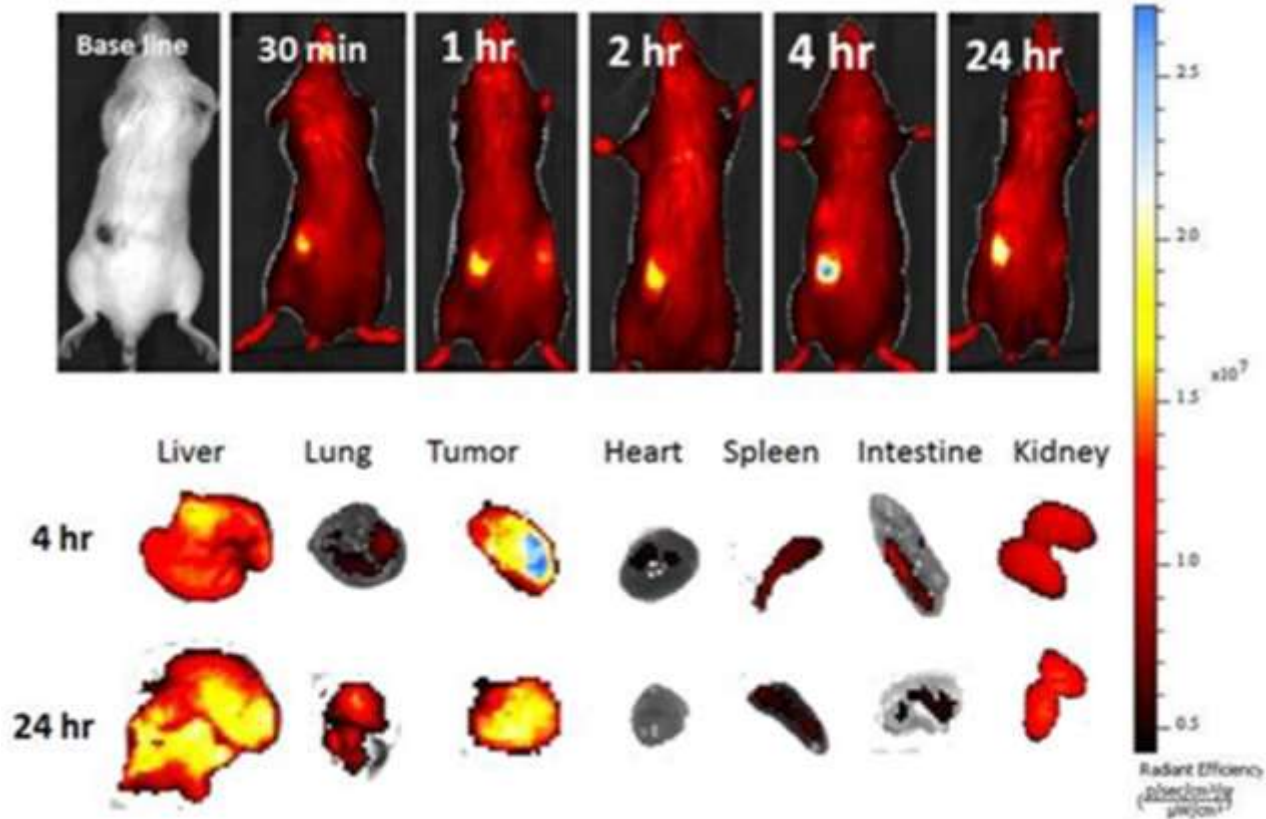
Lip, H., Amini, M. A., Zetrini, A., Cai, P., Abbasi, A. Z., Bristow, R. G., ... & Wu, X. Y. (2022). Redox-responsive nanoparticles enhance radiation therapy by altering multifaceted radio-resistance mechanisms in human castration-resistant prostate cancer cells and xenografts. *Radiotherapy and Oncology*, 170, 213-223.

Hypotheses

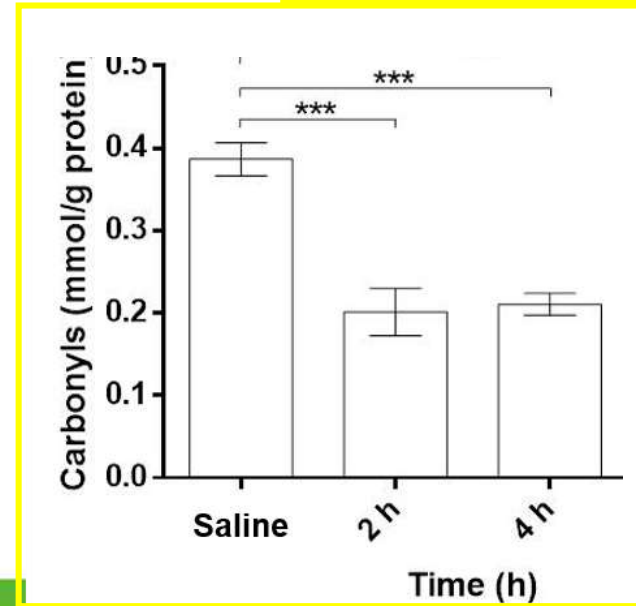
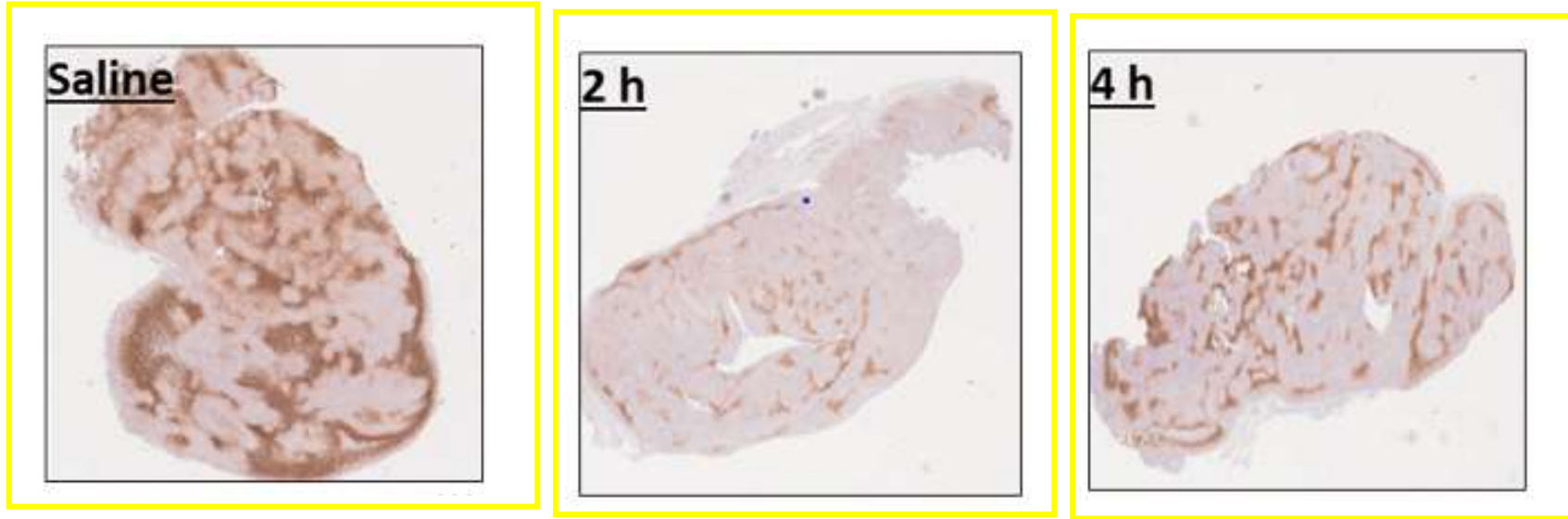
We hypothesize that TME modulation using PLMDs could:

- Enhance radiation induced DNA damage response
- Improve immune response and enhance the efficacy of RT in castration resistant prostate cancer

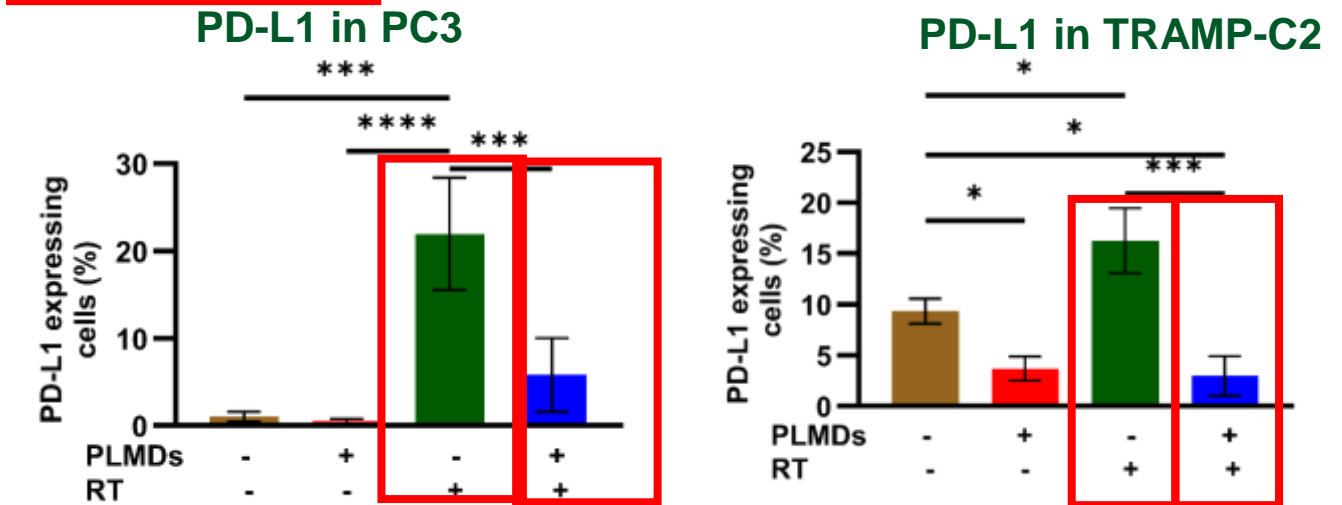
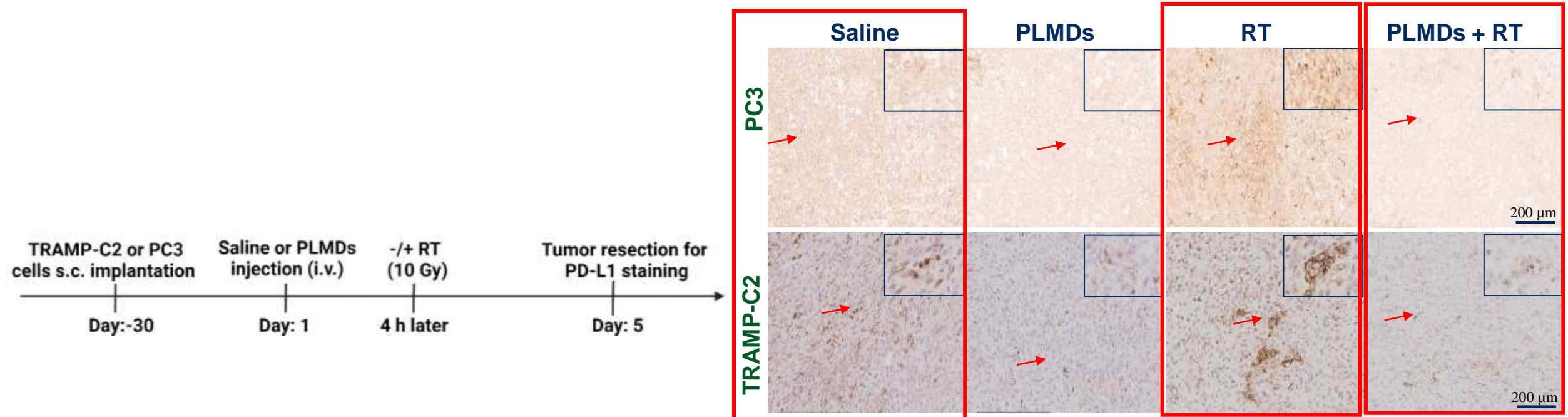
In vivo biodistribution of PLMD NPs.



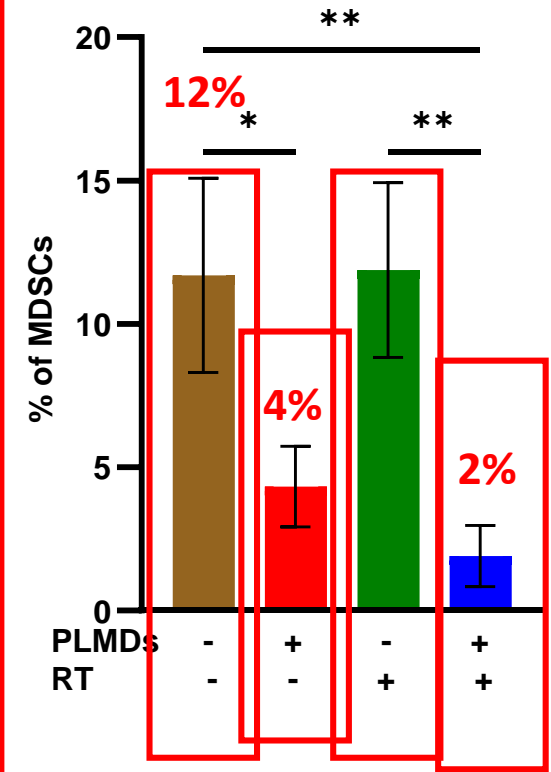
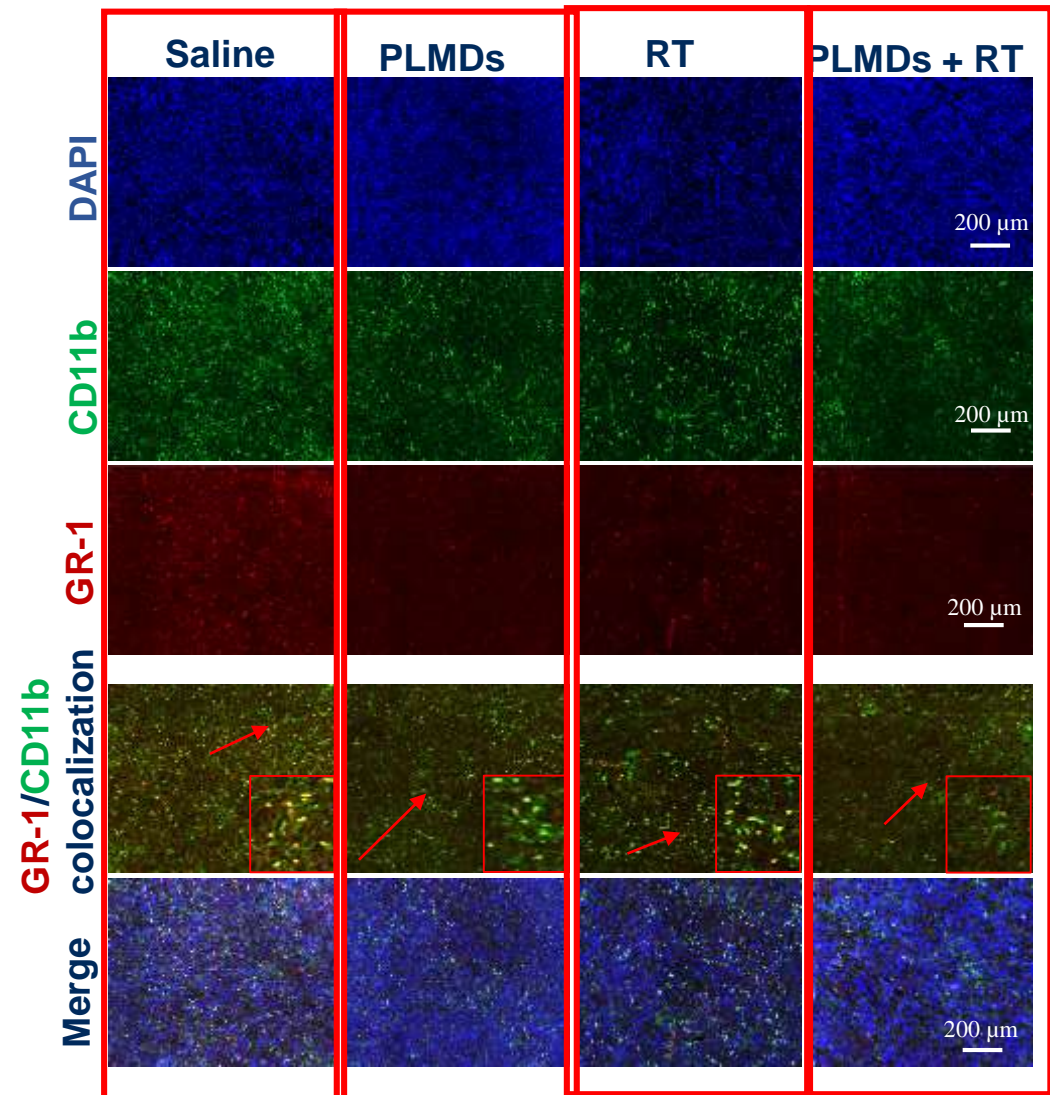
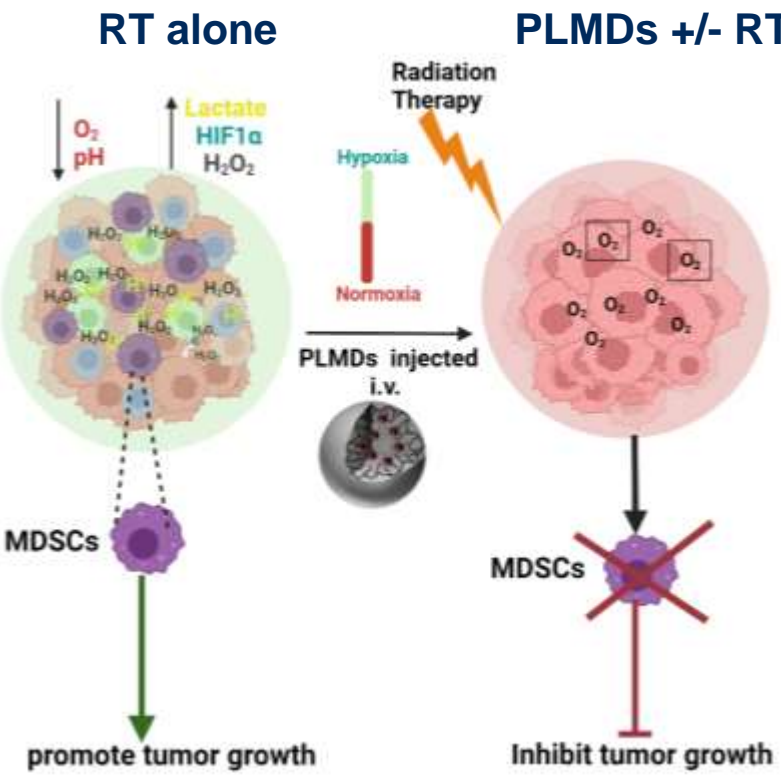
PLMDs reduced hypoxia and oxidative stress in PC3 tumor-bearing mice



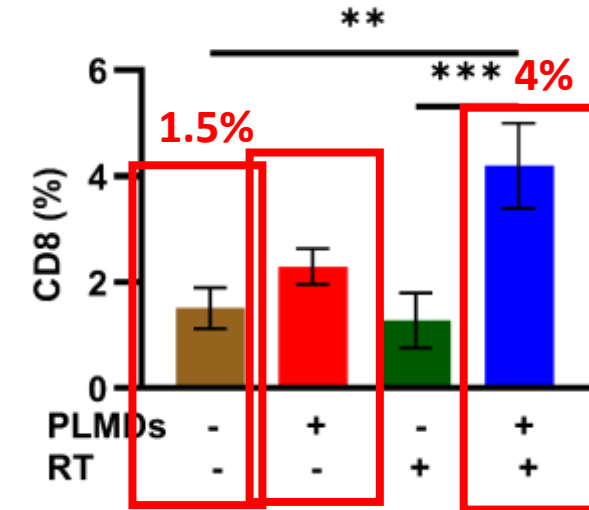
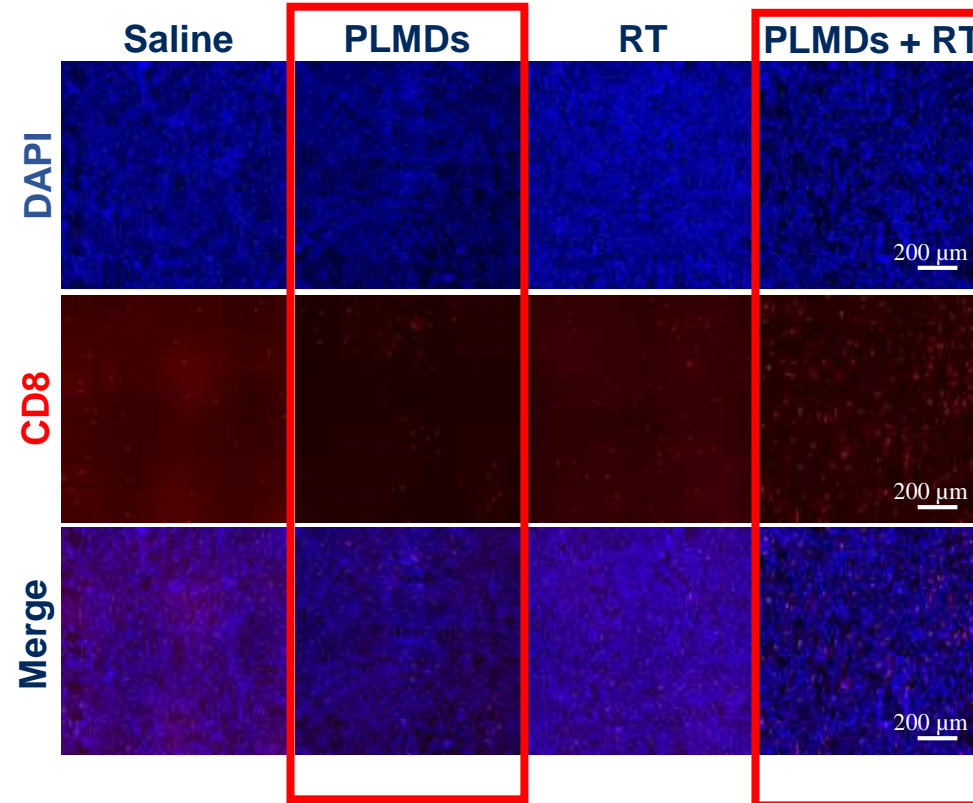
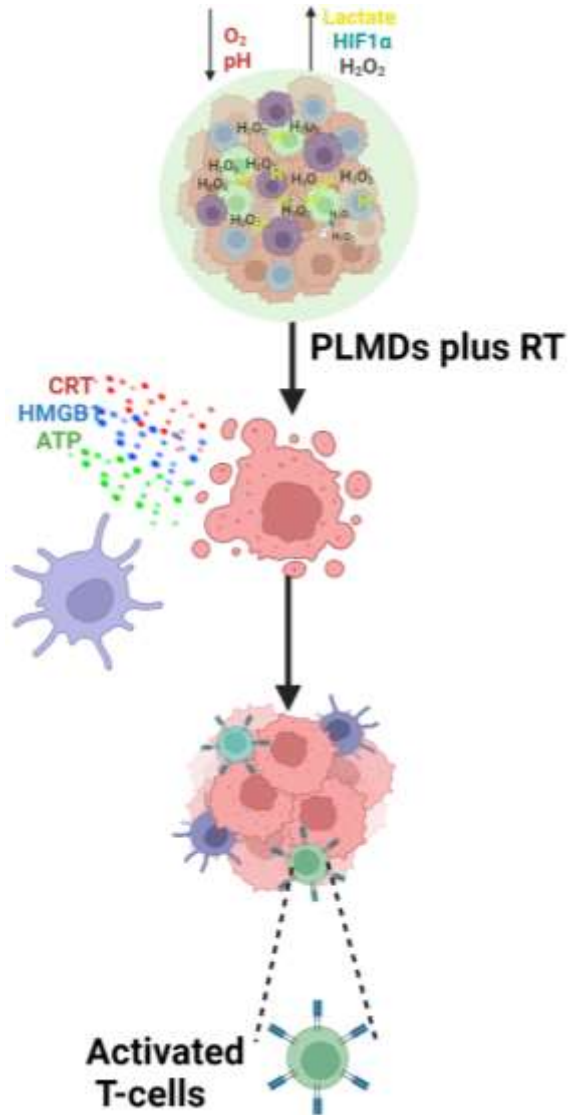
Hypoxia downregulation by PLMDs reduced the expression of PD-L1 in PC3 and TRAMP-C2 tumors *in vivo*



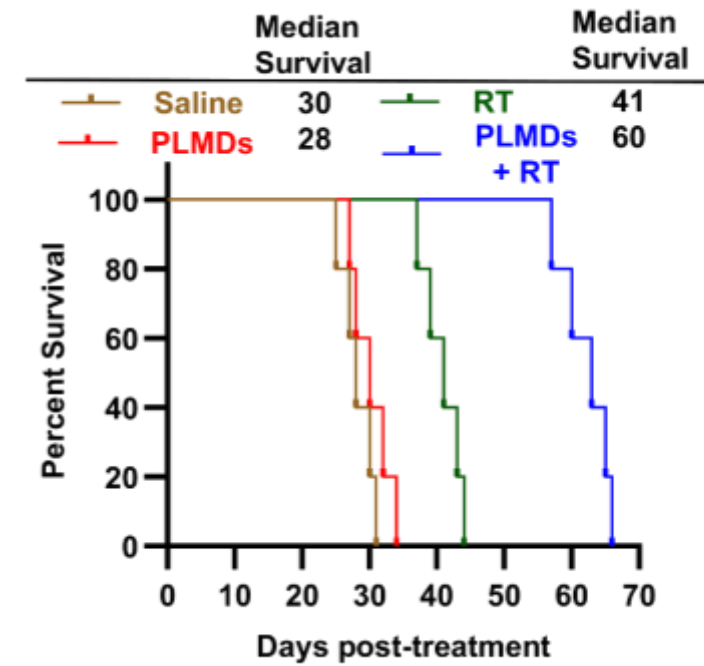
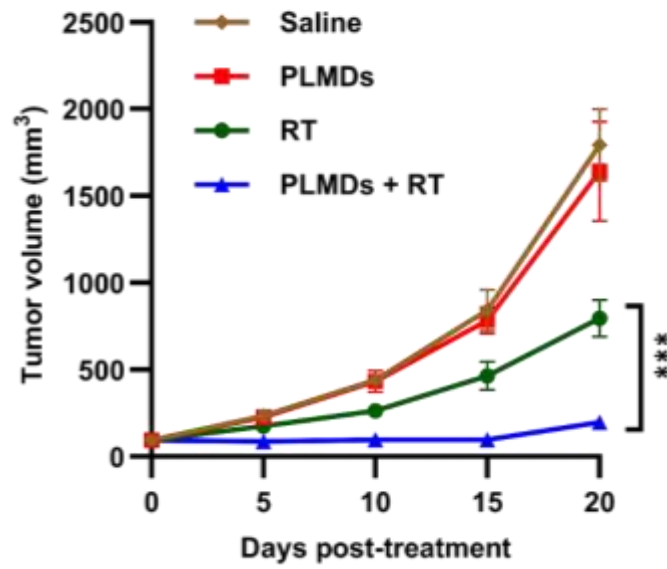
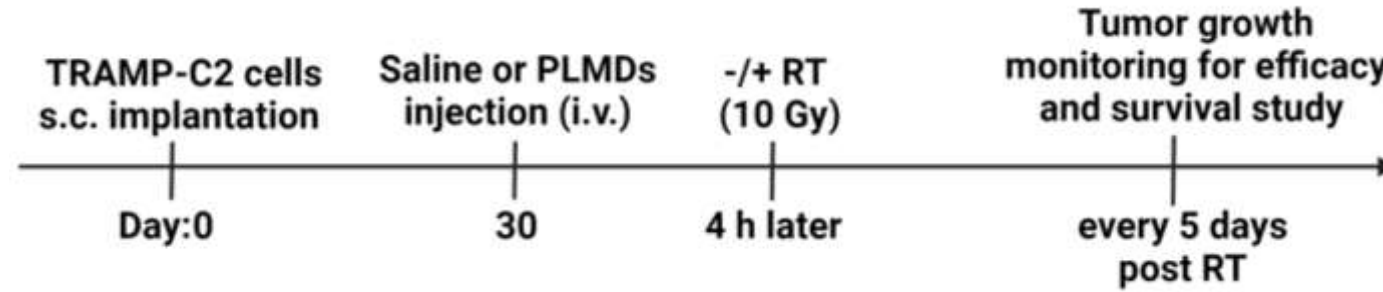
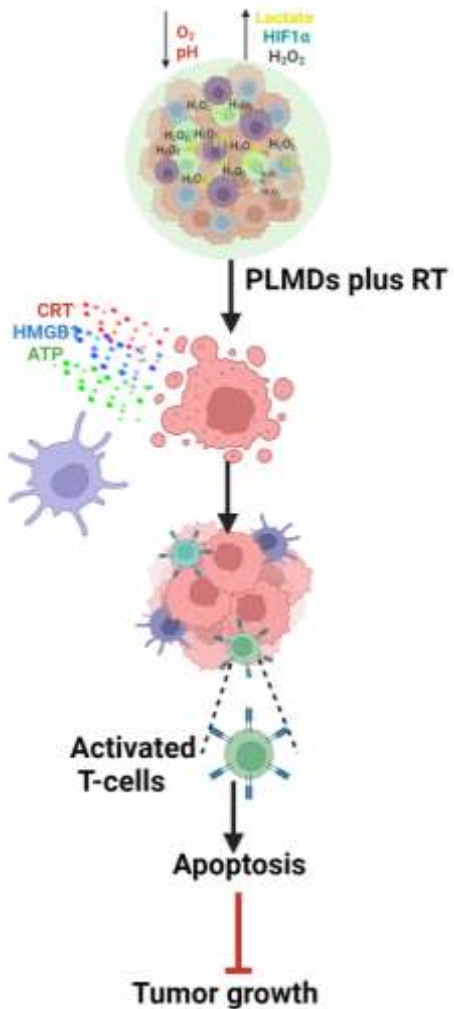
TME Modulating PLMDs reduced while RT increased the recruitment of MDSCs into tumors



PLMDs plus RT enhanced the infiltration of antitumor T- cells



PLMDs plus RT inhibited tumor growth and prolonged median survival of TRAMP-C2 tumor-bearing mice



Summary

- 1- i.v injection of PLMDs reoxygenate the tumor and ROS
- 2-i.v injection of PLMDs results in PD-L1 downregulation i.v
- 3-injection of PLMDs reduced MDSCs while increased infiltration of CTL in tumors, leading to apoptosis



My supervisor:

Prof. Xiao Yu (Shirley) Wu

My project manager:

Dr. Azhar Abbasi

Committee members:

Prof. Peter G. Wells

Prof. Peter Chung

Previous committee

member:

Prof. Andrew M. Rauth

Examiners:

Prof. Michael Weinfeld

Prof. Michael Milosevic

Collaborator:

Prof. Jeffry

Henderson

Wu Lab members: Dr. HoYin Lip, Dr. Chanson He.

Dr. Ibrahim Alradwan. Dr. Taksim Ahmed.



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Thank you



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Faculty of Pharmacy



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