

Xkr8 Knockdown Enhances Chemotherapy Efficacy Through Modulating Tumor Immune Microenvironment

Speaker: Chien-Yu Chen
Advisor: Song Li, M.D. Ph.D.

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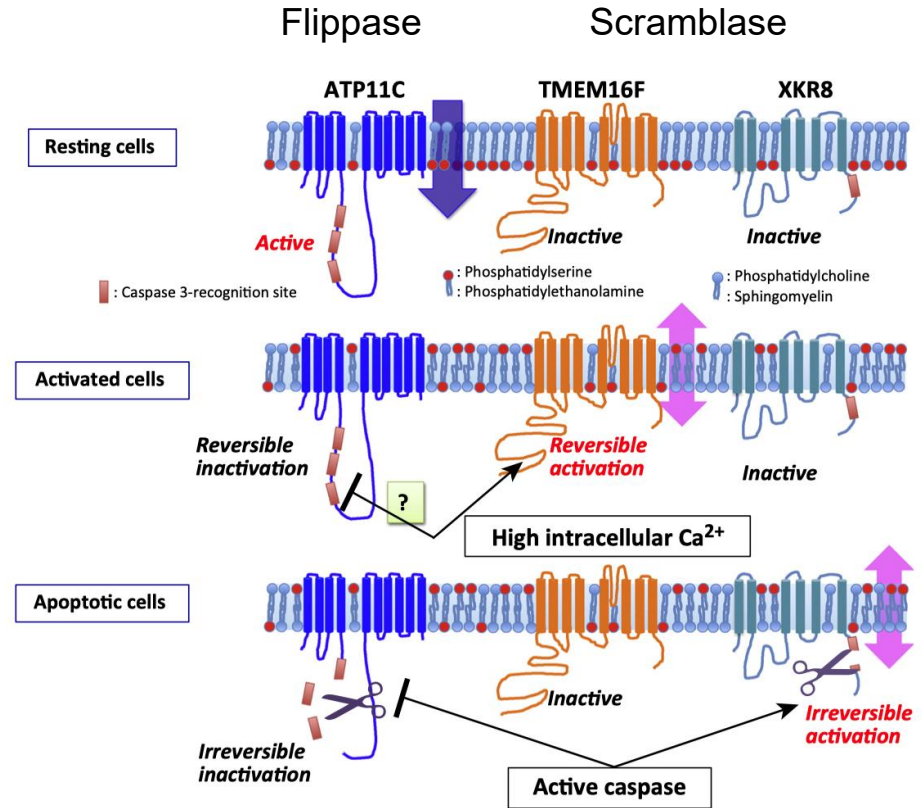


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**NEXT-GENERATION
DELIVERY INNOVATIONS**

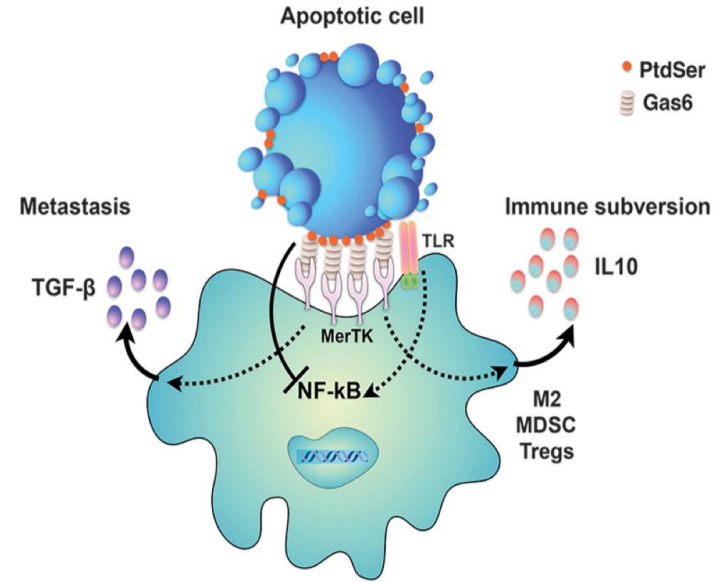
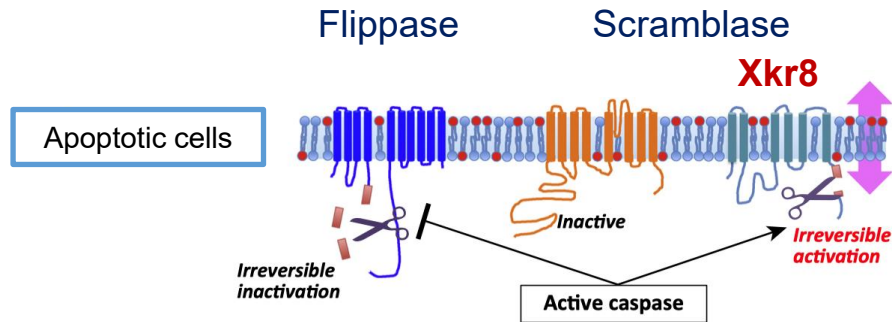
Phosphatidylserine (PS)

- Externalized to cell surface during apoptosis
- Serve as an “eat-me” signal, promoting the clearance of apoptotic cells
- Efferocytosis

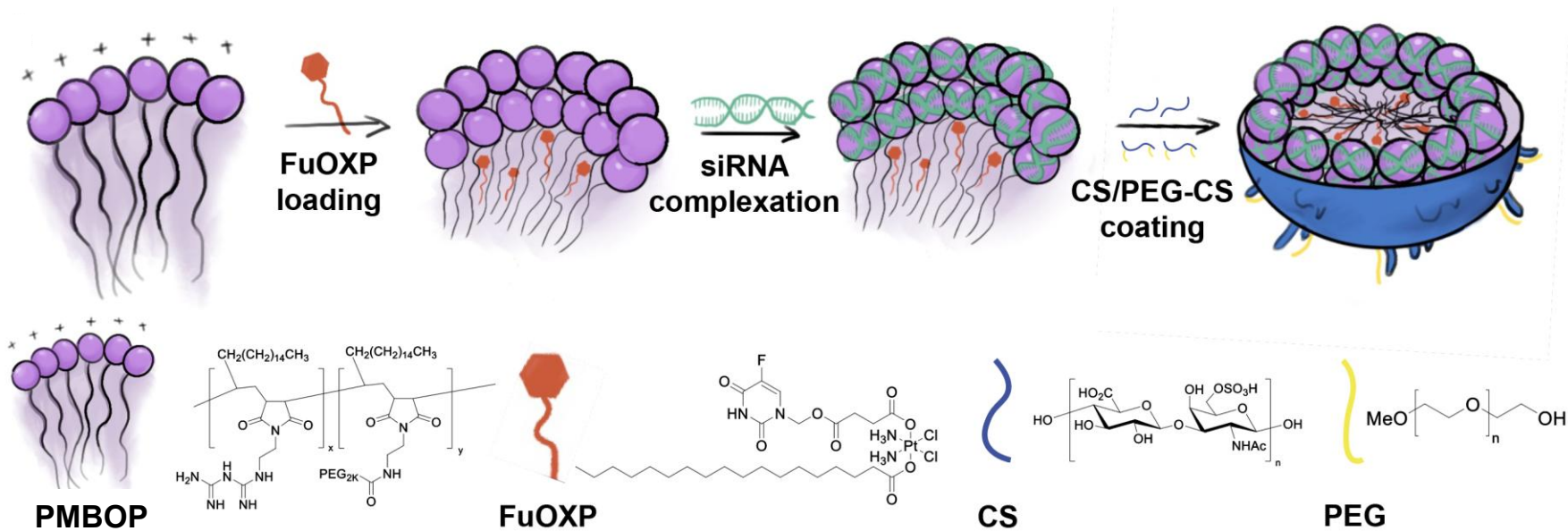


PS-mediated immunosuppression

- PS stimulates the polarization of phagocytes toward immunosuppressive phenotypes.



PMBOP nanoparticles for FuOXp & siXkr8 co-delivery

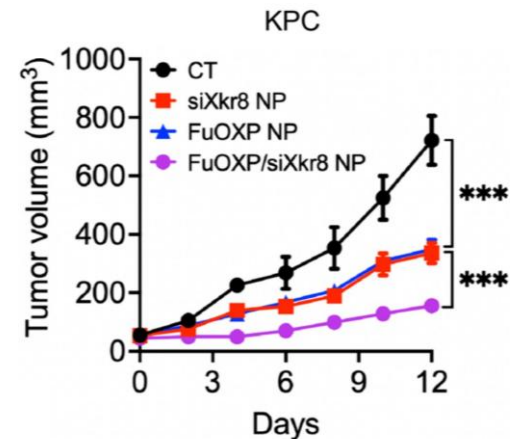
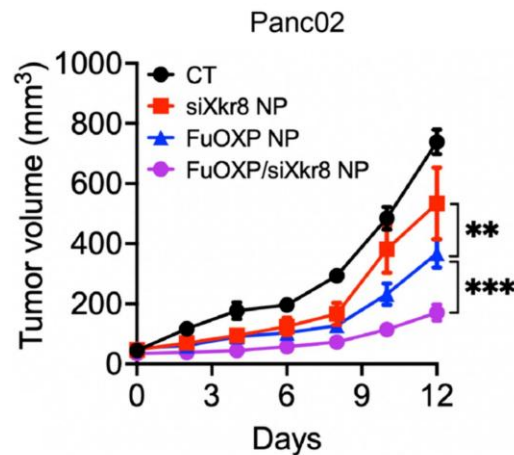
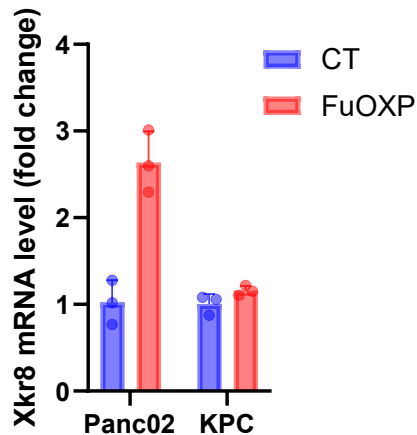


Chen, Y., Huang, Y., Li, Q. *et al.* *Nat. Nanotechnol.* **18**, 193–204 (2023).

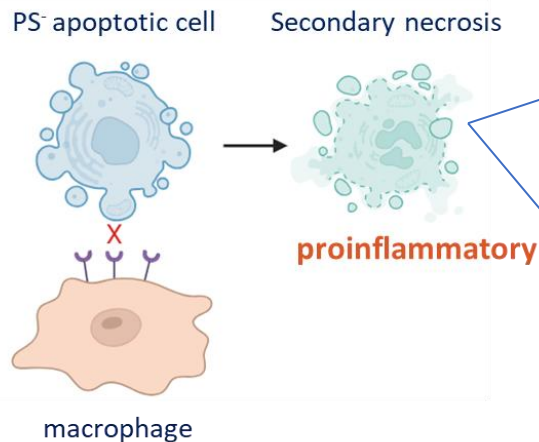
Objectives

- Evaluate the therapeutic effect of Xkr8 knockdown (KD) in models with distinct Xkr8 induction profiles
- Study the death pathway contributing to immune activation
- Assess therapeutic efficacy and characterize the tumor microenvironment in a clinically relevant orthotopic pancreatic tumor model

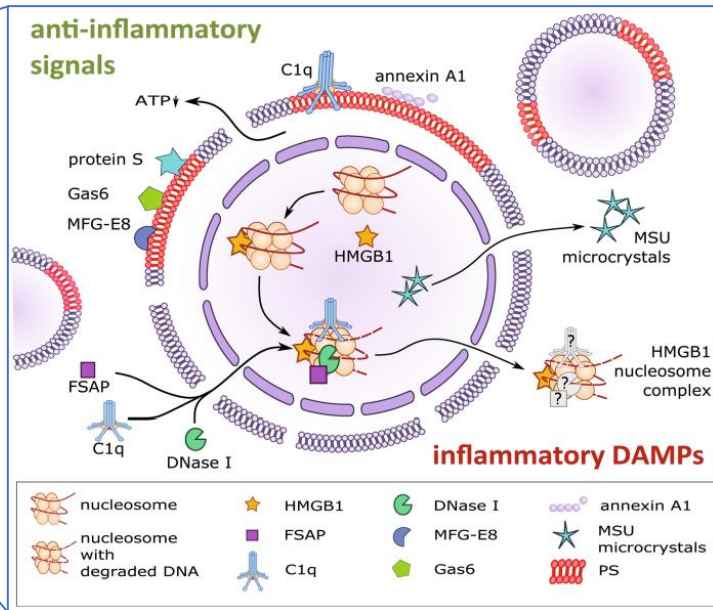
Xkr8 KD suppresses growth of pancreatic tumors with different Xkr8 induction profiles



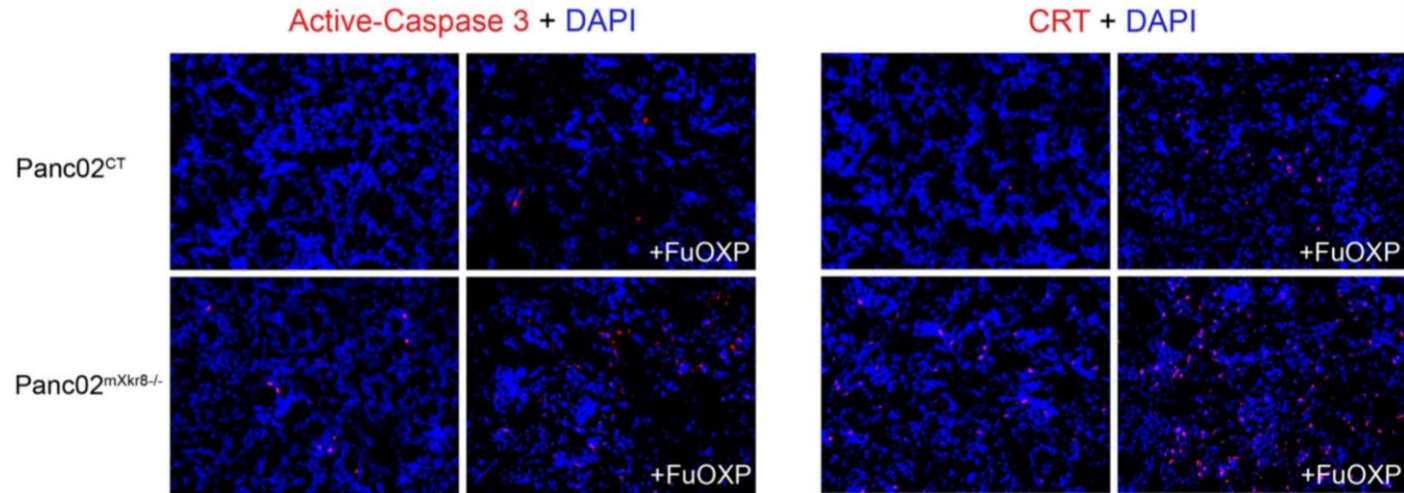
Secondary necrosis



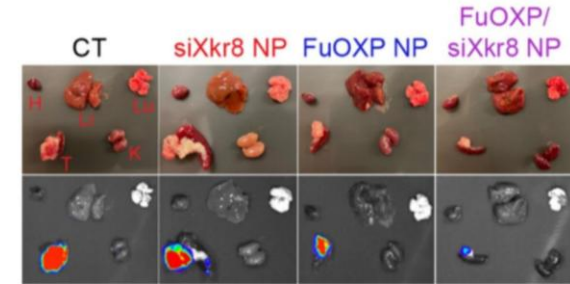
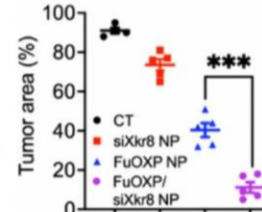
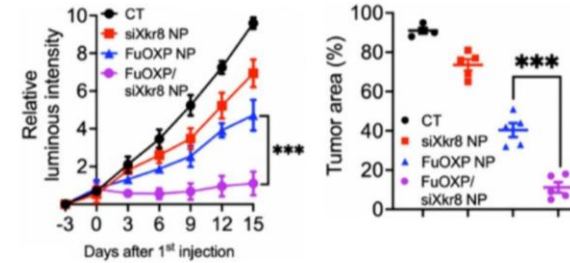
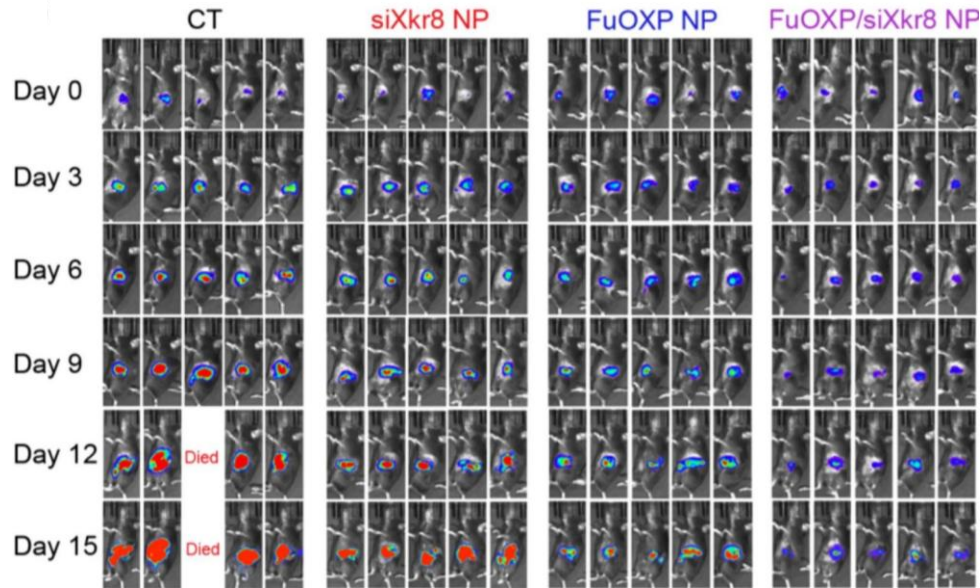
- Secondary necrosis contribute to immunogenic cell death (ICD)



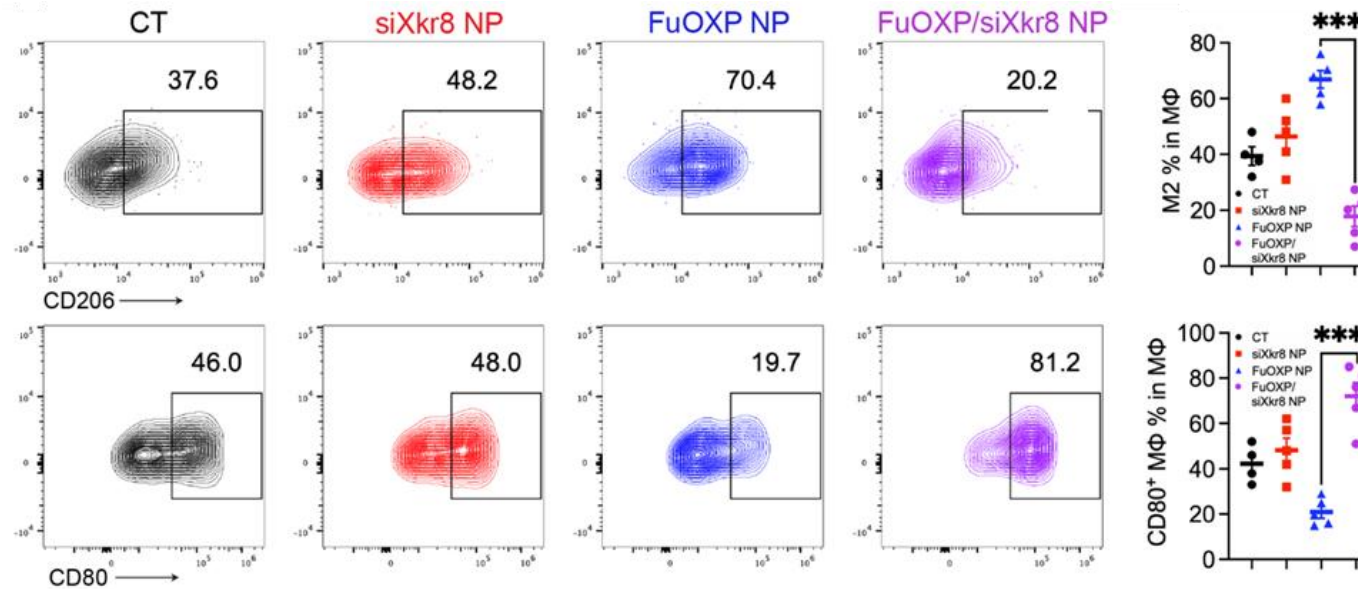
Delayed clearance of apoptotic cells leads to ICD



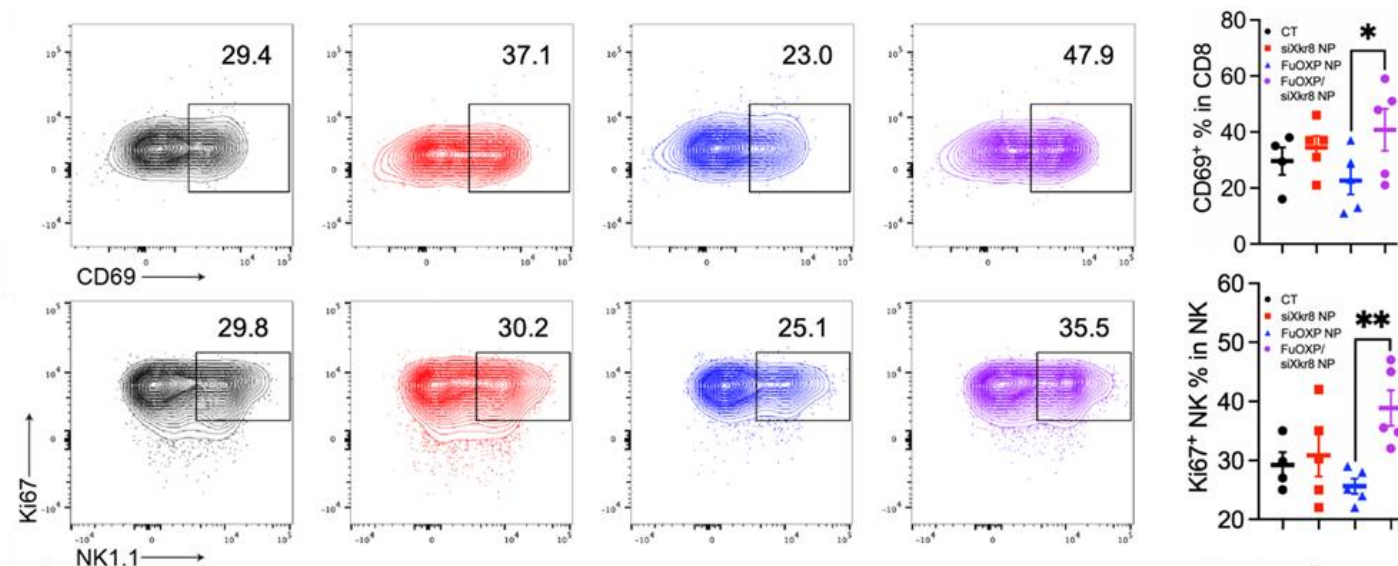
FuOXP/siXkr8 showed enhanced anti-tumor effect in orthotopic pancreatic tumor model



Xkr8 KD promotes MΦ polarization towards M1 phenotype

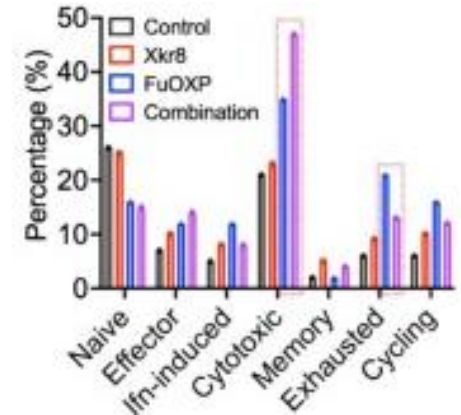
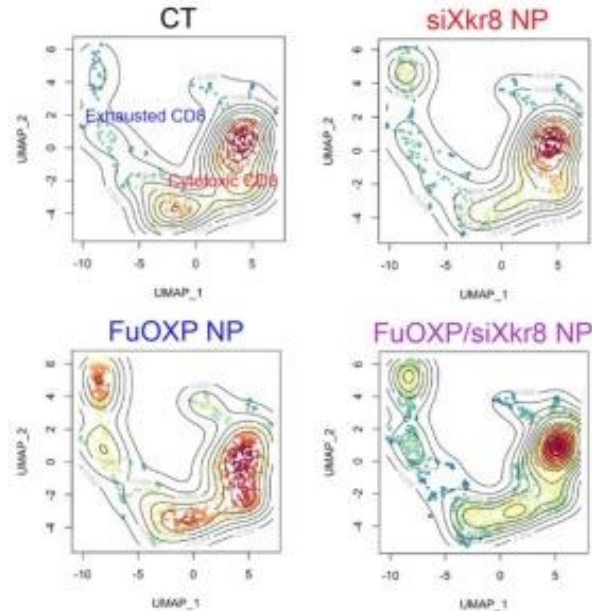
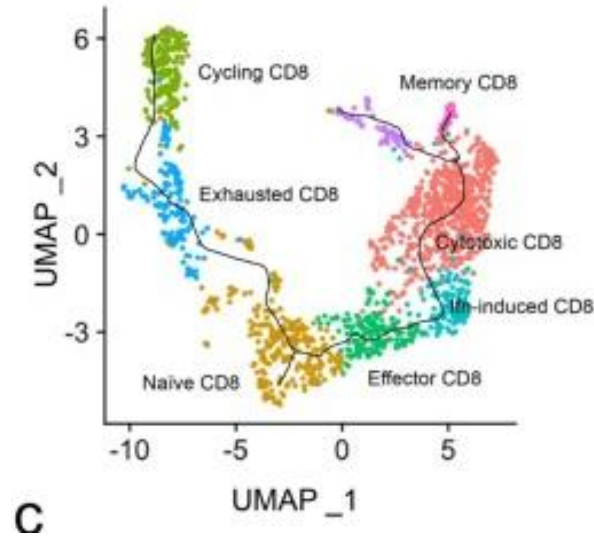


Xkr8 KD promotes CD8 T cells activation and NK cells proliferation

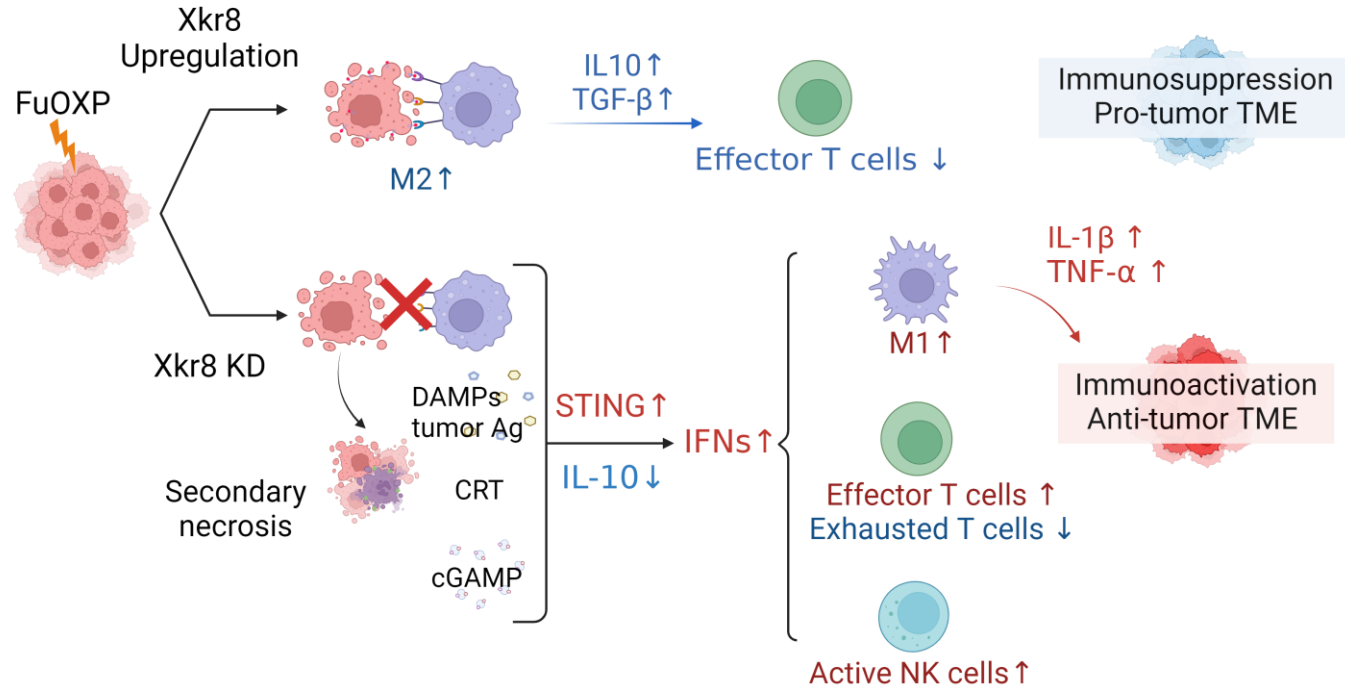


FuOXP/siXkr8 combination treatment alters T cell function in TME

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Summary



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