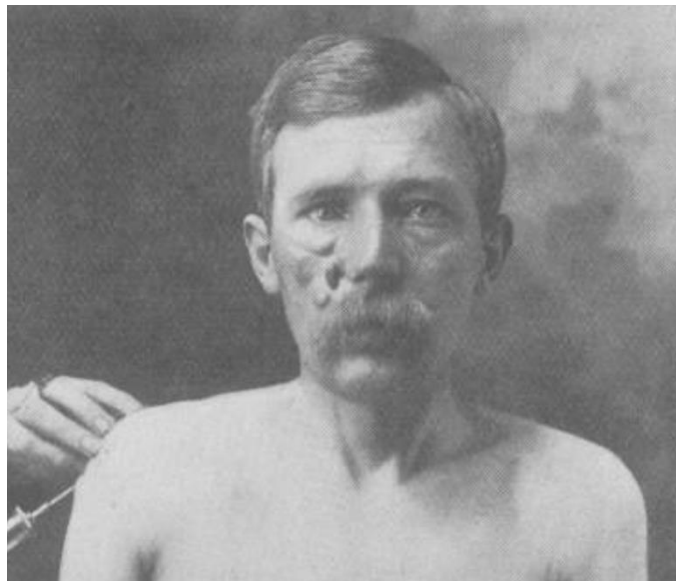
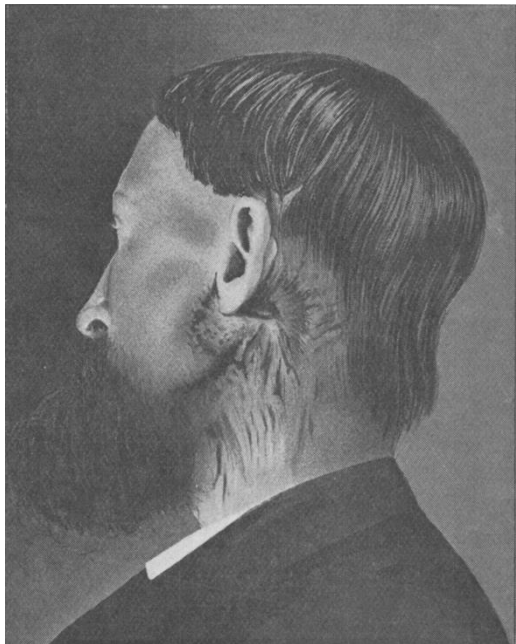


Timely administration of drug combination improves chemoimmunotherapy of an immune-cold tumor

Yanying He

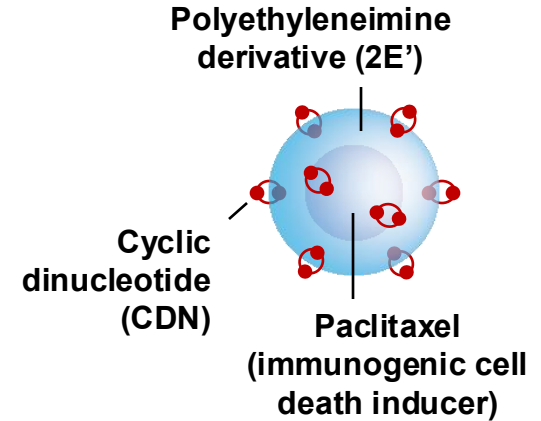
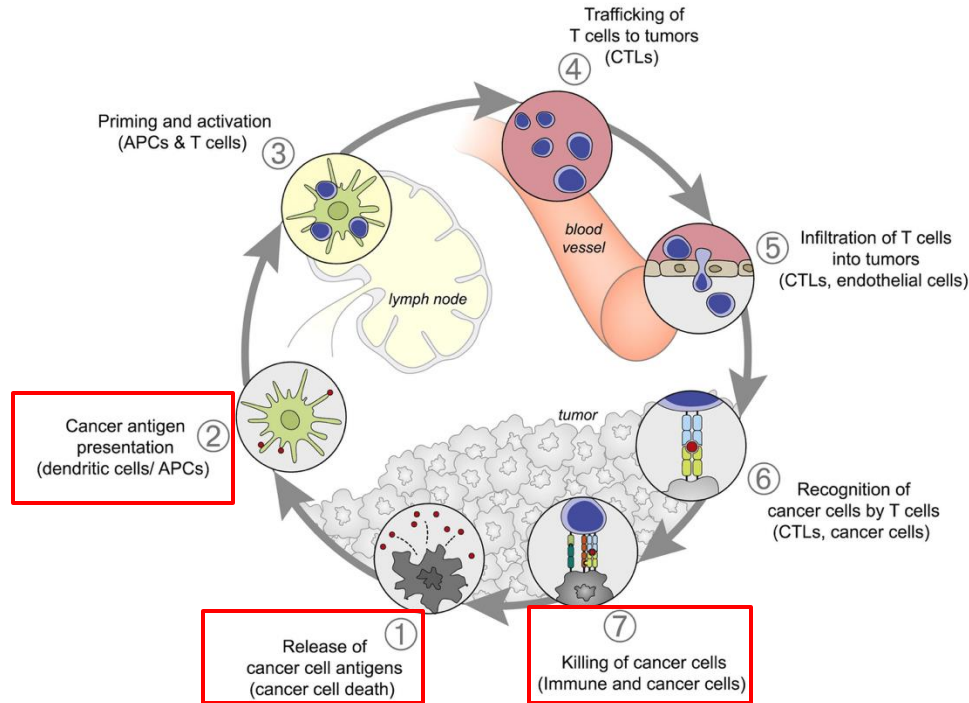
Industrial and Molecular Pharmaceutics
Purdue University

Cancer immunotherapy started 100 years ago



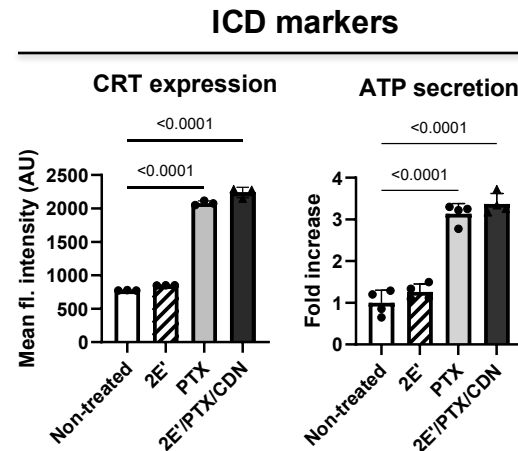
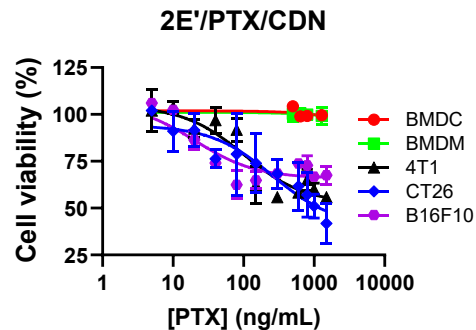
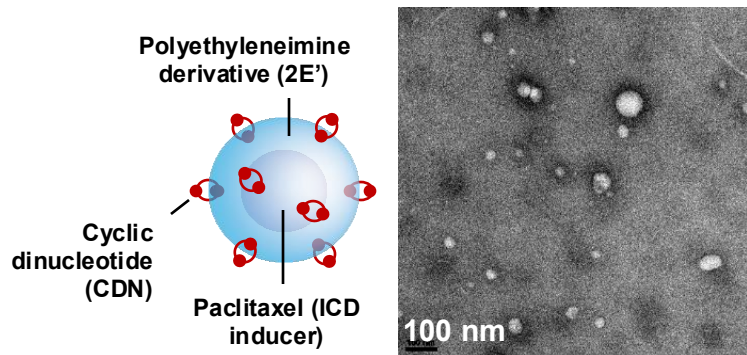
Coley, W. B. (1910). *Proceedings of the Royal Society of Medicine*.

Augmenting cancer immunotherapy with nanoparticles



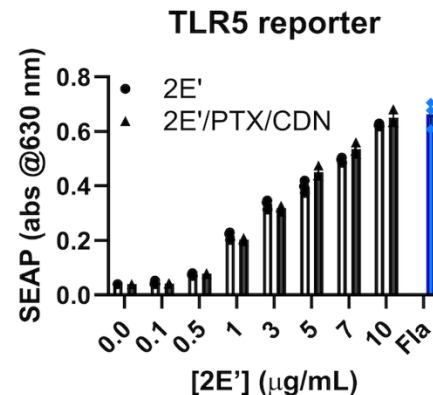
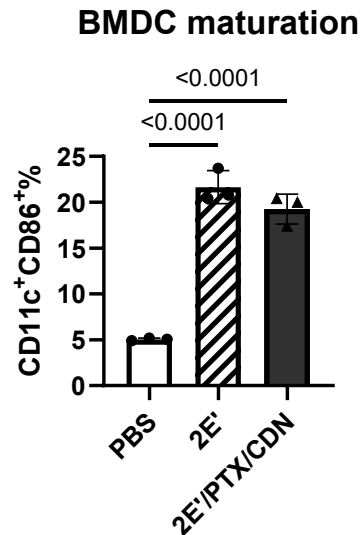
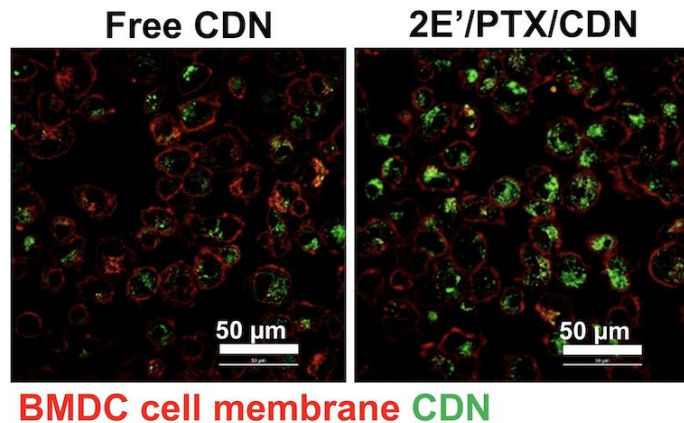
Chen, Daniel S, and Ira Mellman. (2013). *Immunity* vol. 39,1.

2E'/PTX/CDN has selective cytotoxicity to tumor cells and induces immunogenic cell death (ICD)



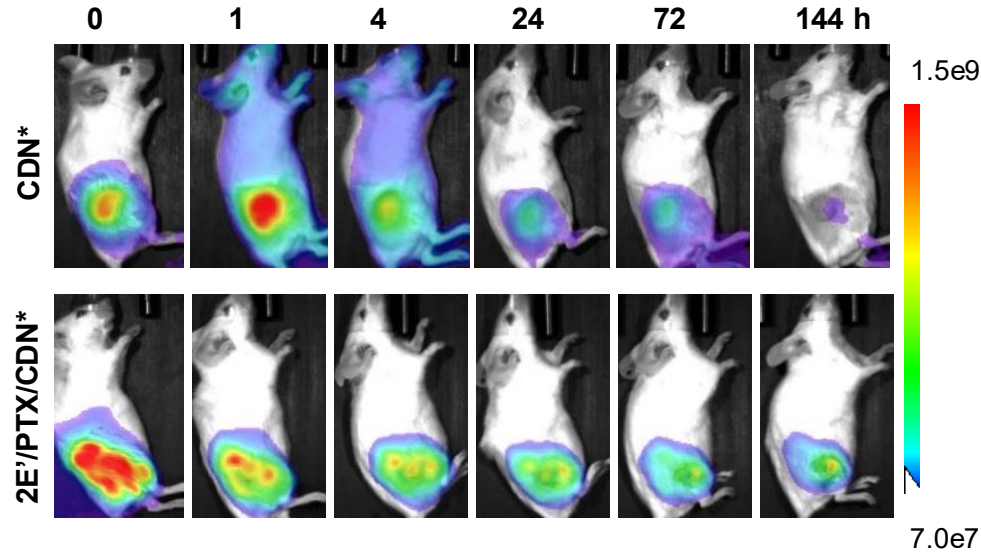
Meng, F., He, Y., Zhao, J., Yuan, Z., Wang, J., Parra, K. G., Fishel, M. L., Ratliff, T. L., & Yeo, Y. (2025). *Journal of Controlled Release*, 381, 113579.

2E'/PTX/CDN facilitates CDN uptake and activates immune cells



Meng, F., He, Y., Zhao, J., Yuan, Z., Wang, J., Parra, K. G., Fishel, M. L., Ratliff, T. L., & Yeo, Y. (2025). *Journal of Controlled Release*, 381, 113579.

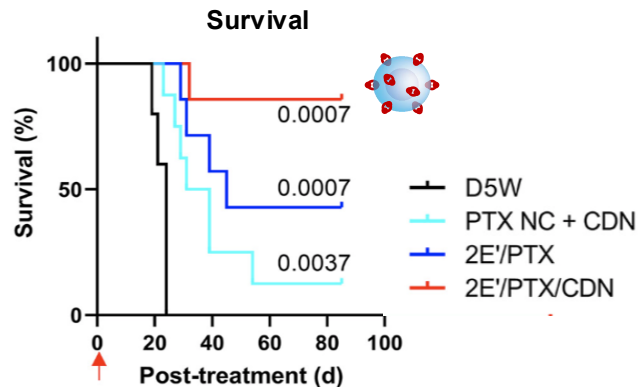
2E'/PTX/CDN prolongs CDN retention in CT26 tumor



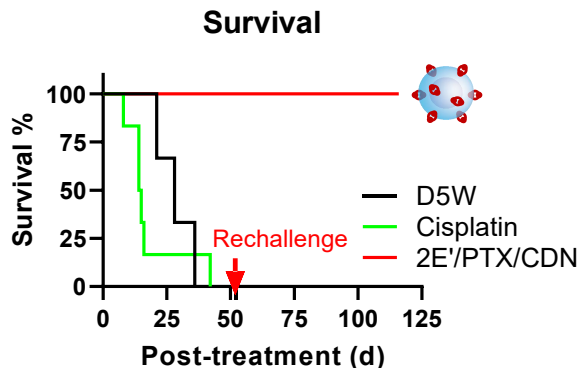
Meng, F., He, Y., Zhao, J., Yuan, Z., Wang, J., Parra, K. G., Fishel, M. L., Ratliff, T. L., & Yeo, Y. (2025). *Journal of Controlled Release*, 381, 113579.

A single local 2E'/PTX/CDN injection eliminates tumor in multiple cancer models

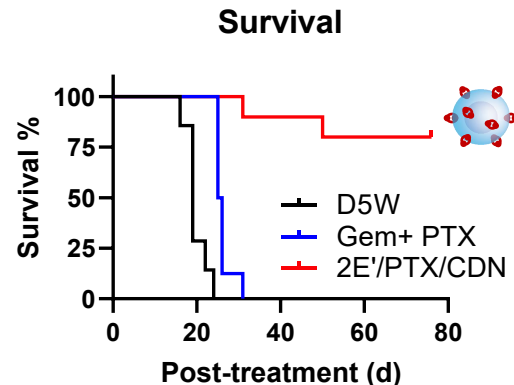
CT26 Colon Tumor



MOC1 Oral Squamous Cell Carcinoma



KPCY (2838c3) Pancreatic Tumor

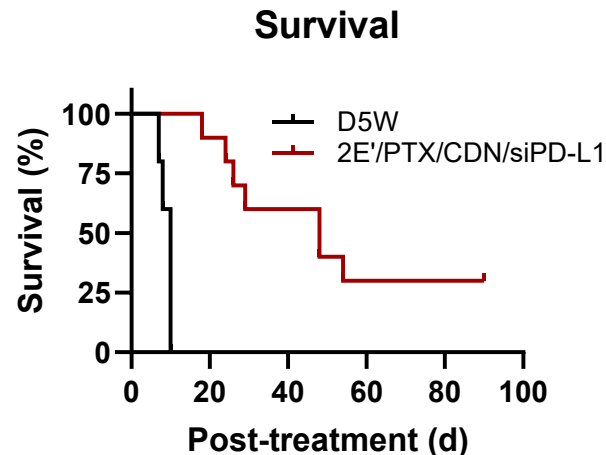
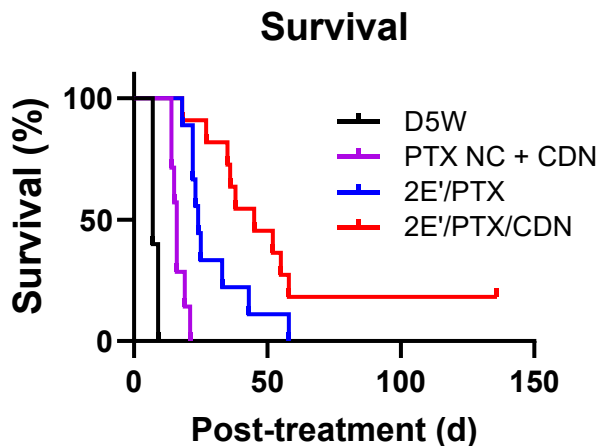


NC: nanocrystal
Gem: gemcitabine

Meng, F., Wang, J., He, Y., Cresswell, G. M., Lanman, N. A., Lyle, L. T., Ratliff, T. L., & Yeo, Y. (2022). *PNAS*, 119(22).
Meng, F., He, Y., Zhao, J., Yuan, Z., Wang, J., Parra, K. G., Fishel, M. L., Ratliff, T. L., & Yeo, Y. (2025). *Journal of Controlled Release*, 381, 113579.

2E'/PTX/CDN shows limited therapeutic efficacy in B16F10 melanoma model

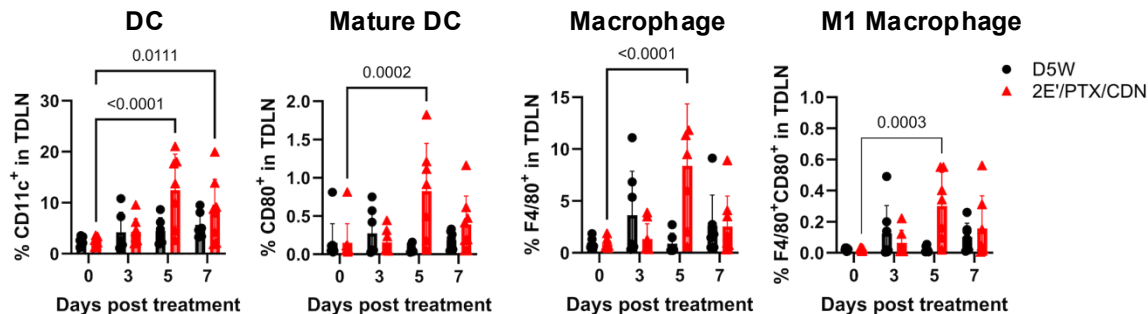
B16F10 melanoma



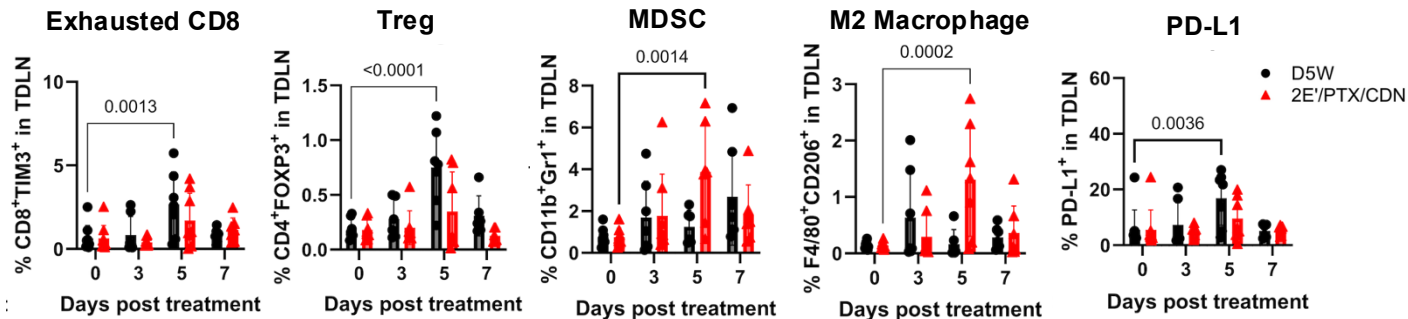
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2E'/PTX/CDN induced a time-dependent shift in the tumor microenvironment in B16F10 melanoma model

Anti-tumor



Pro-tumor

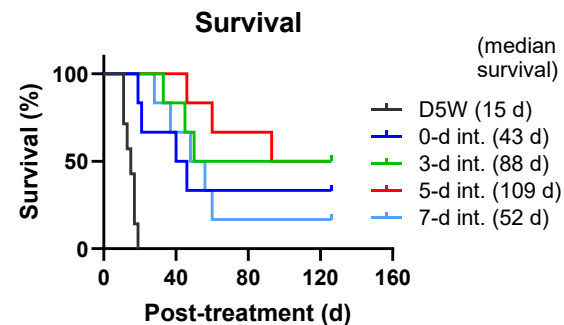
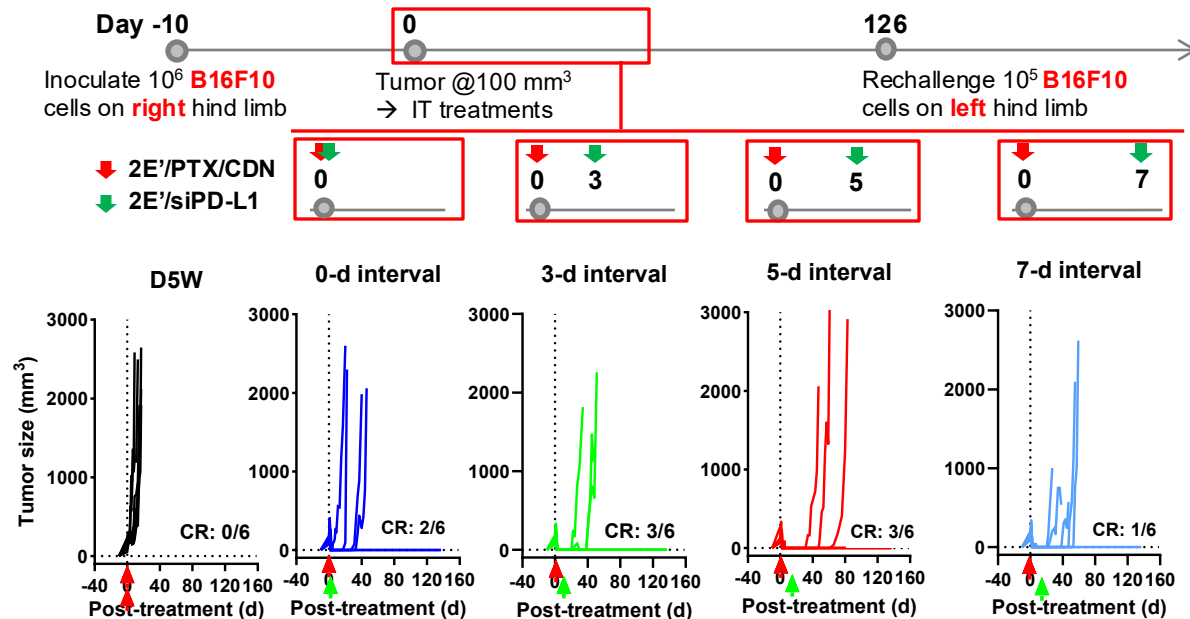
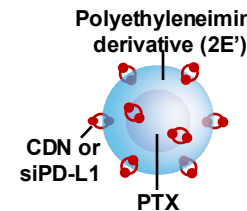


Treg: regulatory T cell

MDSC: myeloid-derived suppressive cell

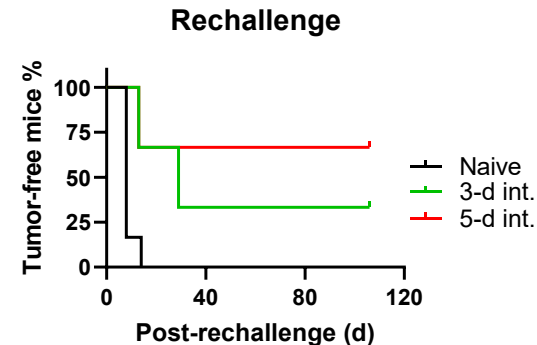
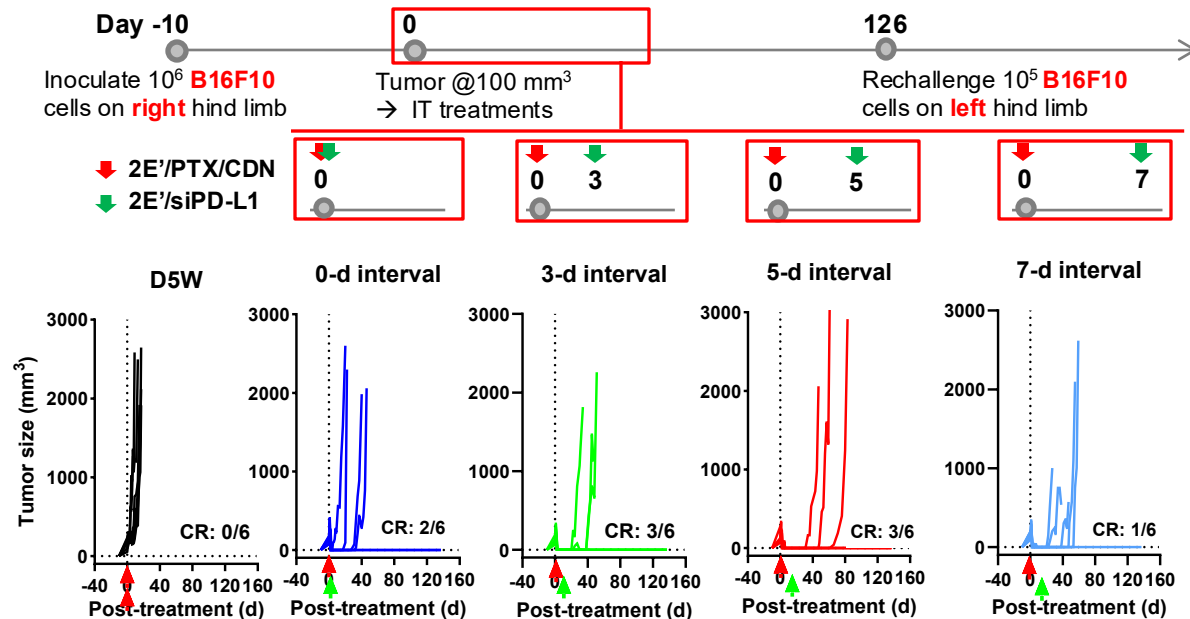
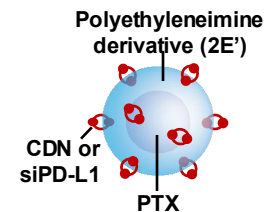
Meng, F., He, Y., Zhao, J., Yuan, Z., Wang, J., Parra, K. G., Fishel, M. L., Ratliff, T. L., & Yeo, Y. (2025). *Journal of Controlled Release*, 381, 113579.

Timely addition of siPD-L1 increases the antitumor activity of 2E'/PTX/CDN in B16F10 model



Meng, F., He, Y., Zhao, J., Yuan, Z., Wang, J., Parra, K. G., Fishel, M. L., Ratliff, T. L., & Yeo, Y. (2025). *Journal of Controlled Release*, 381, 113579.

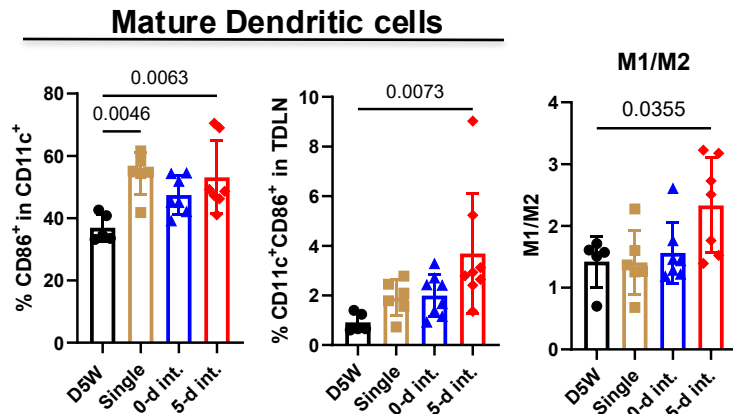
Timely addition of siPD-L1 increases the antitumor activity of 2E'/PTX/CDN in B16F10 model



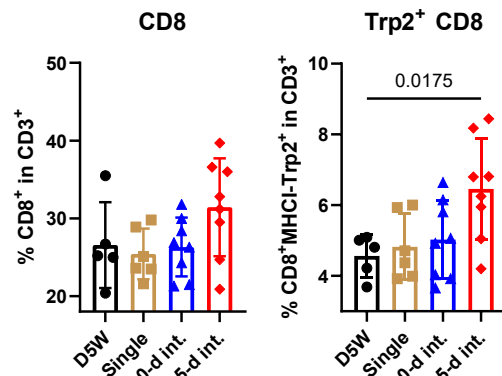
Meng, F., He, Y., Zhao, J., Yuan, Z., Wang, J., Parra, K. G., Fishel, M. L., Ratliff, T. L., & Yeo, Y. (2025). *Journal of Controlled Release*, 381, 113579.

Timely combination of 2E'/PTX/CDN and 2E'/siPD-L1 activates and maintains antitumor immunity in B16F10 model

APCs in TDLN



T cells in spleen



Meng, F., He, Y., Zhao, J., Yuan, Z., Wang, J., Parra, K. G., Fishel, M. L., Ratliff, T. L., & Yeo, Y. (2025). *Journal of Controlled Release*, 381, 113579.

Conclusion

- The antitumor effect of B16F10 depends on the interval between 2E'/PTX/CDN and 2E'/siPD-L1, and a 5-day interval showed the best efficacy.
- Timely administration of additional immune stimulator is critical to counteracting the evolution of immunosuppressive TME following tumor immunotherapy.
- Biomarkers informing temporal changes of a tumor's immune milieu will be highly valuable for designing an optimal regimen.

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Questions?