Pro-tumorigenic cancer-associated fibroblasts are tumor-activated resident lung fibroblasts that are not confined to the tumor microenvironment in NSCLC patients

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AATS 93RD ANNUAL MEETING 2013

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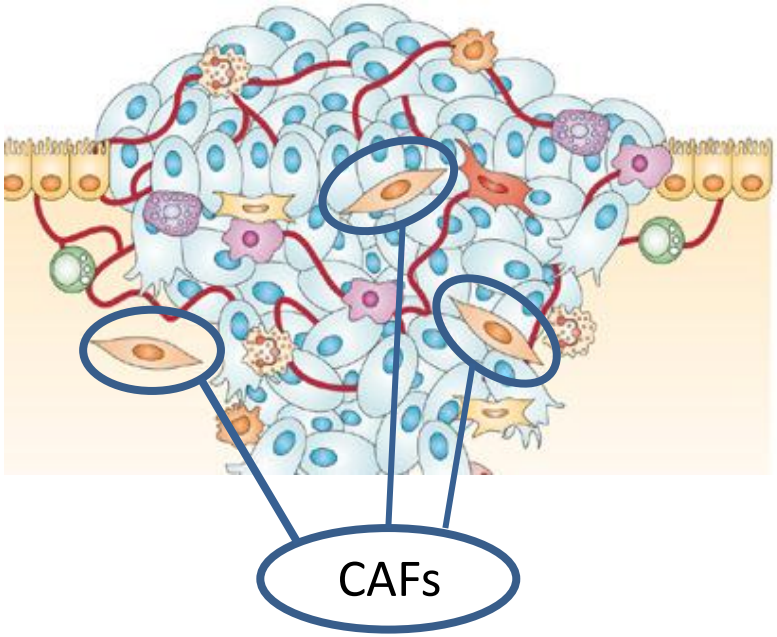
Disclosures: None

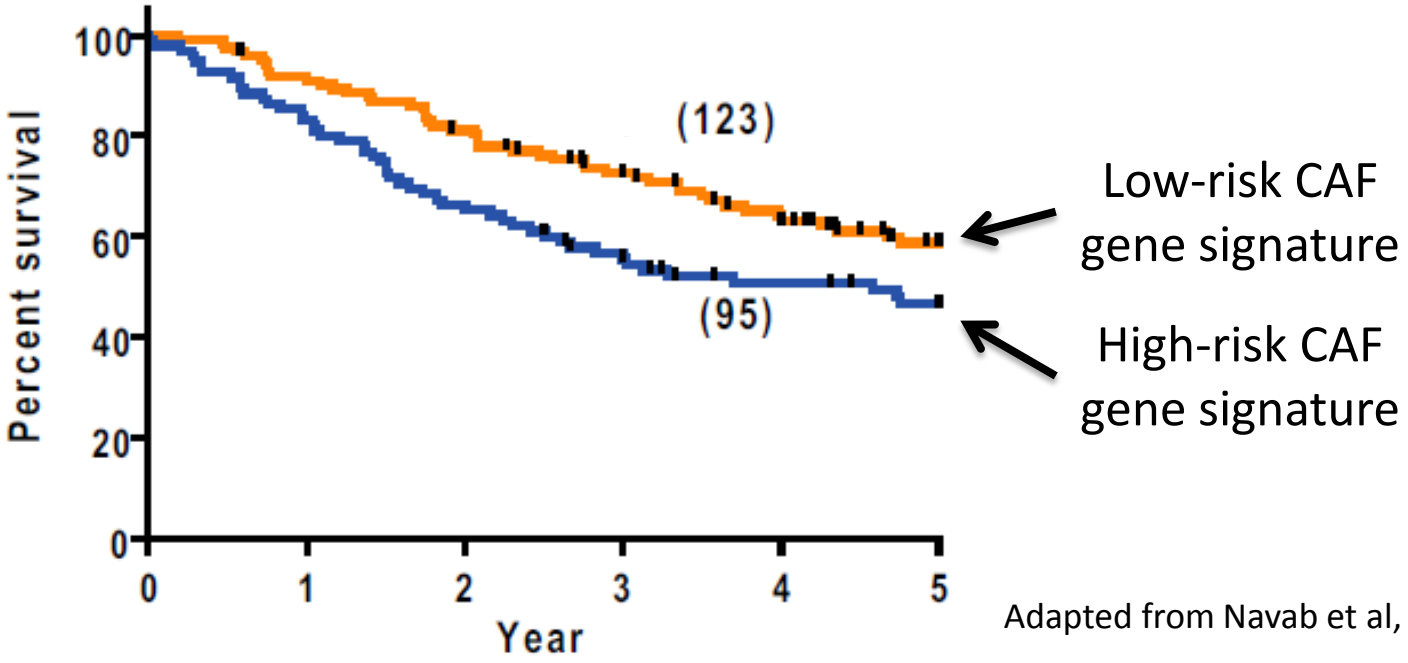
Cancer-Associated Fibroblasts



- Fibroblasts isolated from tumors have an “activated” phenotype
- CAFs, but not NFs, have been shown to be tumorigenic in animal models

Adapted from: Joyce JJ & Pollard JW. *Nature Reviews Cancer,* 2009

CAFs are associated with worse prognosis in NSCLC



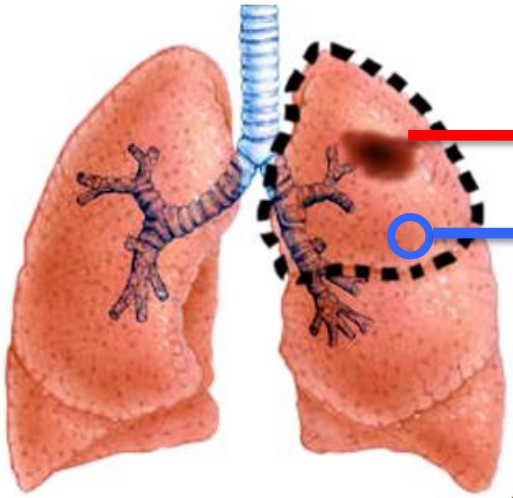
Adapted from Navab et al, *PNAS*, 2011.

- Mechanistic basis of CAFs' role in lung cancer is poorly understood
- Potential therapeutic target especially since they are genetically stable

Objective

- Define and characterize the tumor promoting ability of CAFs compared to normal lung and dermal fibroblasts from patients with NSCLC

Creation of Lung Tumor Cancer-Associated Fibroblast, Normal Fibroblasts, and Dermal Fibroblast Cell Lines



CAFs

> 5cm

NFs

DFs

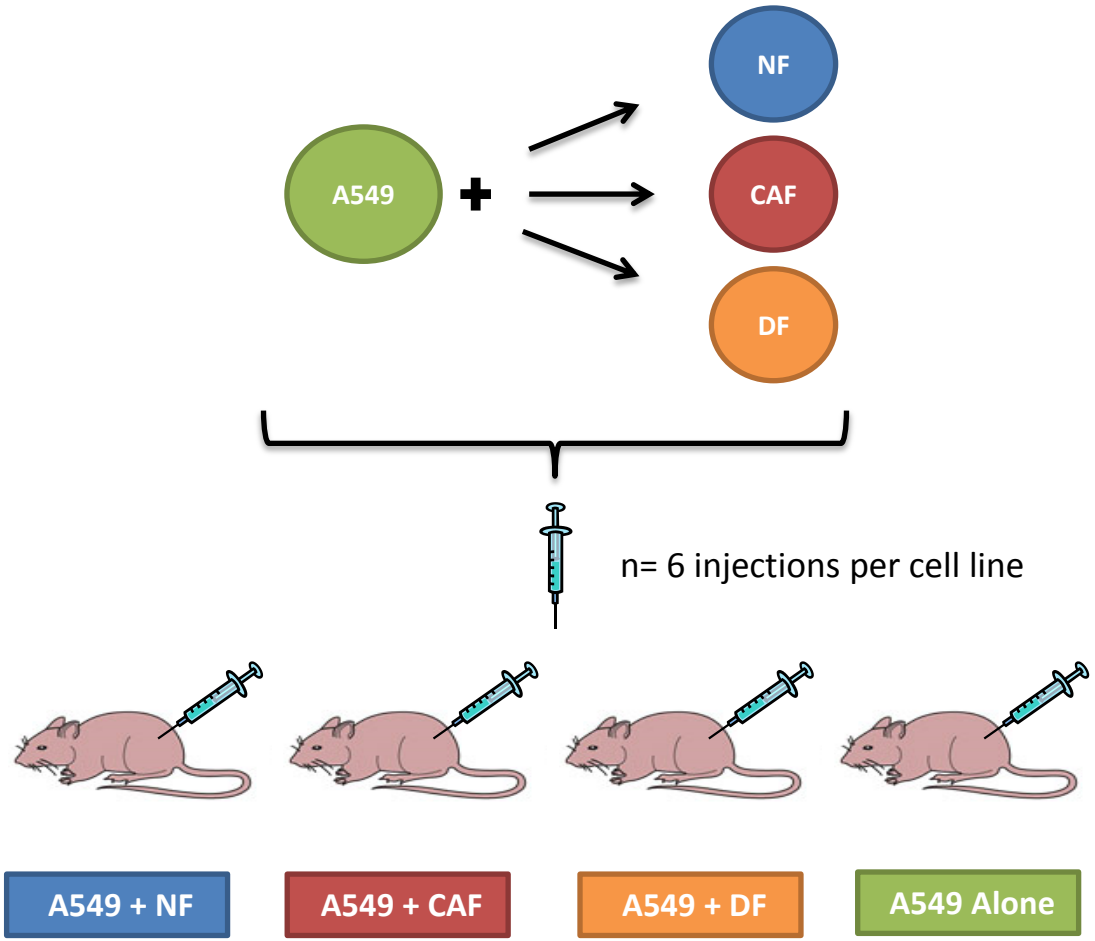
- Enzymatic & mechanical disruption of tissue.
- Plate cells from disrupted tissue.

Expand cells *in vitro*

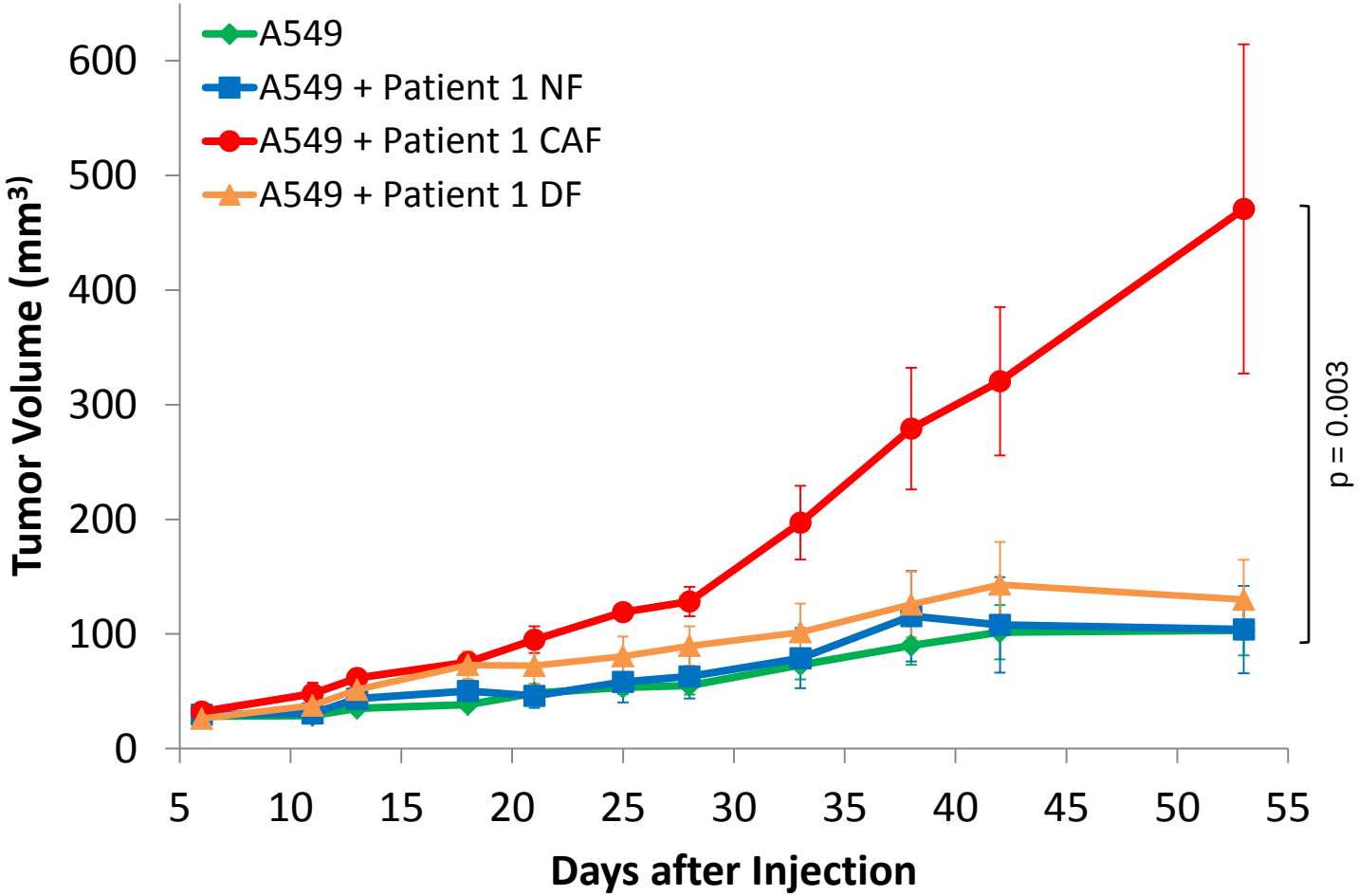
NF CAF DF

- *In vitro / in vivo* studies
- "-omic" studies
  - –Metabolomic
  - –Genomic
  - –Proteomic

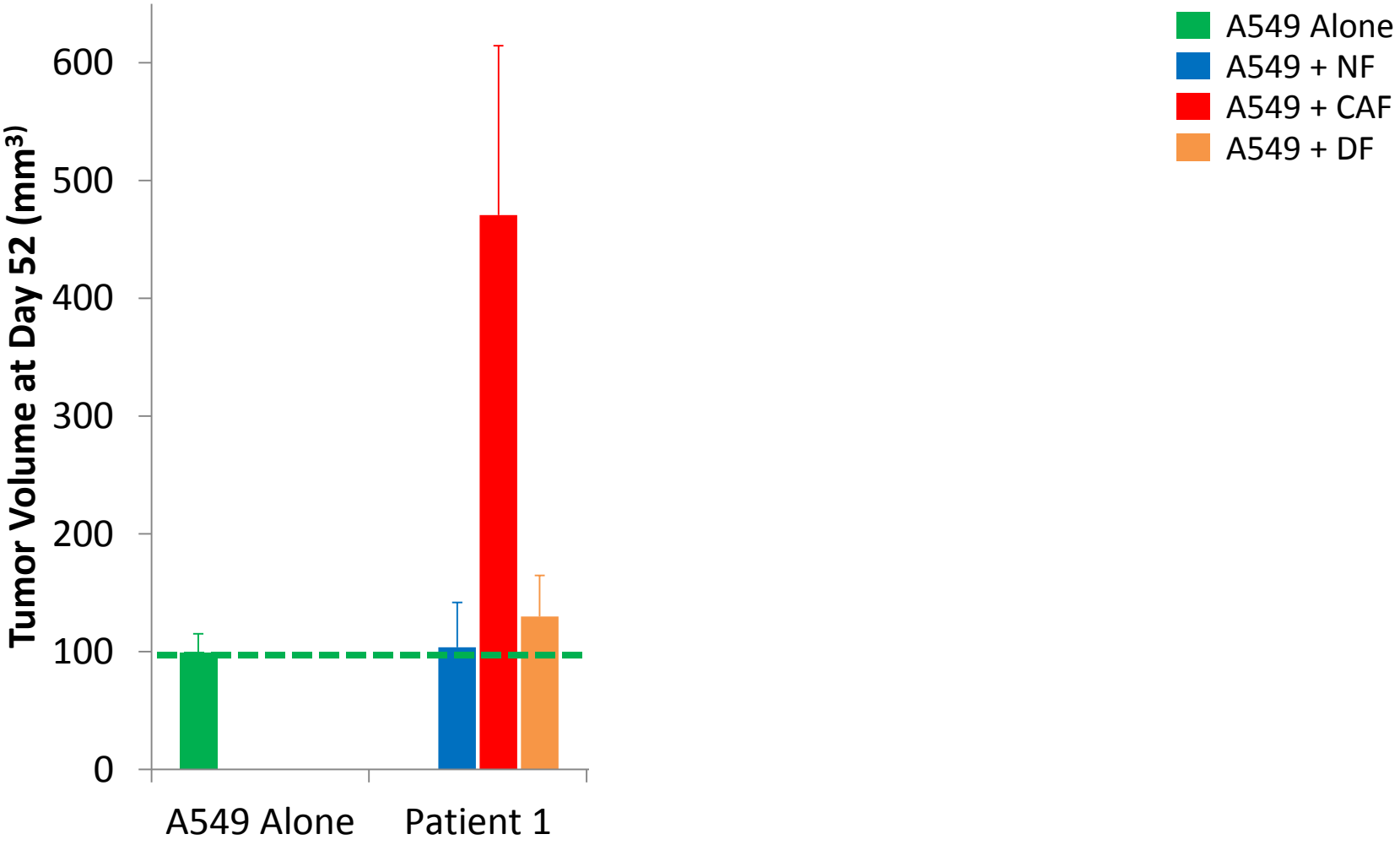
In vivo Tumorigenesis



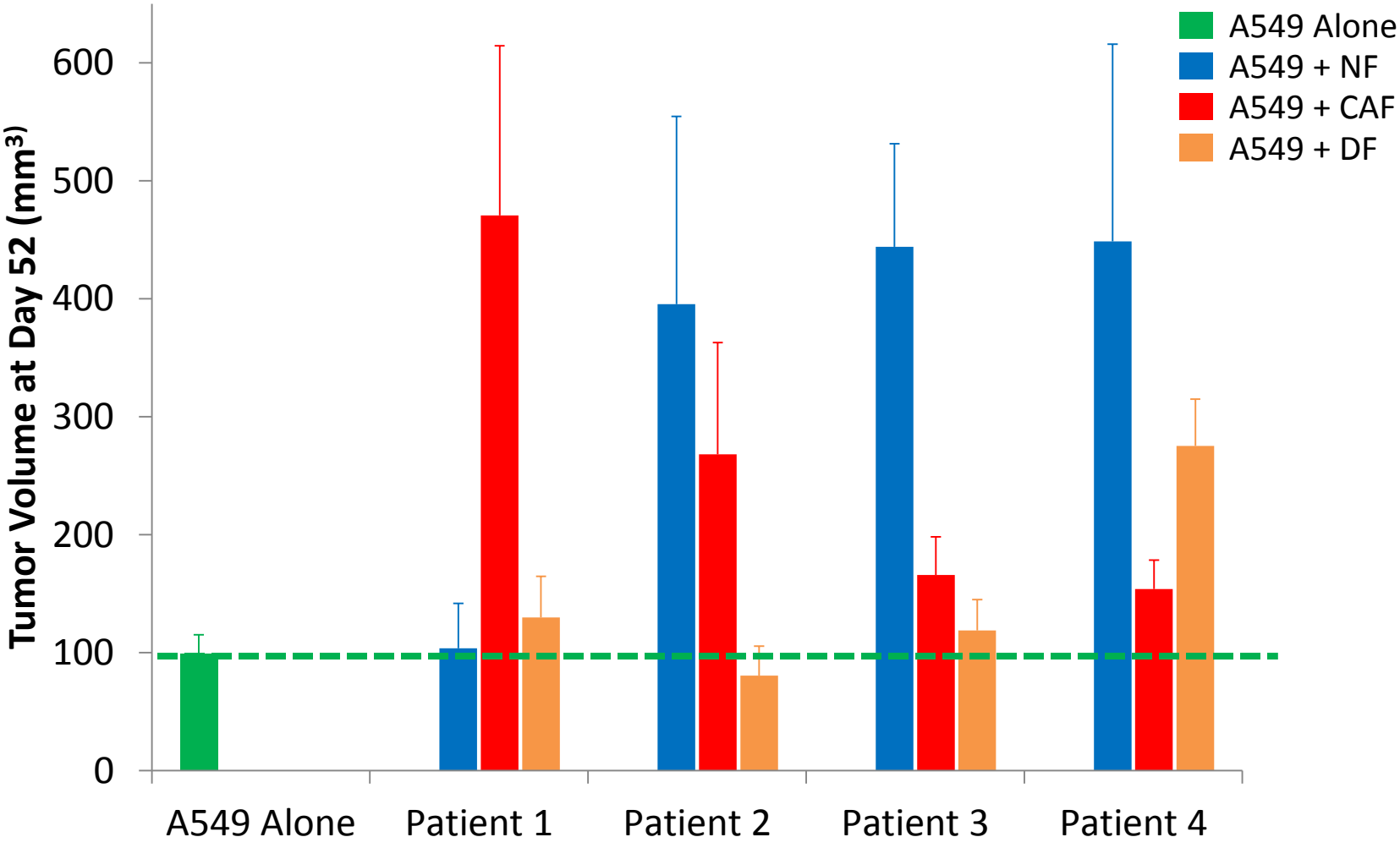
Tumor Growth



Tumor Volume at Day 52



Normal fibroblasts are also pro-tumorigenic

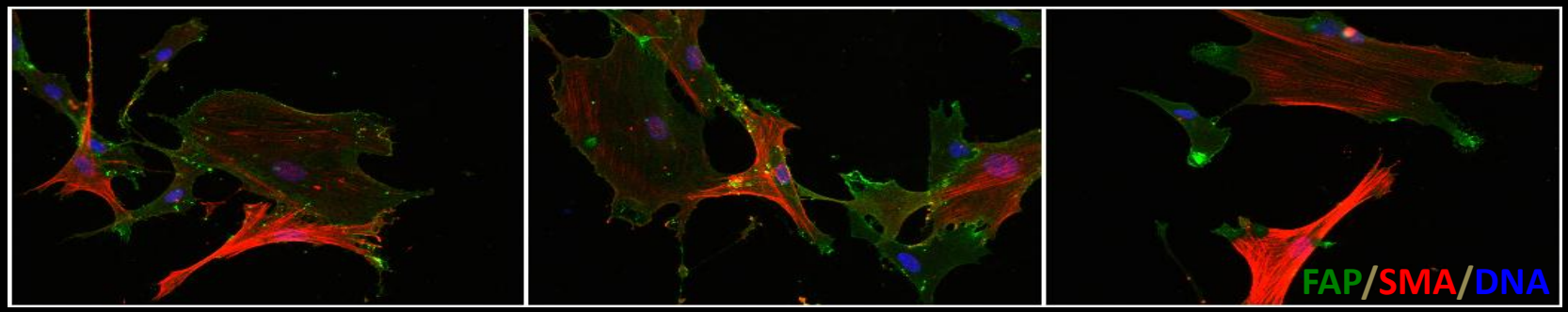


- Tumor-promoting activity is not limited to CAFs
  - Location from which fibroblasts come does not predict tumor-promoting activity

Is activation status related to pro-tumorigenic activity?

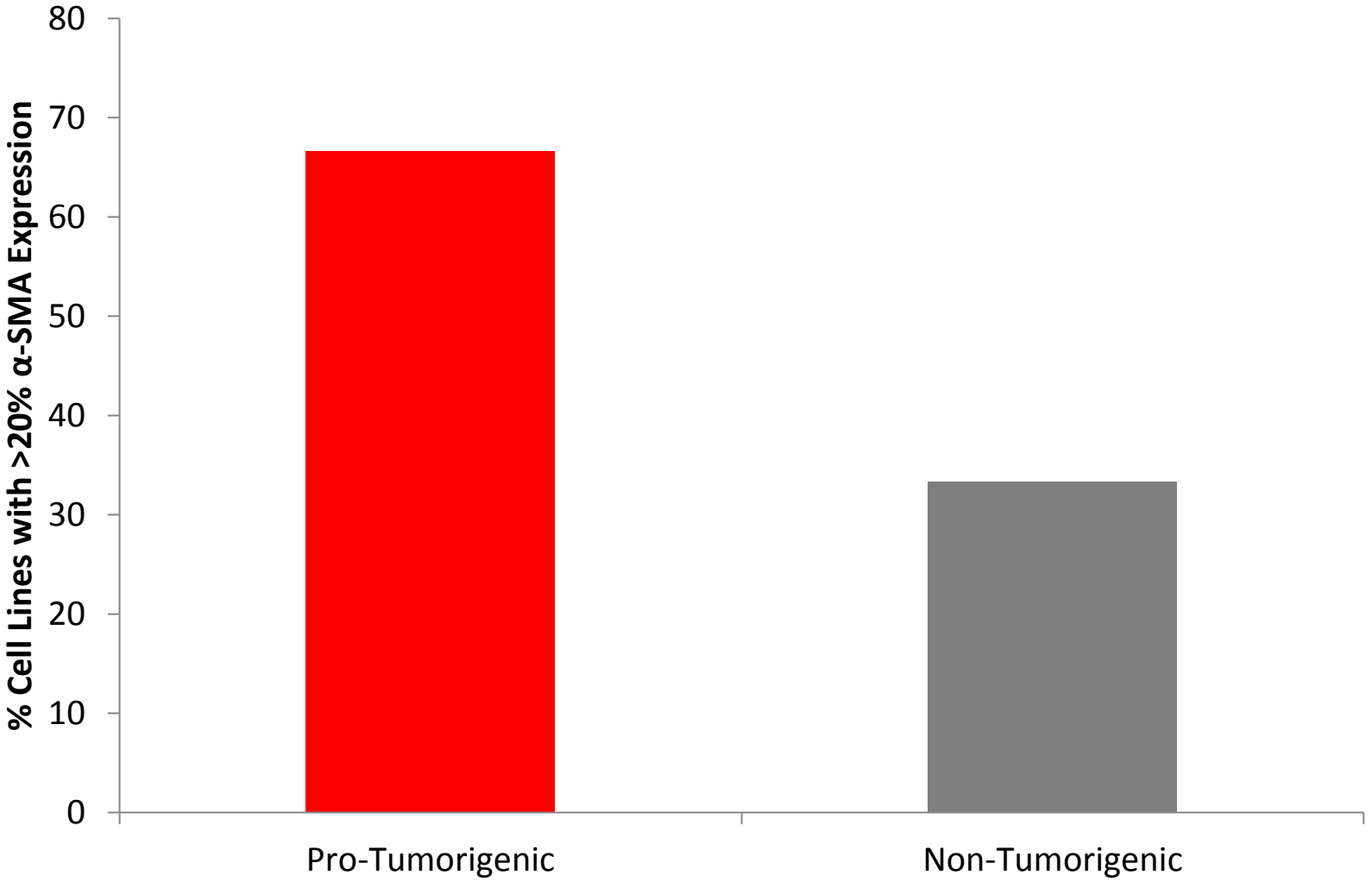
α-SMA Activation Status

CAF



- α-Smooth Muscle Actin (αSMA)
  - CAF marker in literature (“Activated” Fibroblasts)

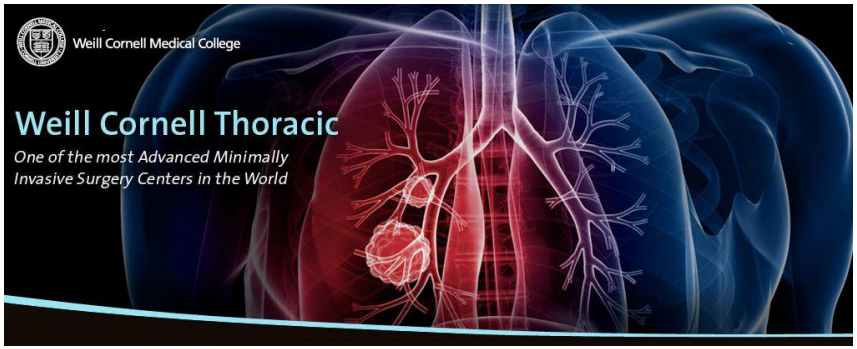
66% of pro-tumorigenic fibroblast cell lines have elevated α-SMA



Conclusions

- Fibroblasts should be grouped as non- or pro-tumorigenic instead of by isolation location
  - Future studies ("-omic," etc.) based on these groupings
- Activation status may better reflect tumor-promoting capability of fibroblast
- Significant heterogeneity exists among fibroblasts from patients with NSCLC

Acknowledgements



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