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## RATIONALE: Cav-1 regulates homeostasis METHODS: donor/IPF lung organoids

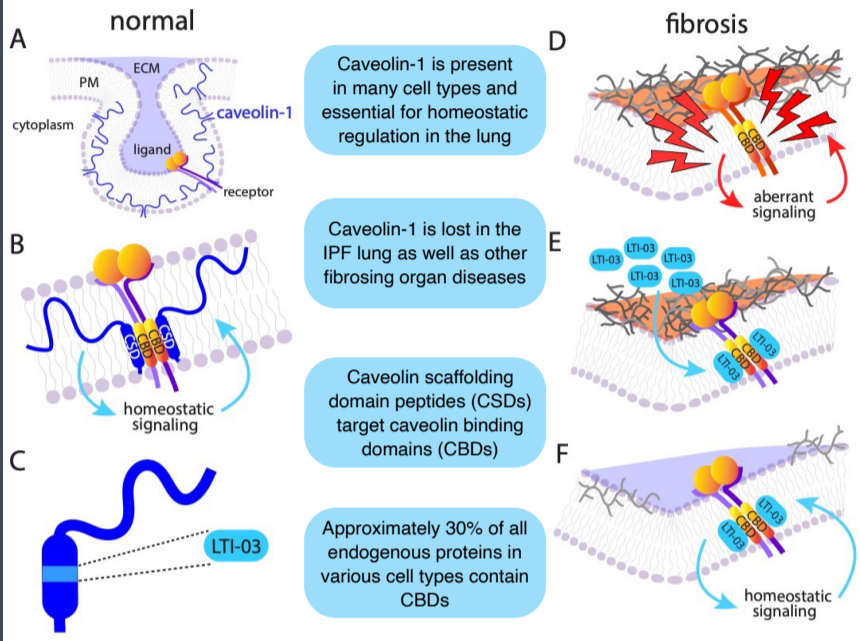
**1** CSD peptides replace the functional domain of Caveolin-1

Caveolin-1 Scaffolding Domain Peptides		
CSD	LTI-03	LTI-2355
molecular weight (Da)	815.92	1886.07
sequence	FTTFTVT	EGKASFTTFTVTKGS
solubility (pH 7.5)	1.43mg/mL	28.3mg/mL
formulation	excipient free dry powder	1. PBS - IP 2. PBS - SC-IR 3. novel-XR

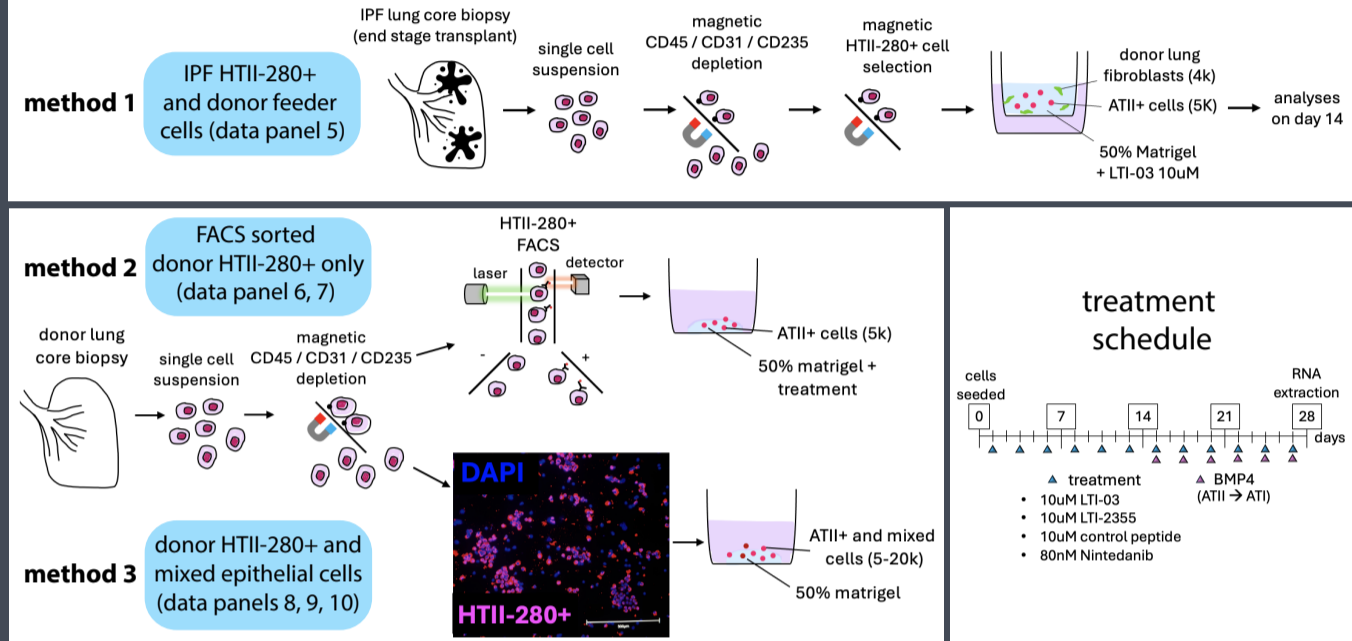
Caveolin-1: a critical regulator of lung fibrosis in idiopathic pulmonary fibrosis (IPF) and CTL

J Exp Med 2006 Dec 25;203(13):2895-906.

**2** Caveolin-1 protein is lost in the IPF lung; LTI-03 and LTI-2355 replace the homeostatic regulator domain (CSD) of Cav-1

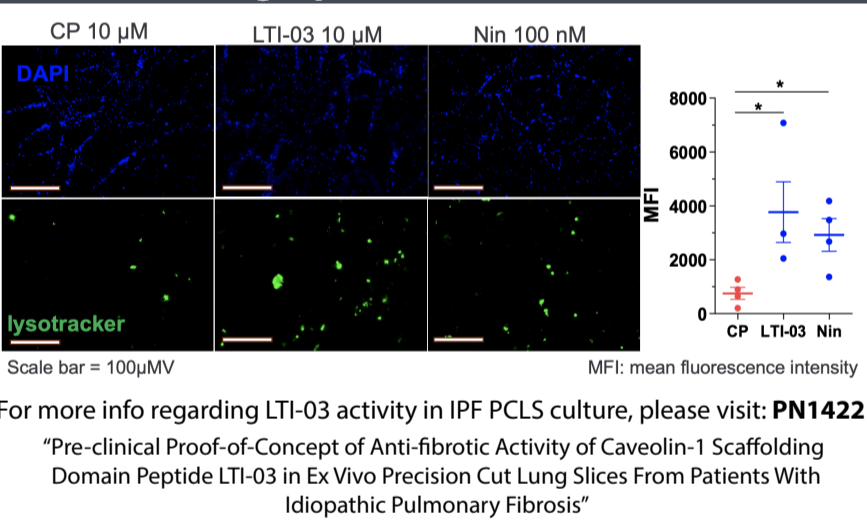


**3** Magnetic beat sorting or FACS were used to isolate IPF or donor lung epithelial cells which were grown in matrigel with or without donor fibroblast feeder cells

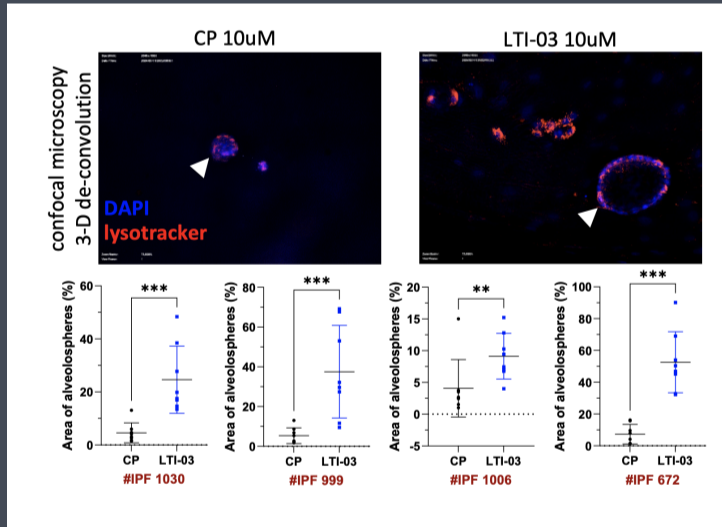


## DATA: CSD peptides sustain IPF and alveolar organoids

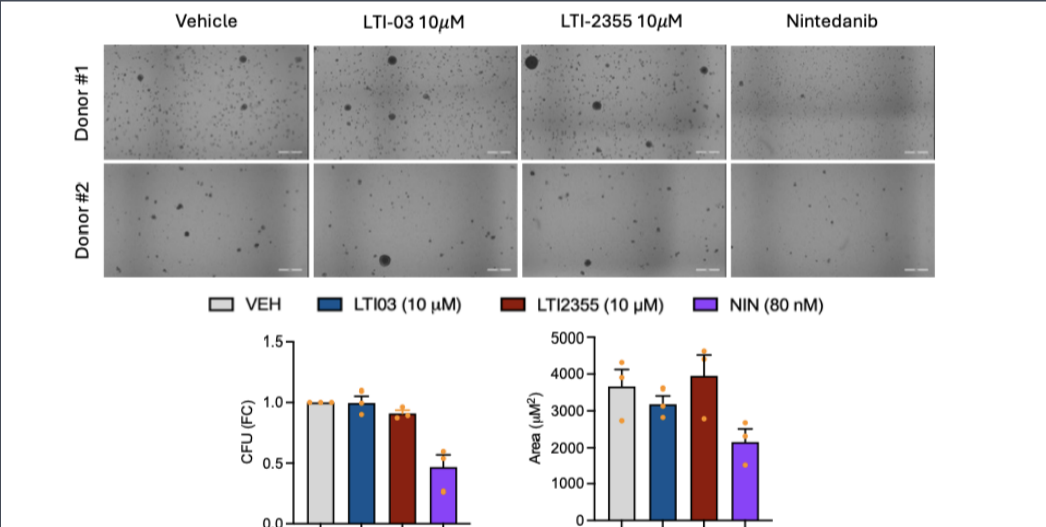
**4** LTI-03 increased lysotracker staining in IPF precision cut lung slices (PCLS) indicating a positive effect on AEC2 cells



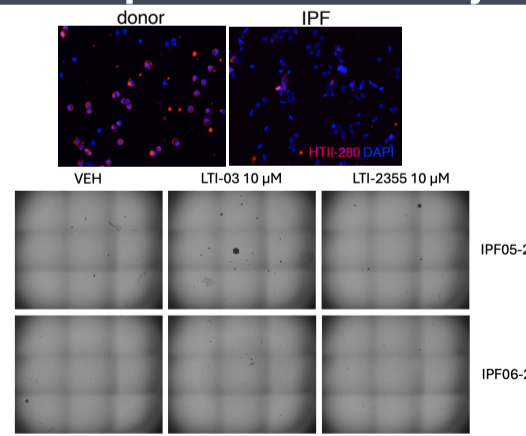
**5** LTI-03 treatment increased alveolar organoid area in 4 distinct IPF patients



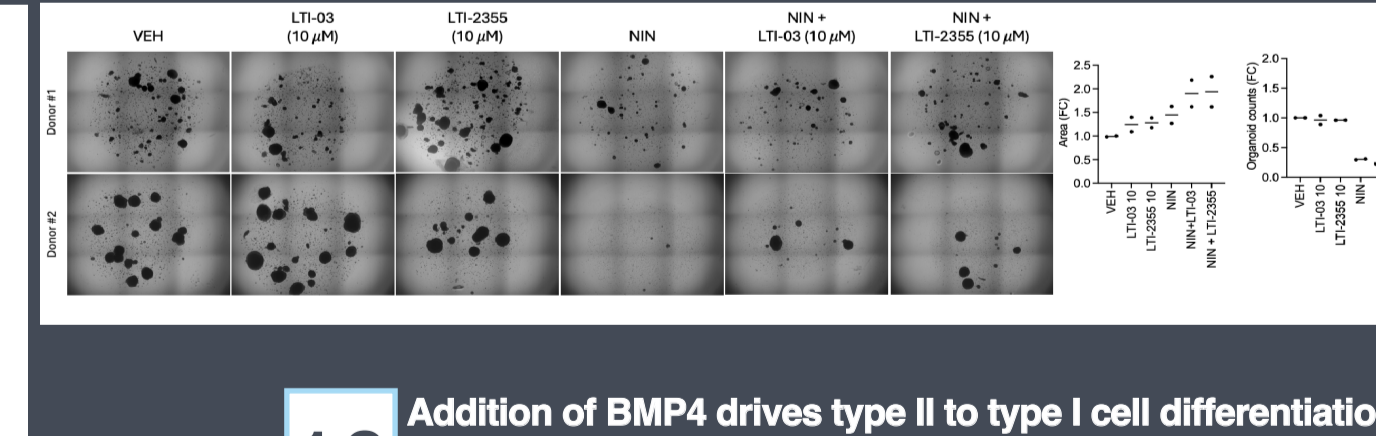
**6** Compared to LTI-03, Nintedanib impaired the growth of organoids in a fibroblast free donor lung organoid culture system



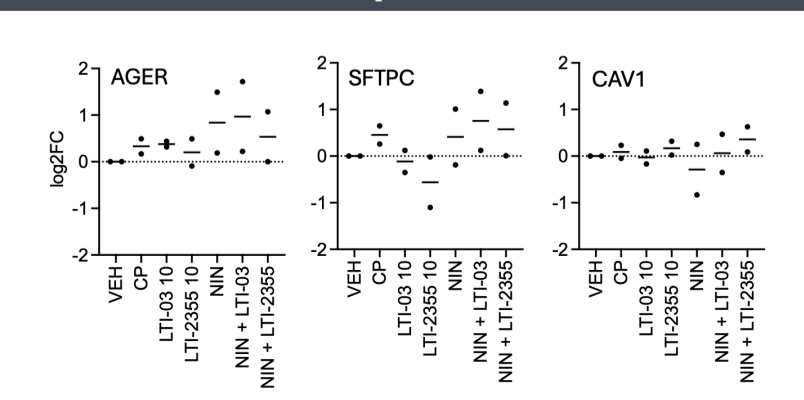
**7** AEC2 outgrowth did not occur in most IPF cell cultures due to poor epithelial cell recovery



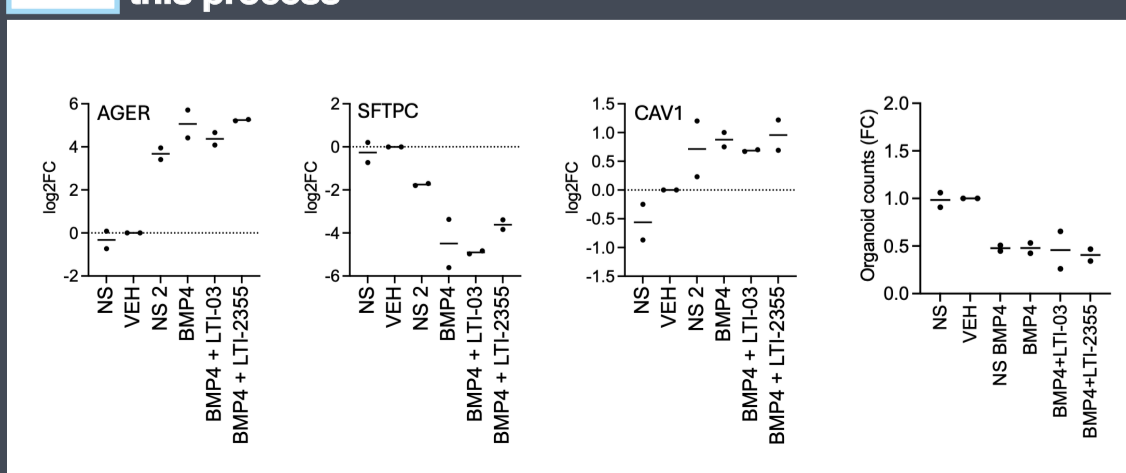
**8** CSDs sustained alveolar organoid outgrowth and appeared to counter inhibitory effects of Nintedanib on organoid growth



**9** CSD peptides increase type 1 and type II cell RNA in the presence of Nintedanib



**10** Addition of BMP4 drives type II to type I cell differentiation in normal lung organoids; CSD peptides did not impair this process



**11** CSD peptides sustain AEC2s in IPF cultures and do not inhibit AEC2 to AEC1 differentiation in donor lung organoids

