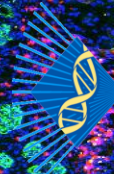


Reprogramming the Tumor Microenvironment to Improve Responses to Therapy



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SITC
November 10th, 2018



SITEMAN CANCER CENTER
BARNES-JEWISH HOSPITAL • WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

Disclosures

SAB Member

Adhere

Gossamer

Research Funding

Verastem

BMS

Speakerships

Merck

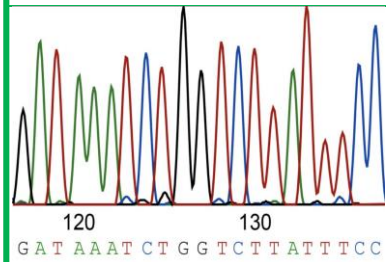
BMS

Verastem

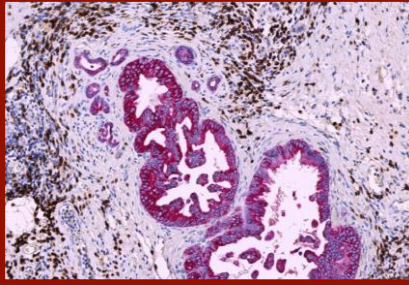
Halozyne

Immunotherapeutic Failures in Pancreas Cancer; Why?

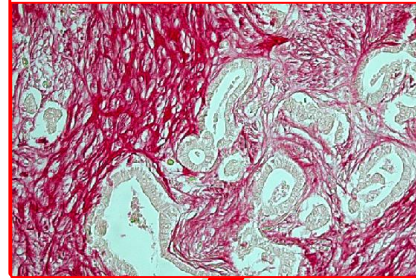
Poor TMB



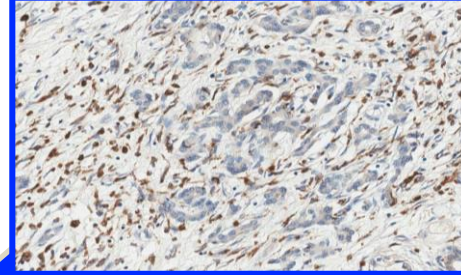
Poor T cell Infiltrate



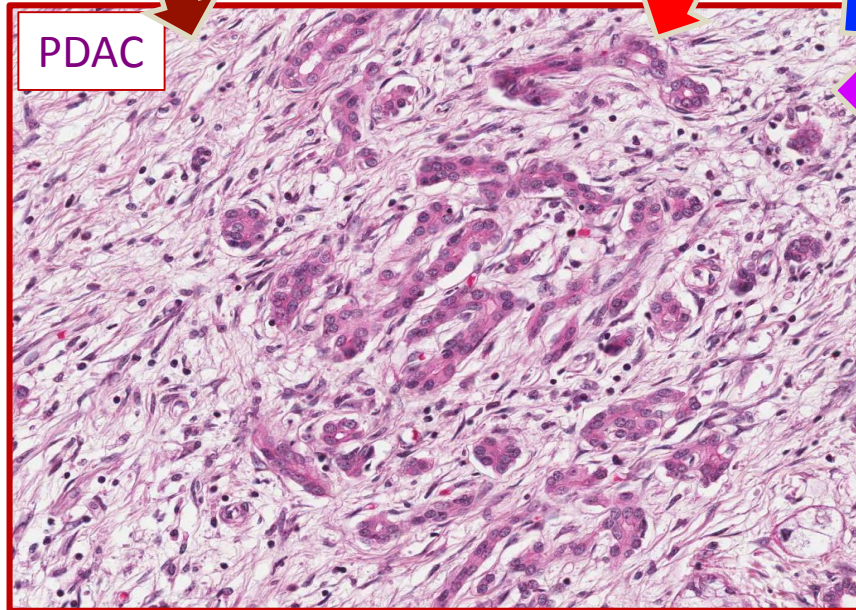
Fibrosis/Dense ECM



Heavy Myeloid Infiltrates

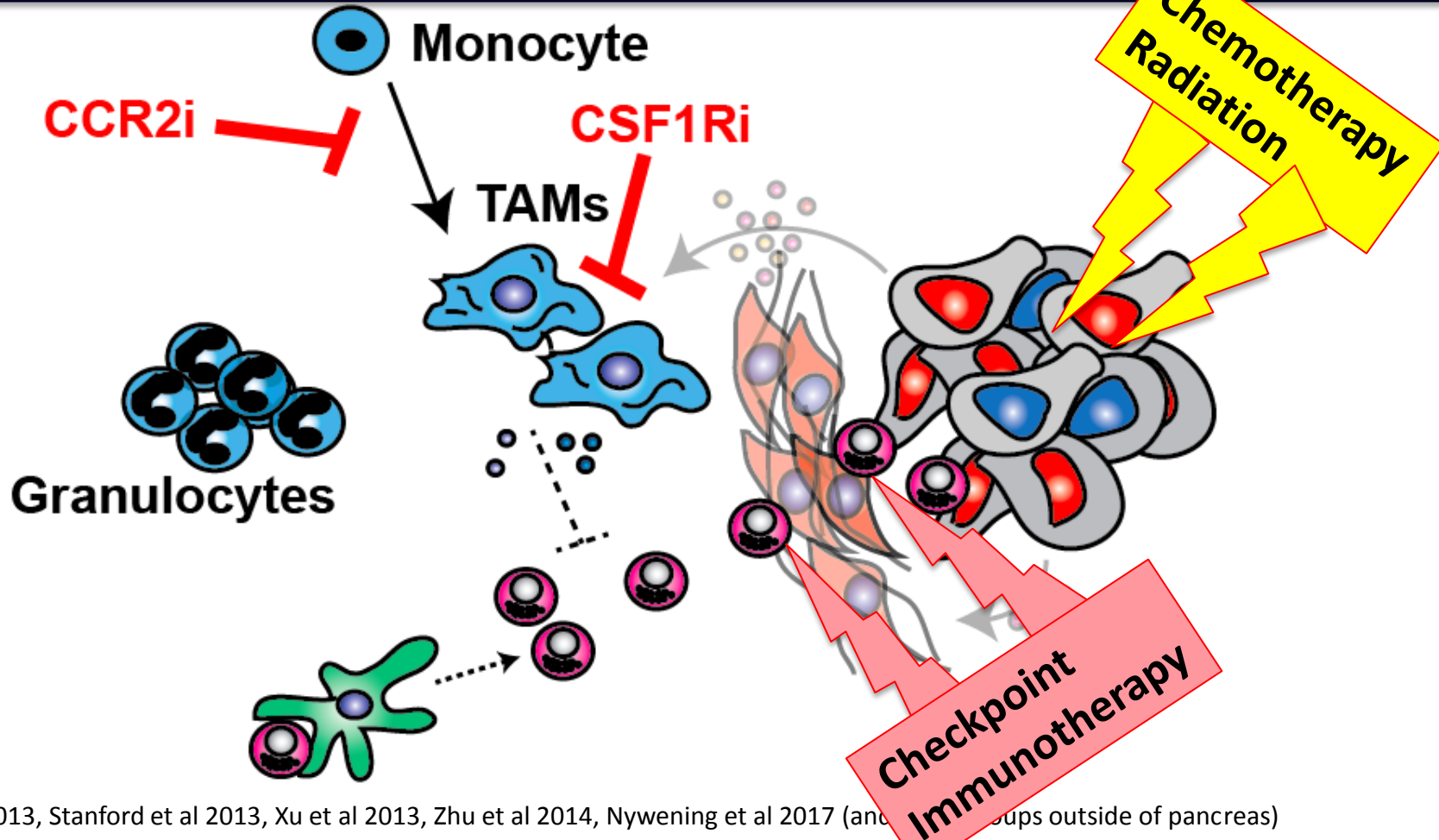


PDAC



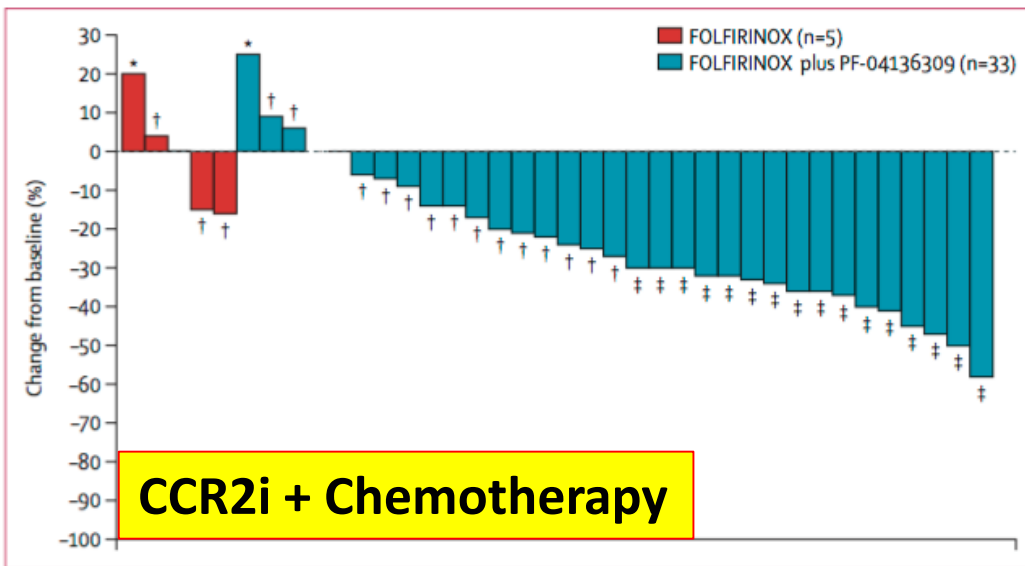
- Hypoxia
- Vasculature Dysfunction
- Metabolism

Targeting Macrophages To Improve Response to Therapy



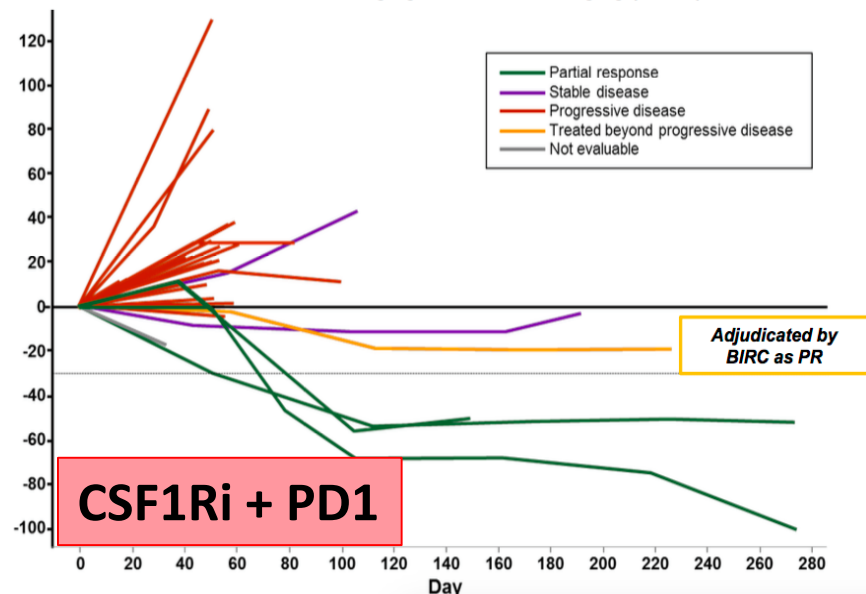
Hints of Activity in PDAC

Chemotherapy Combination



Checkpoint Combination

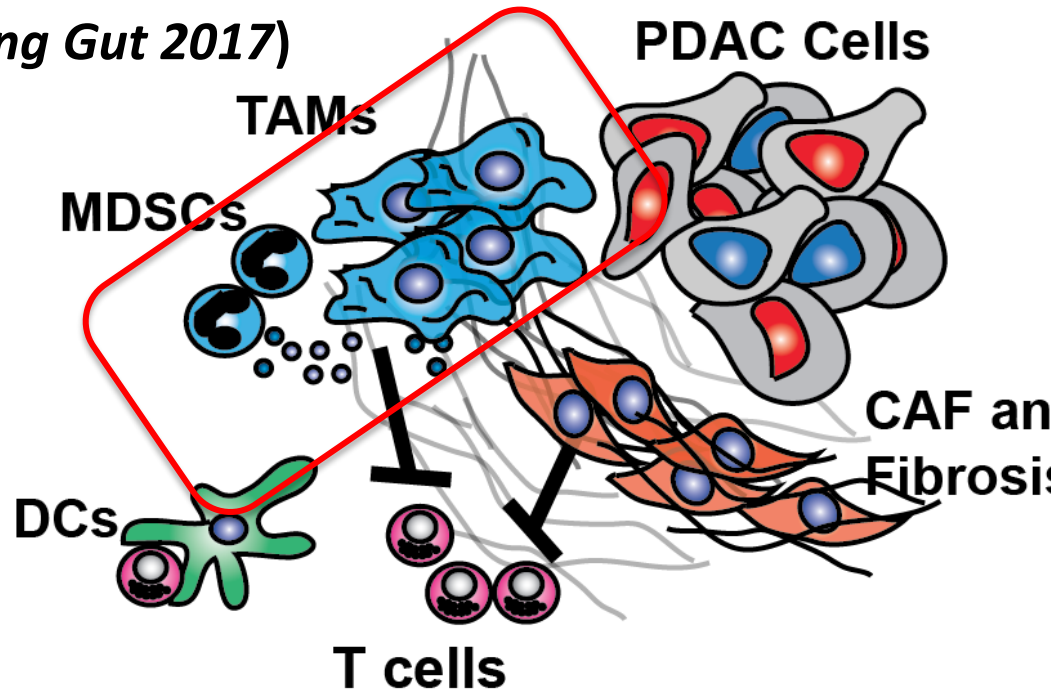
Best change in tumor burden over time in efficacy-evaluable patients treated with cabiralizumab 4 mg/kg + nivolumab 3 mg/kg (n = 31)^a



SWOT Analysis

Problem

- Myeloid Compensation
(*Kumar Cancer Cell 2018, Nywening Gut 2017*)
- Tissue Resident Macrophages
(*Zhu Immunity 2017*)

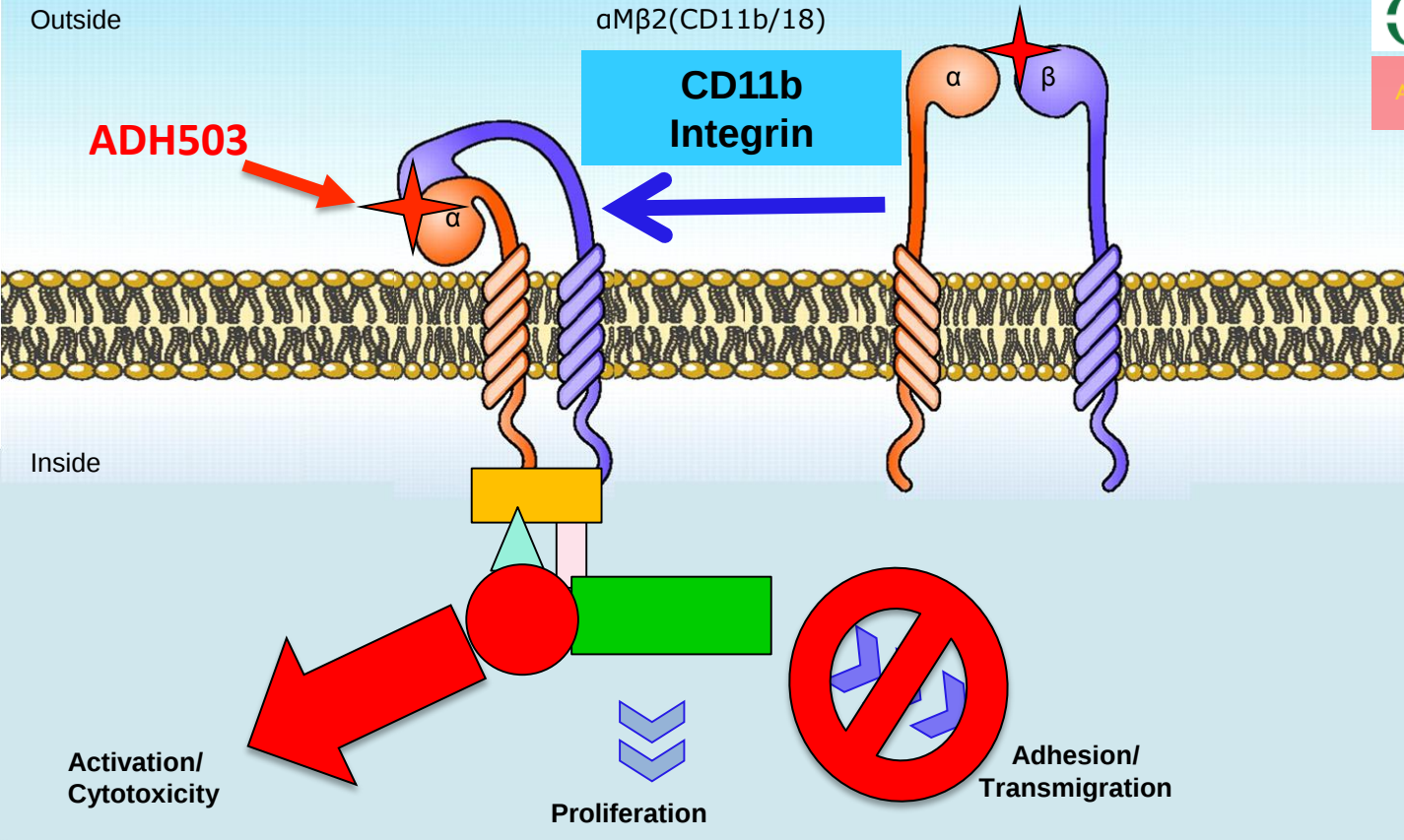


Teaching an Old Dog New Tricks (Targeting CD11b)

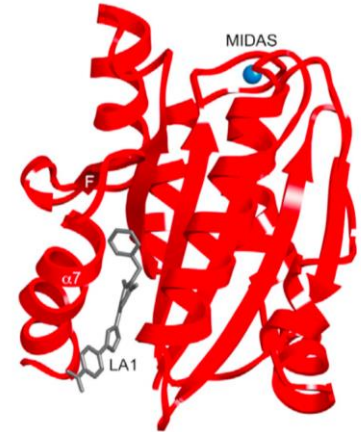


RUSH UNIVERSITY

ADHAERE PHARMACEUTICALS, INC.



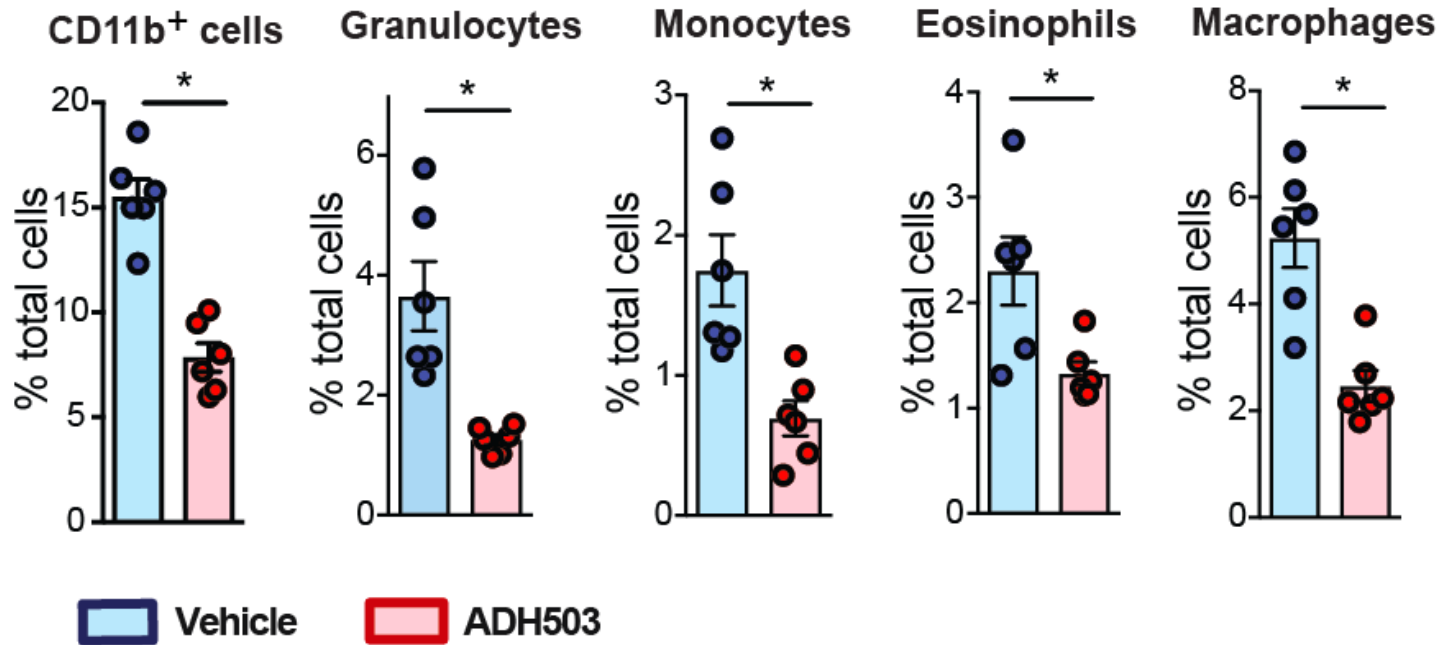
Vineet Gupta, PhD



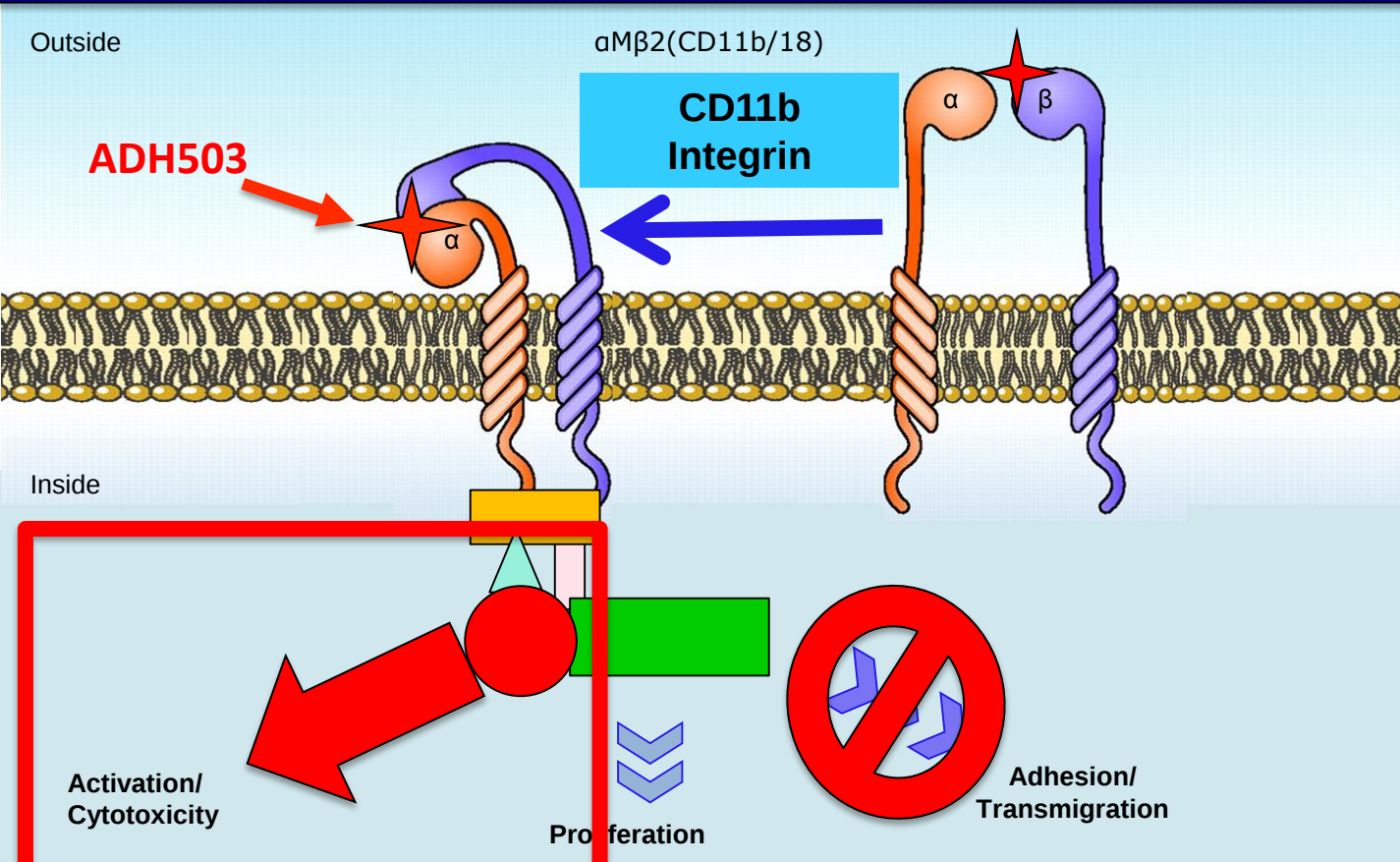
ADH503 Disrupts Multiple Myeloid Cell Populations

Orthotopic PDAC (KP2)

Tumor Myeloid Infiltrate (Orthotopic KPC-2.0)



Teaching an Old Dog New Tricks (Targeting CD11b)



Farid M. Crit. Care Med. May, 2002

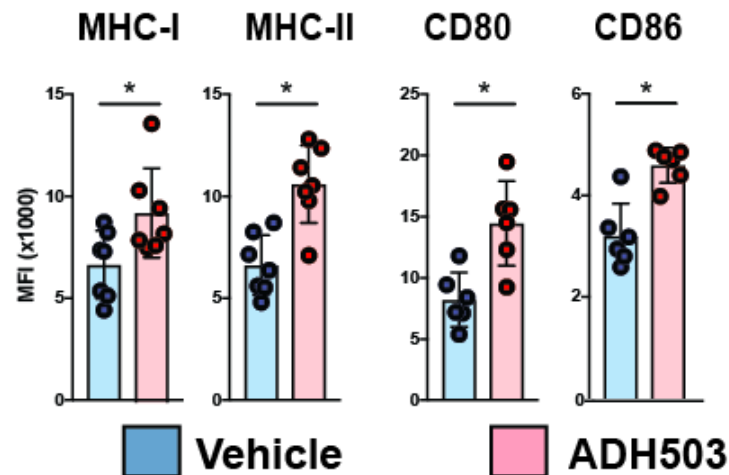
Jagtap S. Am J Respir Cell Mol Biol. Dec, 2013

Farid M. Biochim Biophys Acta. Jun, 2013

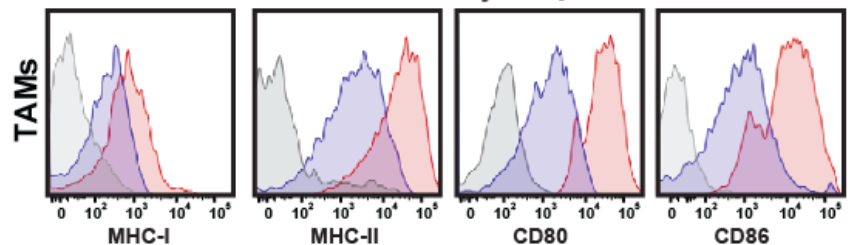
Celik E. Biophys J. Dec, 2013

CD11-Agonists Re-polarize Macrophages

In-vivo TAMs



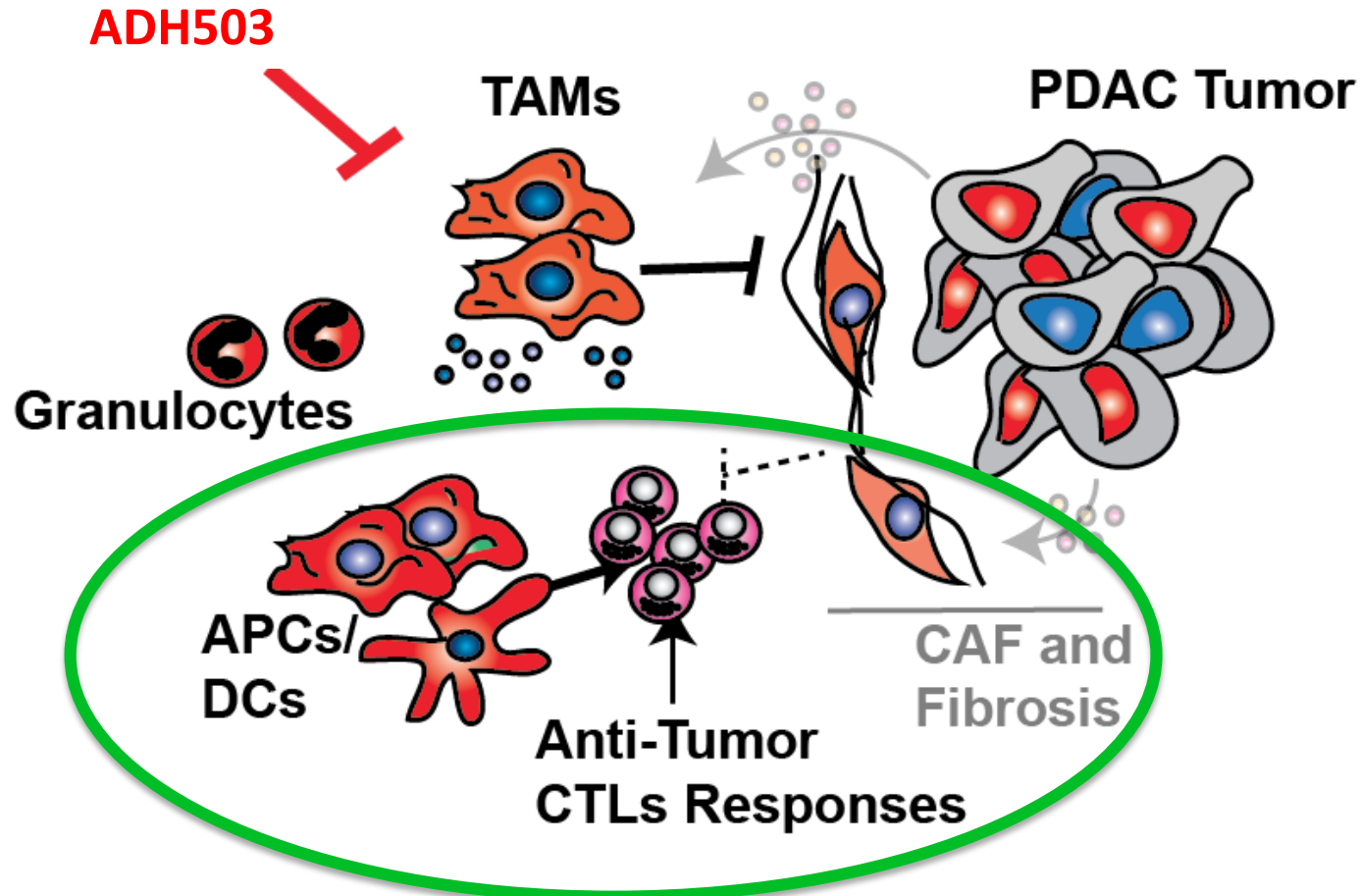
Gated on $CD45^{+}CD3^{-}CD19^{-}CD11b^{+}Ly6G^{-}Ly6C^{Low}/F4/80^{+}MHCII^{+}$



Consistent Across Two PDAC Models

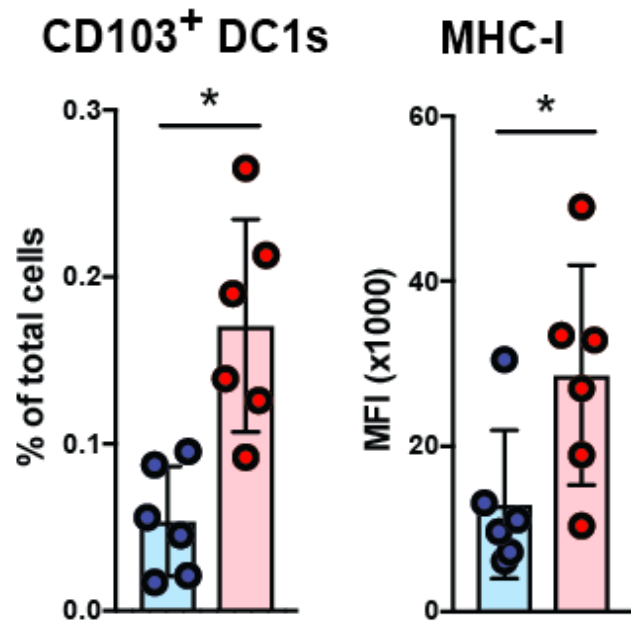
Panni et al Sci. Transl. Med. In Revision

Targeting Myeloid Cells

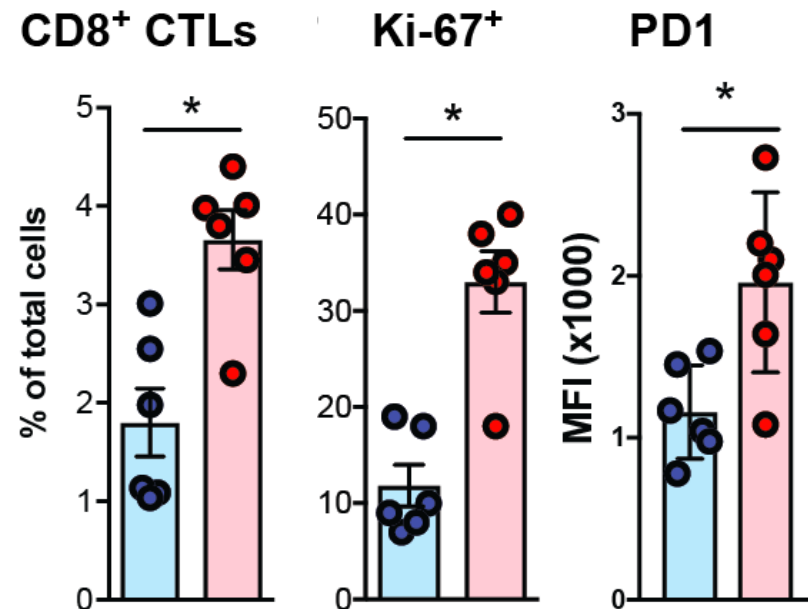


CD11B-Agonists Invigorate cDC and T cell Responses

cDC Support



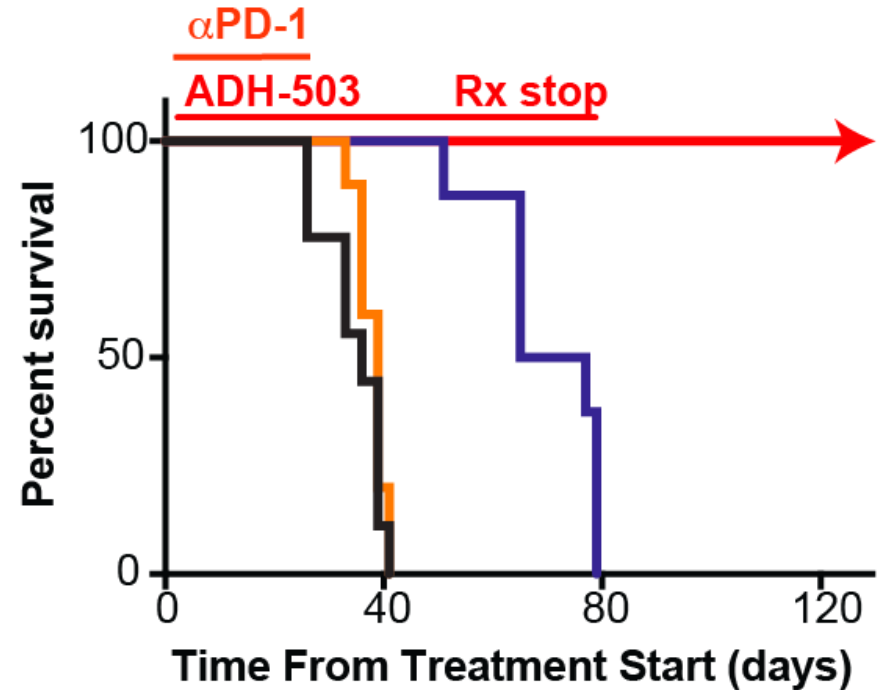
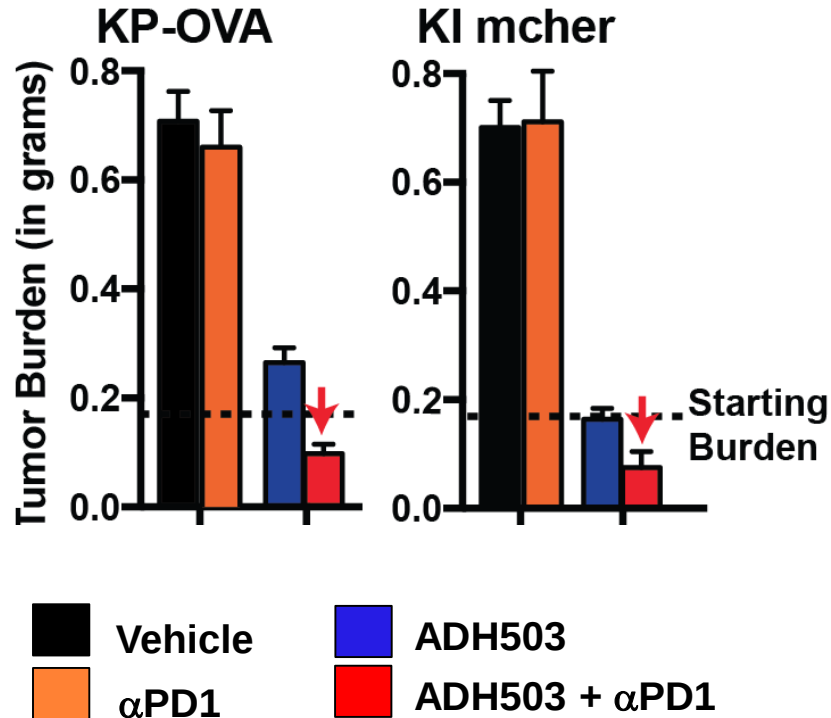
T cell Response



Vehicle
ADH503

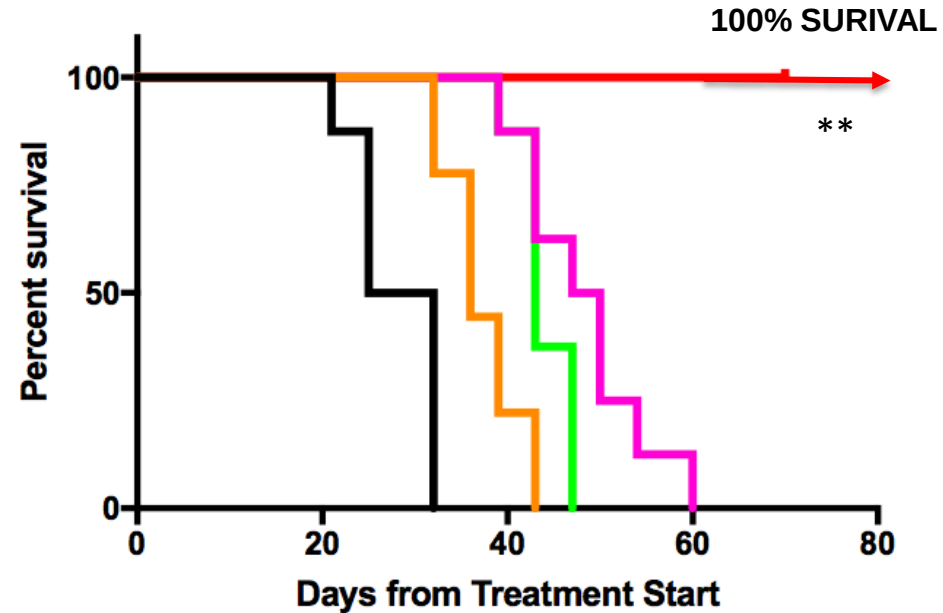
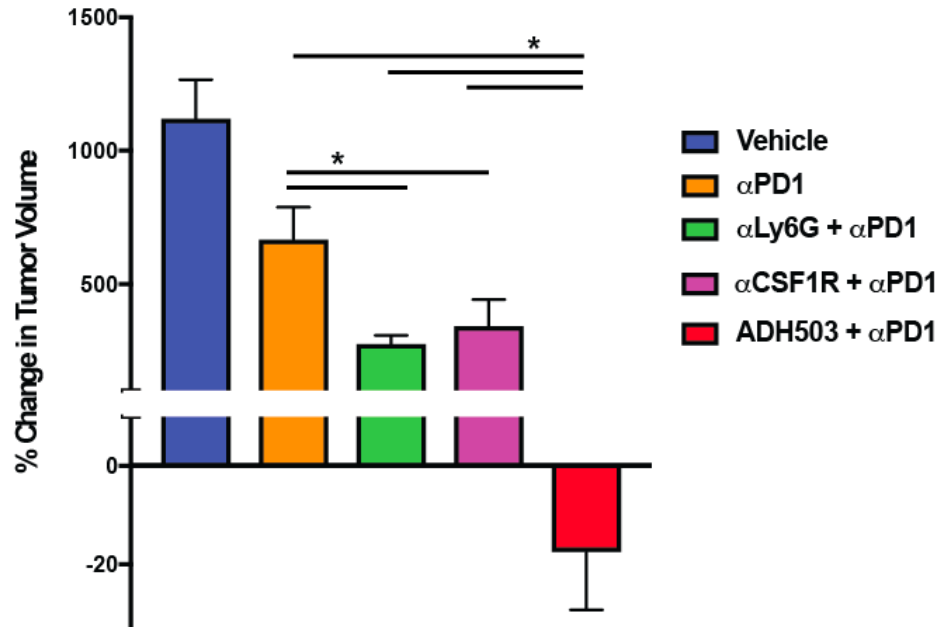
ADH503 improves checkpoint immunotherapy

Orthotopic Tumors



Head to Head vs. Other Approaches

Orthotopic PDAC (KP2)

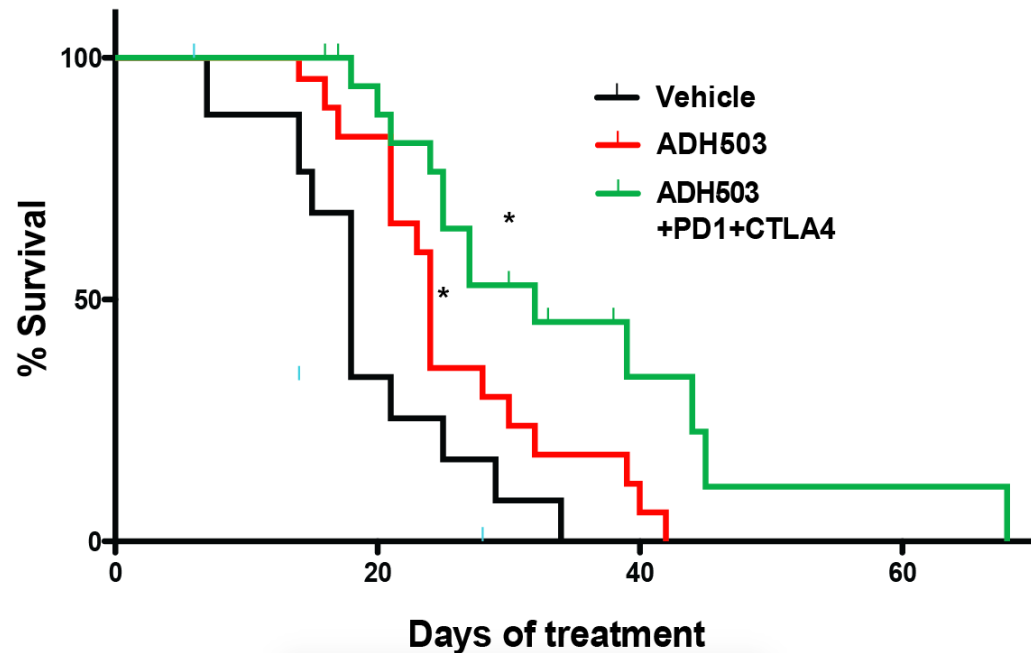
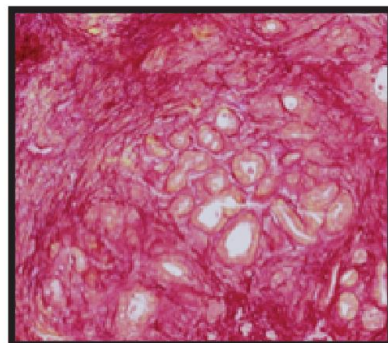
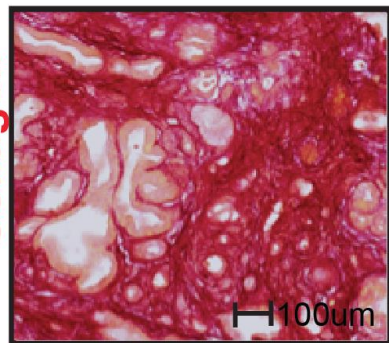
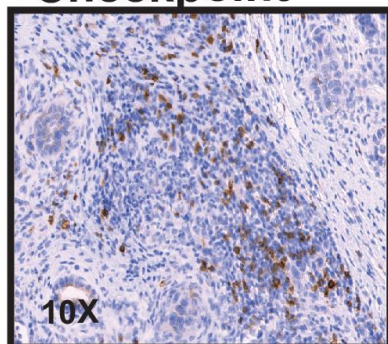
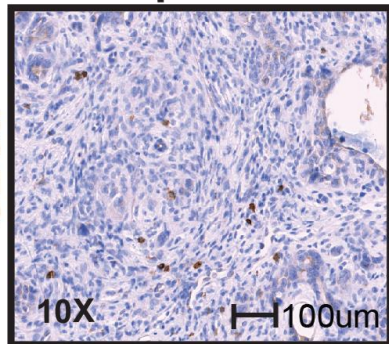


ADH503 improves immunotherapy

KPC GEMM

ADH503 +Checkpoint

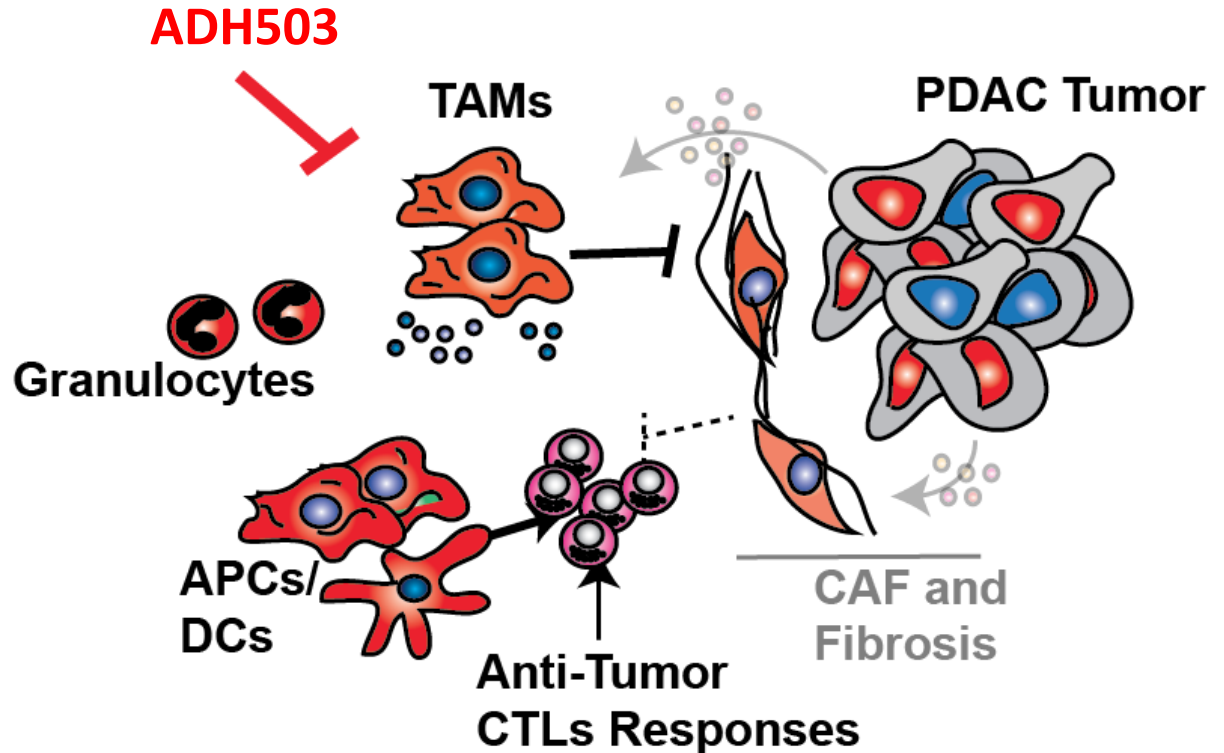
Checkpoint



Therapeutic Model

Take homes

- Target Integrins
- Myeloid/DC Interface





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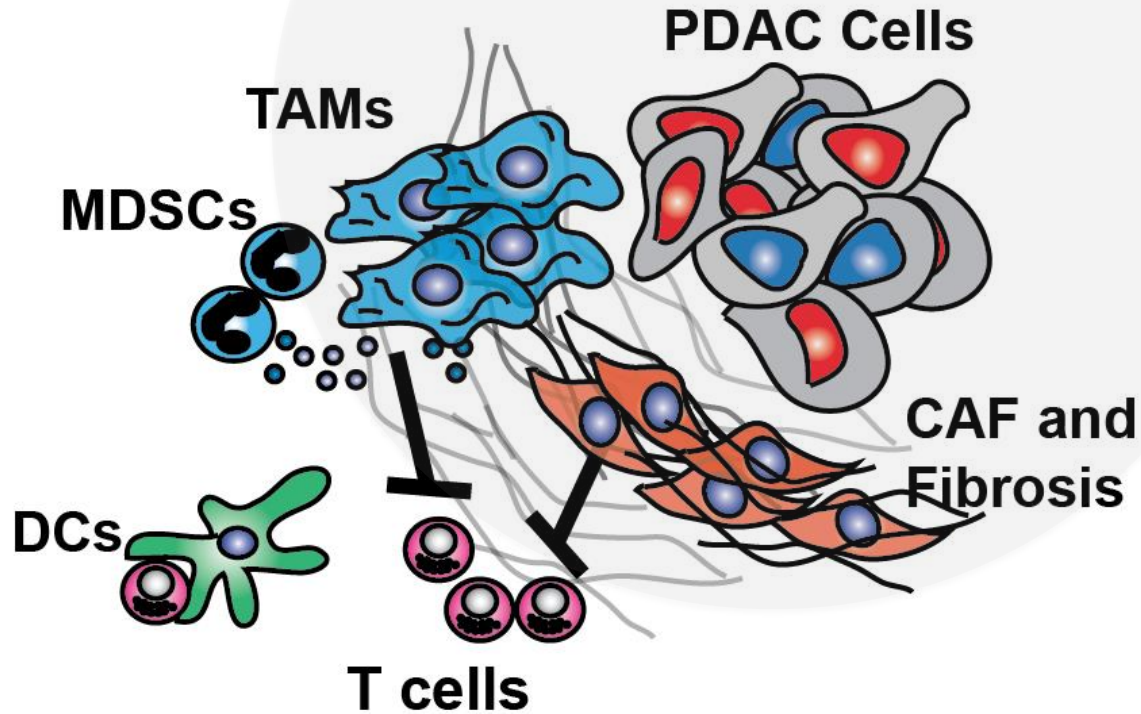
Funding

NCI R01-CA177670
NCI R01-CA203890
NCI P50-CA196510
AACR/PANCAN
DOD-BCRP
PRMA/BICIH



“QUESTIONS?”

Targeting PDAC Microenvironment



Targeting Myeloid Cells

