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Early Human Insights

人类精确切割组织切片：
药物开发和疾病研究的转化模型

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临床前合同研究组织（CRO）

➤ 通过人体组织评估疗法，以推动项目进入IND阶段

◆ **成立于2009年** —— 由科学家创办

◆ **总部位于加利福尼亚州圣地亚哥**

◆ **高级管理团队具备以下经验：**

➤ 大型制药和生物技术研发

➤ 合同研究组织（CRO）

AnaBios 与监管机构及国家卫生与科学研究院密切合作

- 已与超过350家制药企业及高等科研机构建立合作关系
- 共发表48篇经同行评审的科学研究论文

AnaBios 与监管机构及国家卫生与科学研究院密切合作

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- 共发表48篇经同行评审的科学研究论文

frontiers in Physiology

ORIGINAL RESEARCH
published: 19 December 2017
doi: 10.3389/fphys.2017.01073

Adult Human Primary Cardiomyocyte-Based Model for the Simultaneous Prediction of Drug-Induced Inotropic and Pro-arrhythmia Risk

*Nathalie Nguyen, William Nguyen, Brynna Nguyenton, Phachareeya Ratchada, Guy Page, Paul E. Miller, Andre Ghetti and Najah Abi-Gerges**

AnaBios Corporation, San Diego, CA, United States

frontiers in Physiology

ORIGINAL RESEARCH
published: 05 January 2018
doi: 10.3389/fphys.2017.01109

Action Potential Recording and Pro-arrhythmia Risk Analysis in Human Ventricular Trabeculae

Yusheng Qu[1], Guy Page[2], Najah Abi-Gerges[2], Paul E. Miller[2], Andre Ghetti[2] and Hugo M. Vargas[1]*

[2] AnaBios Corporation,

PNAS RESEARCH ARTICLE PHARMACOLOGY

Modulation of human dorsal root ganglion neuron firing by the Nav1.8 inhibitor suzetrigine

Robert G. Stewart[a,1], Tomás Osorno[a,1], Akie Fujita[a,1], Sooyeon Jo[a,1], Alyssa Ferraiuolo[b], Kevin Carlin[b], and Bruce P. Bean[a,2]

Contributed by Bruce P. Bean; received February 14, 2025; accepted April 16, 2025; reviewed by Robert W. Gereau and Stephen G. Waxman

Nav1.8 voltage-gated sodium channels are strongly expressed in human primary pain-sensing neurons (nociceptors) and a selective Nav1.8 inhibitor VX-548 (suzetrigine) has shown efficacy for treating acute pain in clinical trials express other sodium channels, notably Nav1.7, raising the que

Significance

frontiers Frontiers in Molecular Neuroscience

TYPE Original Research
PUBLISHED 05 October 2023
DOI 10.3389/fnmol.2023.1258823

Check for updates

OPEN ACCESS

EDITED BY
Martin Schmelz,
Heidelberg University, Germany

REVIEWED BY
Masanori Fujii,
Kyoto Pharmaceutical University, Japan
Jing Feng,
Shanghai Institute of Materia Medica (CAS), China

Type 2 cytokines sensitize human sensory neurons to itch-associated stimuli

Madison R. Mack[1]*, Yannick Miron[2], Fanny Chen[2], Paul E. Miller[2], Annie Zhang[3], Andrew Korotzer[4], Daniel Richman[3] and Paul J. Bryce[1]

[1]Immunology and Inflammation Research Therapeutic Area, Sanofi, Cambridge, MA, United States,

Systems/Circuits

The Cancer Chemotherapeutic Paclitaxel Increases Human and Rodent Sensory Neuron Responses to TRPV1 by Activation of TLR4

Tan Li, Pavel Adamek, Haijun Zhang, Claudio Esteves Tatsui, Lawrence D. Rhines, Petra Mrotkova, Qin Li, Alyssa K. Kosturakis, Ryan M. Cassidy, Daniel S. Harrison, Juan P. Cata, Kenneth Supiro, Hongmei Zhang, Rose M. Kennamer-Chapman, Abdul Basit Jawad, Andre Ghetti, Jiusheng Yan, Jiri Palecek, and Patrick M. Dougherty

www.nature.com/scientificreports

scientific reports

Check for updates

OPEN **Arrhythmogenic and antiarrhythmic actions of late sustained sodium current in the adult human heart**

Anh Tuan Ton[1,2], William Nguyen[1,2], Katrina Sweat[1,2], Yannick Miron[1], Eduardo Hernandez[1], Tiara Wong[1], Valentyna Geft[1], Andrew Macias[1], Ana Espinoza[1], Ky Truong[1], Lana Rasoul[1], Alexa Stafford[1], Tamara Cotta[1], Christina Mai[1], Tim Indersmitten[1], Guy Page[1], Paul E. Miller[1], Andre Ghetti[1] & Najah Abi-Gerges[1]

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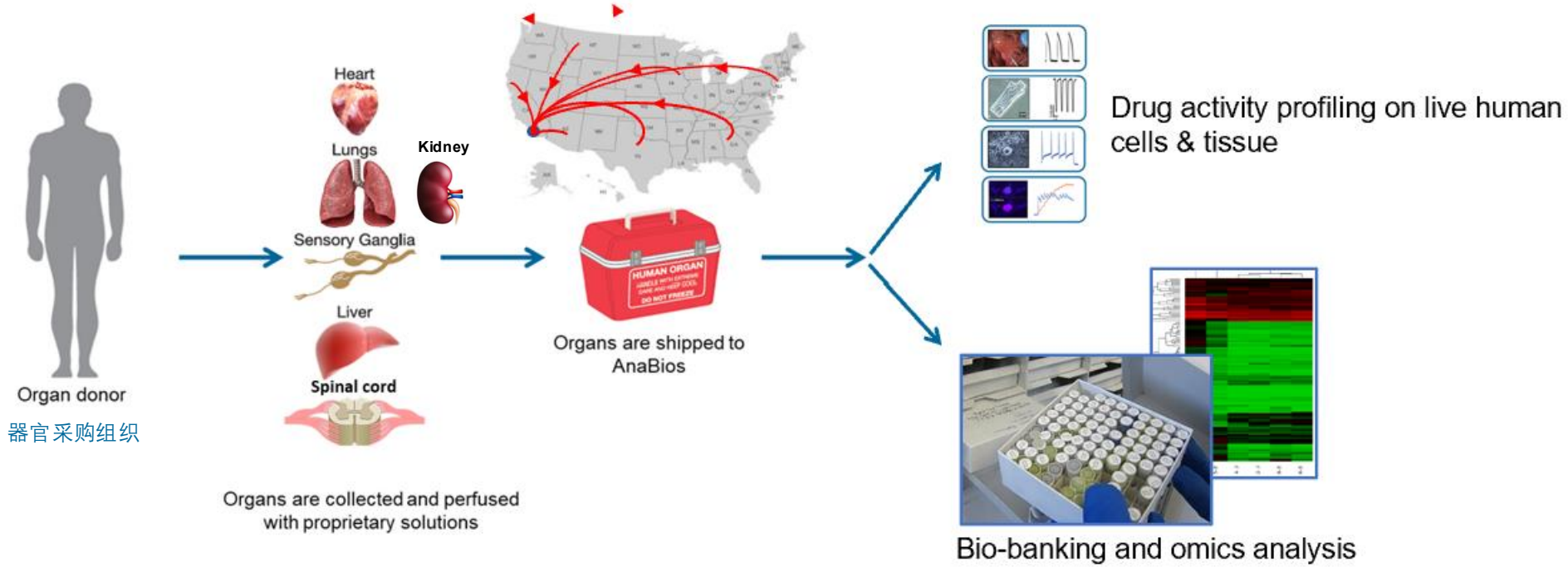
美国食品药品监督管理局（FDA）和国家卫生研究院（NIH）推动以人为本的新药物测试方向

- **美国食品药品监督管理局（FDA）新闻发布（2025年4月）**
  📌 链接：https://www.fda.gov/news-events/press-announcements/fda-announces-plan-phase-out-animal-testing-requirement-monoclonal-antibodies-and-other-drugs
- *“**今日，美国食品**药品监督管理局迈出了具有里程碑意义的一步，旨在通过采用**更高效、与人体更相关的方法，逐步取代在开**发单克隆抗体疗法和其他药物过**程中**对动物的测试，以推动公共健康的发展。”*

- **◆ 美国国家卫生研究院（NIH）新闻发布（2025年4月）**
  📌 链接：https://www.nih.gov/news-events/news-releases/nih-prioritize-human-based-research-technologies
- *“**美国国家**卫生研究院（NIH）**正在启**动一项全新倡议，以扩大创新型、以人为**本的科学研究，并减少**对动物的使用。”*

AnaBios 专有的人体组织获取技术

推动人体转化科学发展



- 方法标准化
- 避免缺血与再灌注损伤
- 高容量器官获取网络
- 每个器官均有详细注释

减少制药行业的损耗
从动物模型转向预测性人源模型

动物模型

- 超过90%的损耗率
- 缺乏预测能力
- 安全性与有效性数据无法转化为人类结果
- 早期药物发现预测不准确
- 无法反映人类生物学和疾病

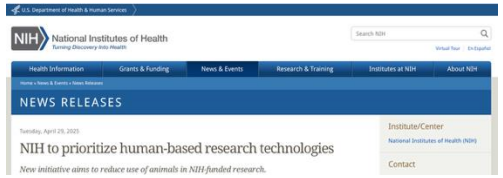
人体模型

- 更可能反映人类生物学和疾病
- 人类数据弥合了与临床试验之间的差距
- 深入了解患者对新疗法的潜在反应
- 监管机构关注以人为本的模型

2025年及以后临床前药物发现的未来

Human-based Models

通量



https://www.nih.gov/news-events/news-releases/nih-prioritize-human-based-research-technologies

生物相关性

FDA Roadmap to Reducing Animal Testing in Preclinical Safety Studies

https://www.fda.gov/media/186092/download?attachment

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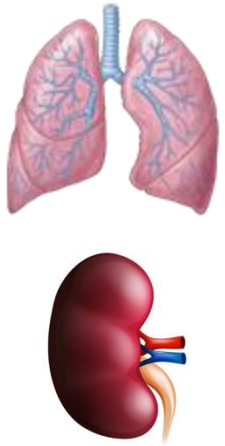
人类肺/肾精准切割组织切片模型

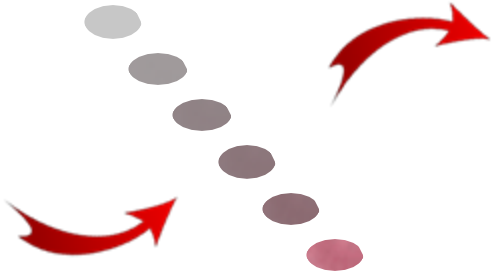
提供正常与病变供体的肺和肾组织

PCLS/PCKS 制备流程

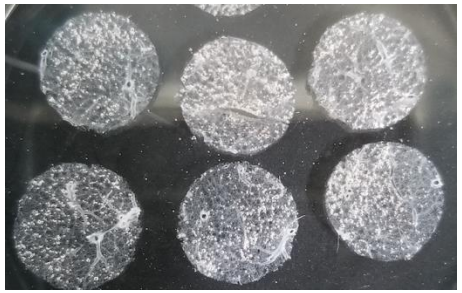


获取供体肺/肾

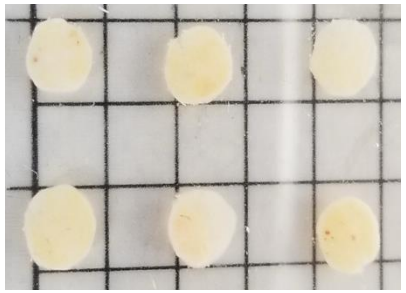
振荡切片



切片培养或冷冻保存



肺切片（PCLS）：350/450微米厚度，5或10毫米直径



肾切片（PCKS）：350微米厚度，5或10毫米直径

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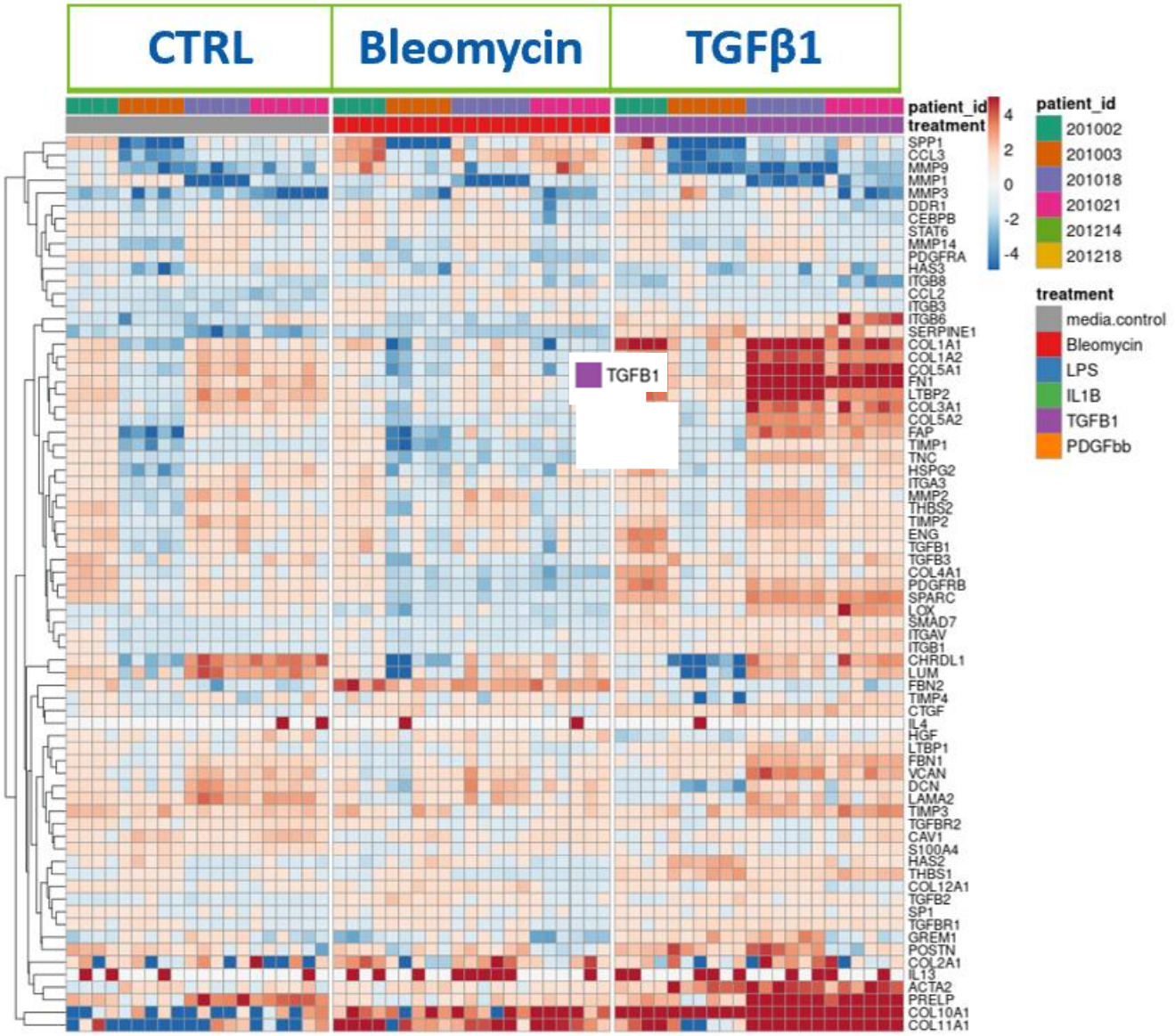
人类PCLS模型实验数据

通过RNA表达分析评估纤维化调控因子的响应机制

正常人类PCLS模型

（PCLS = 精准切割肺组织切片，Precision-Cut Lung Slices）



Bleomycin
(10 μM, 0.06 Unit)

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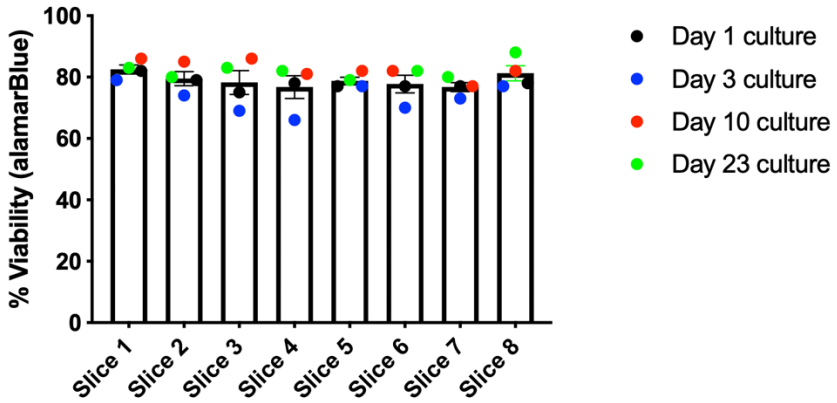
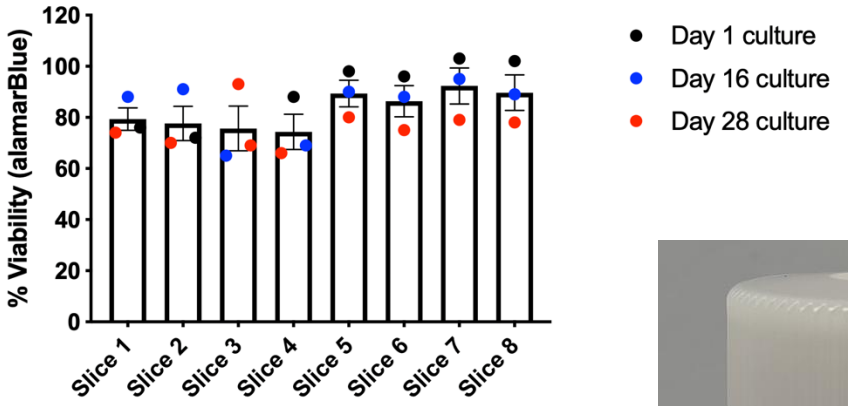
长期活力：alamarBlue™ 细胞活力数据（正常供体）

Donor 1



Donor 2



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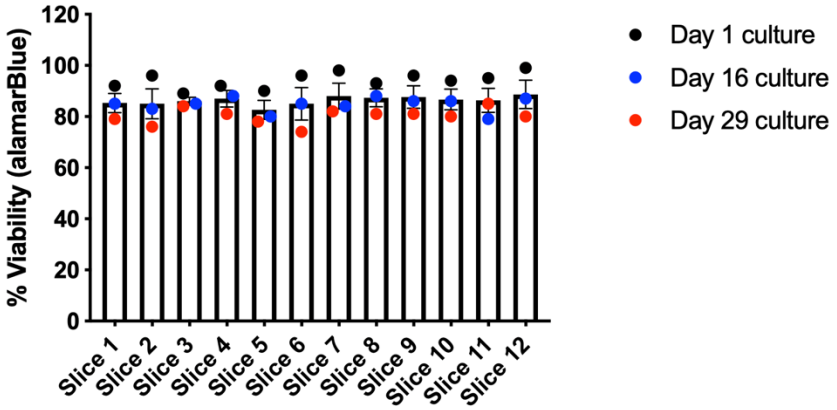
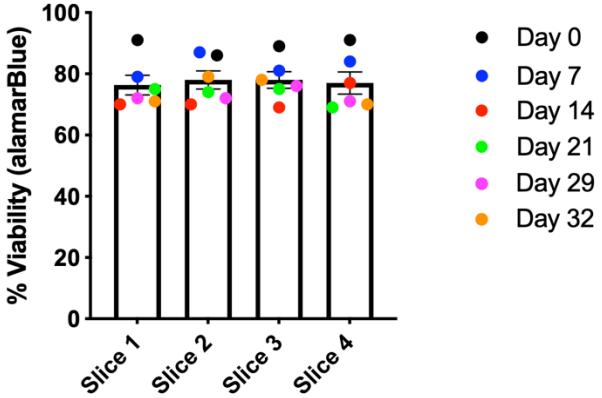


Donor 4



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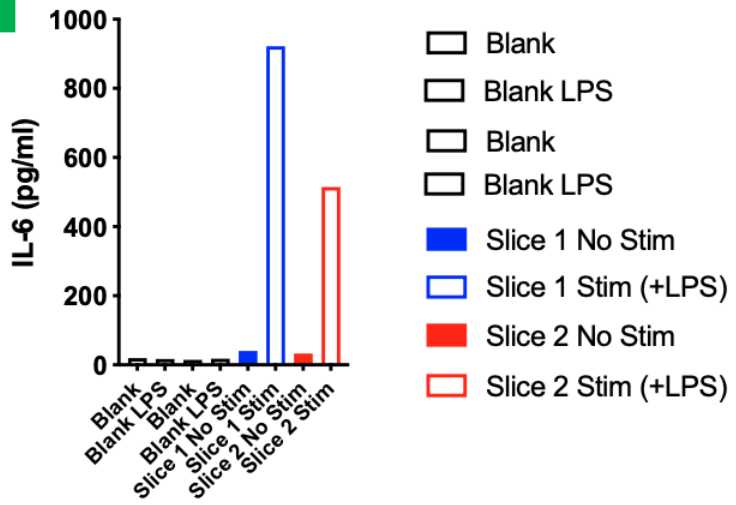
炎症反应：LPS刺激后24小时 IL-6水平检测 (正常供体)
正常供体 - 人肺精准切割组织切片（PCLS）培养上清液 - 处理5天

Donor 1



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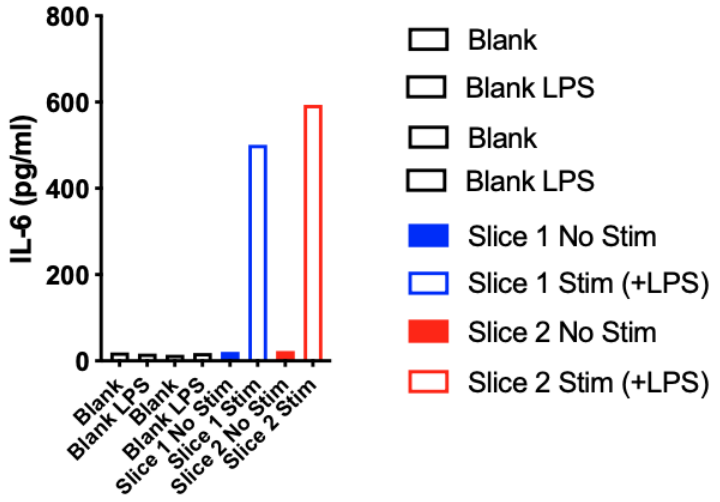

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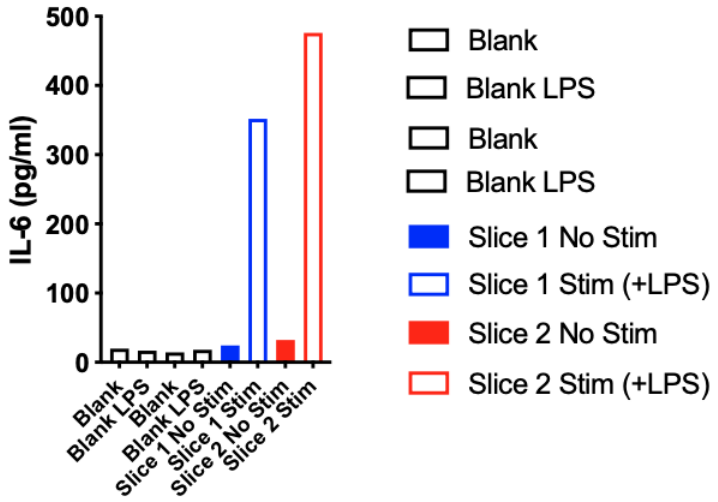

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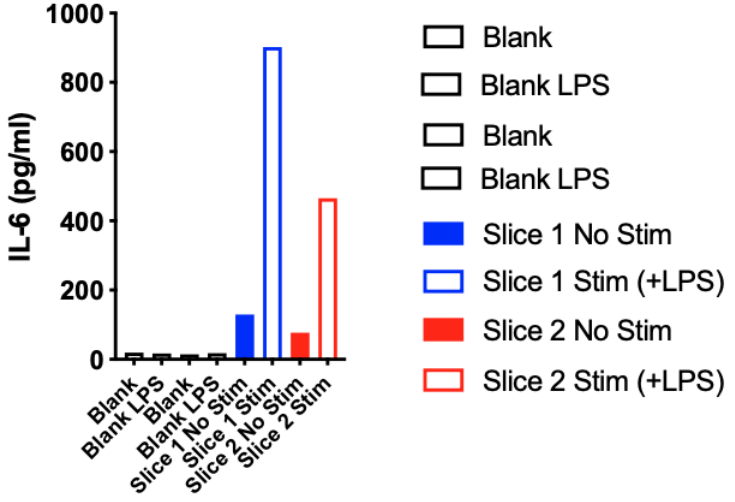

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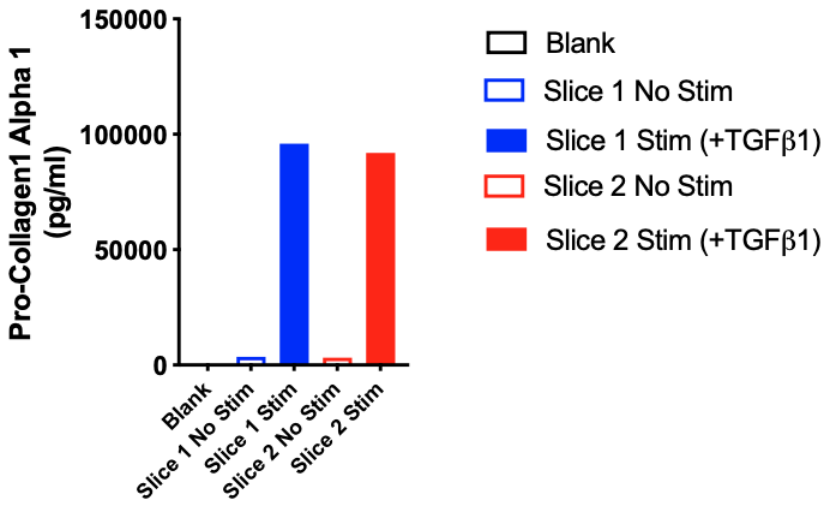
TGF-β1刺激 - 前胶原蛋白1水平 - 纤维化反应
正常供体 - 人肺精准切割组织切片（PCLS）培养上清液 - 处理5天

Donor 1



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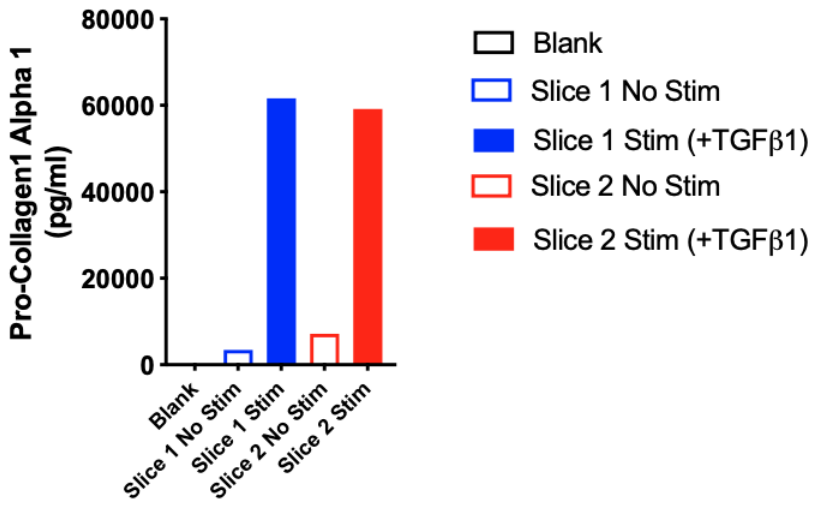

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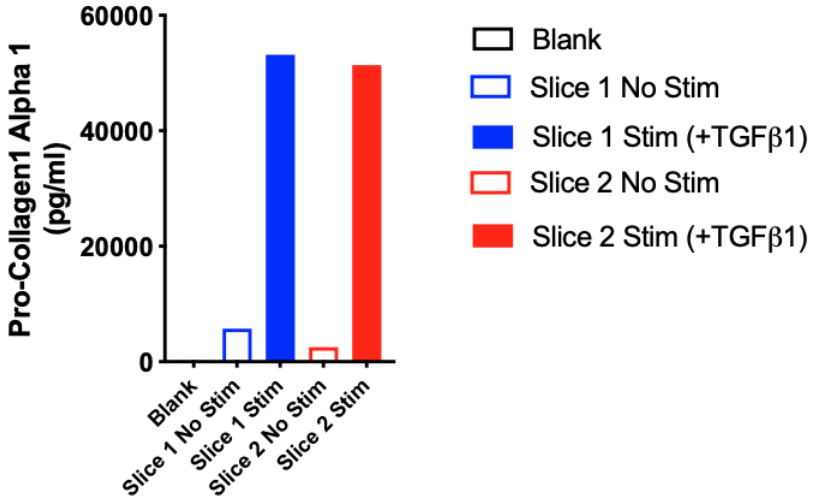

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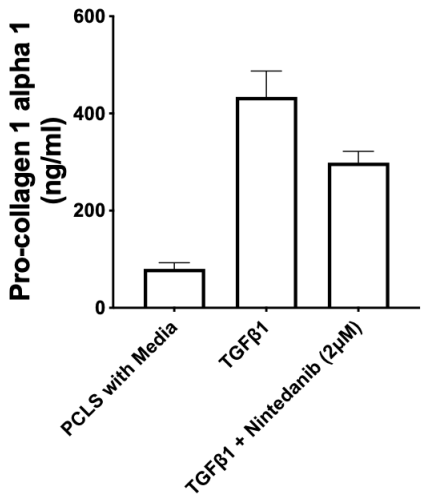
尼达尼布 (Nintedanib) 调节TGF-β1诱导的前胶原蛋白1α1水平升高
正常供体 - 人肺精准切割组织切片（PCLS）培养上清液 - 处理5天

Donor 1



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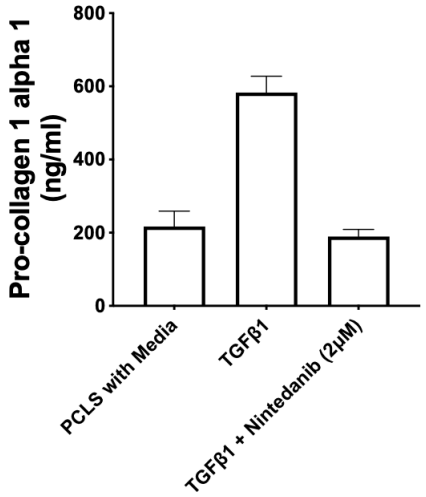

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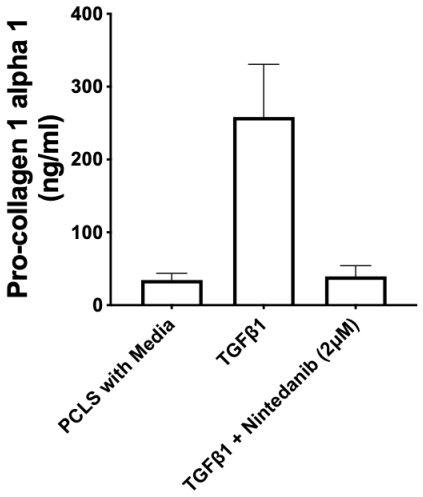

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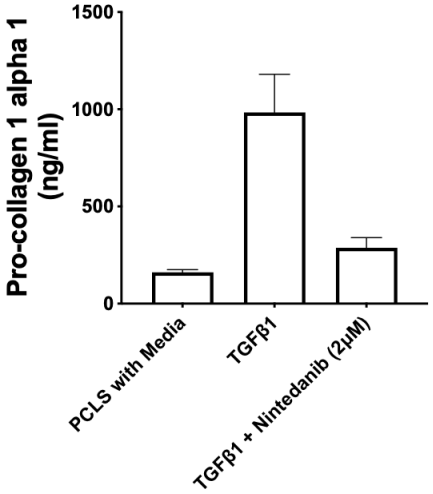

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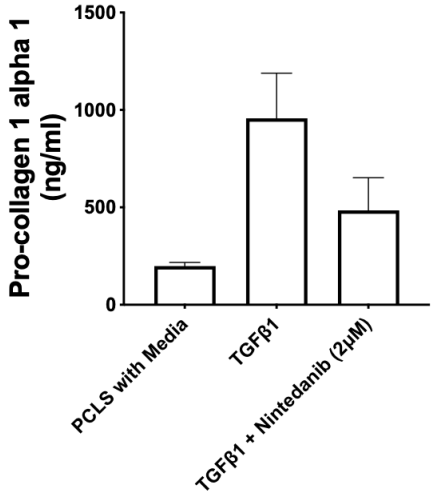

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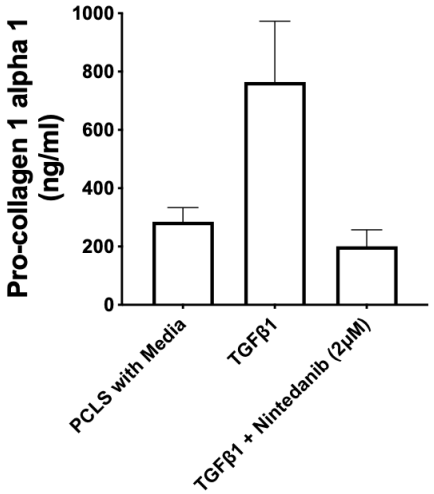

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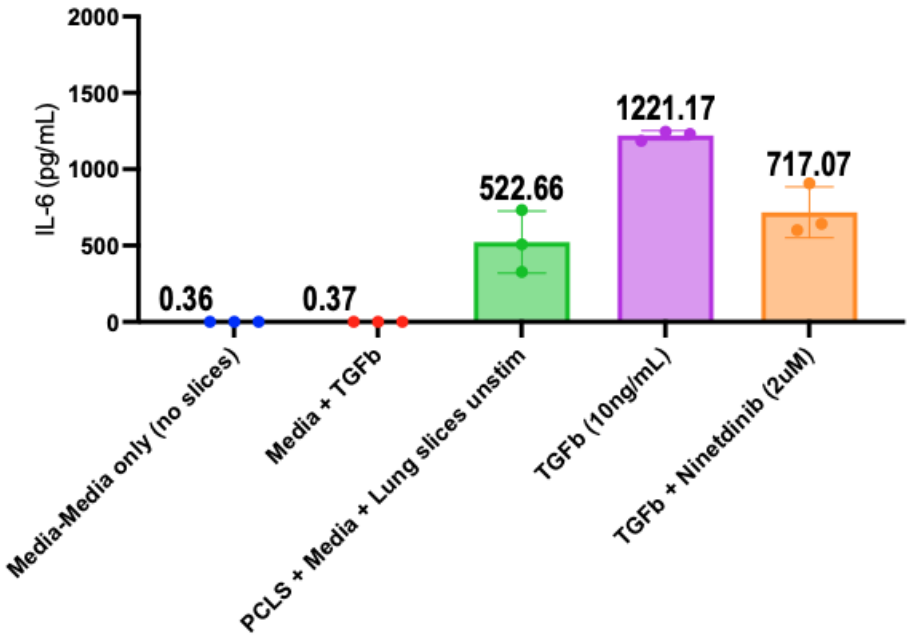
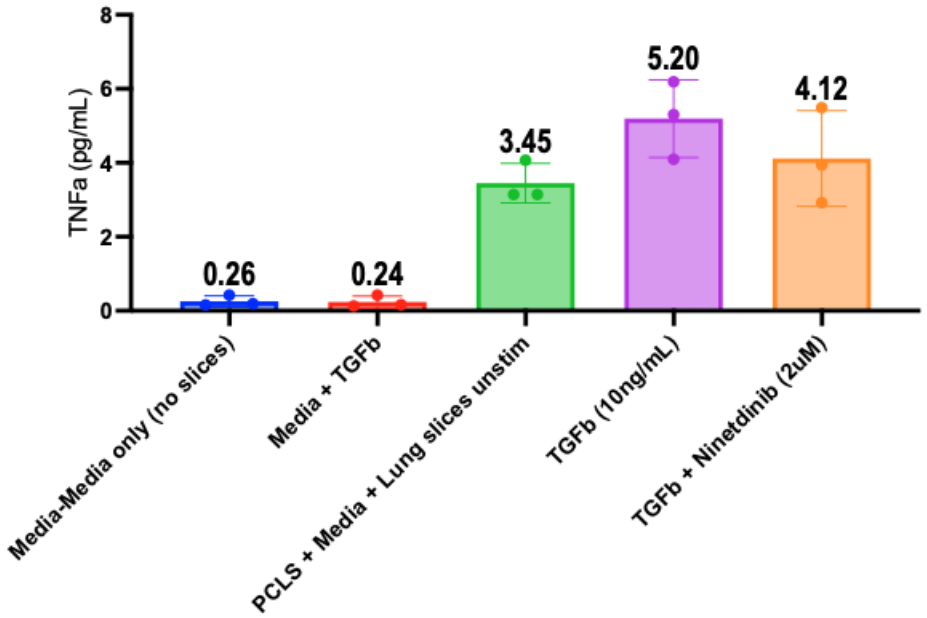
尼达尼布(Nintedanib) 调节TGF-β1诱导的细胞因子表达上调
正常供体 - 人肺精准切割组织切片（PCLS）培养上清液 - 处理5天 – 与制药公司合作





PCLS不仅可用于评估新疗法的抗纤维化潜力，还可提供机制性洞察。

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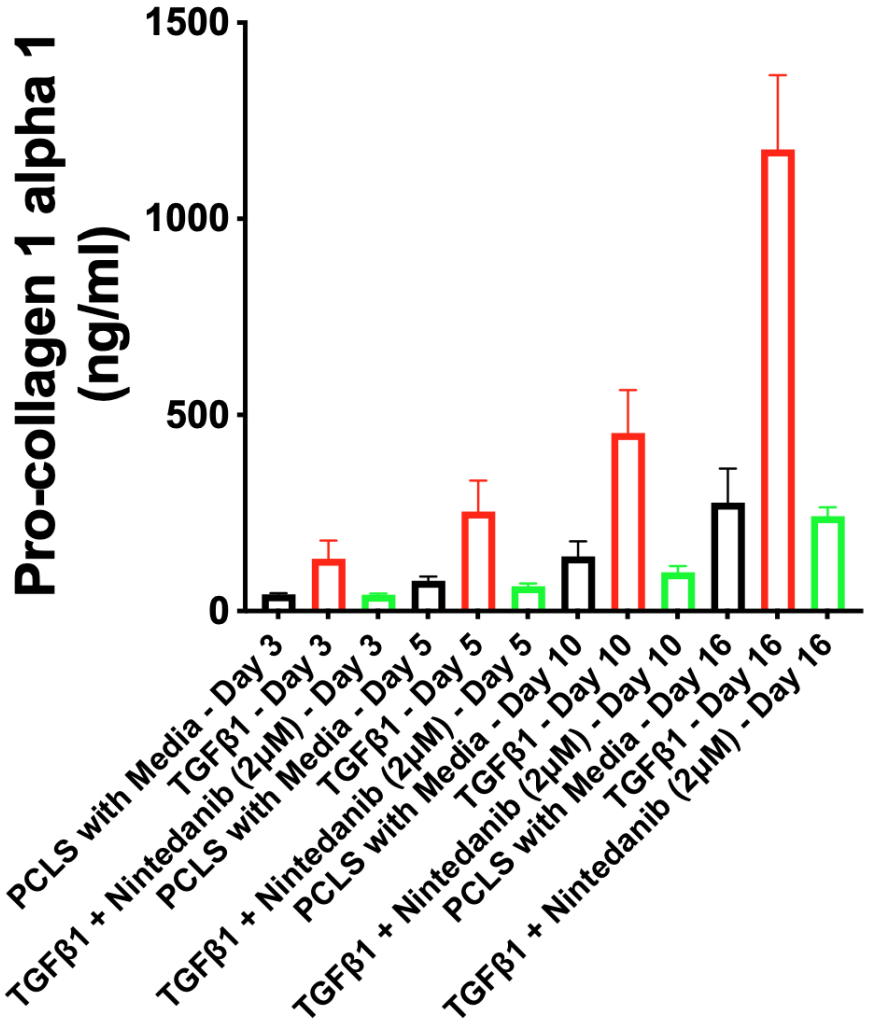
尼达尼布(Nintedanib) 调节TGF-β1诱导的胶原蛋白1α1水平升高
正常供体 - 人肺精准切割组织切片（PCLS）培养上清液 - 多日处理



不同的时间窗口可为每种治疗方式提供足够时间以发挥其抗纤维化作用。

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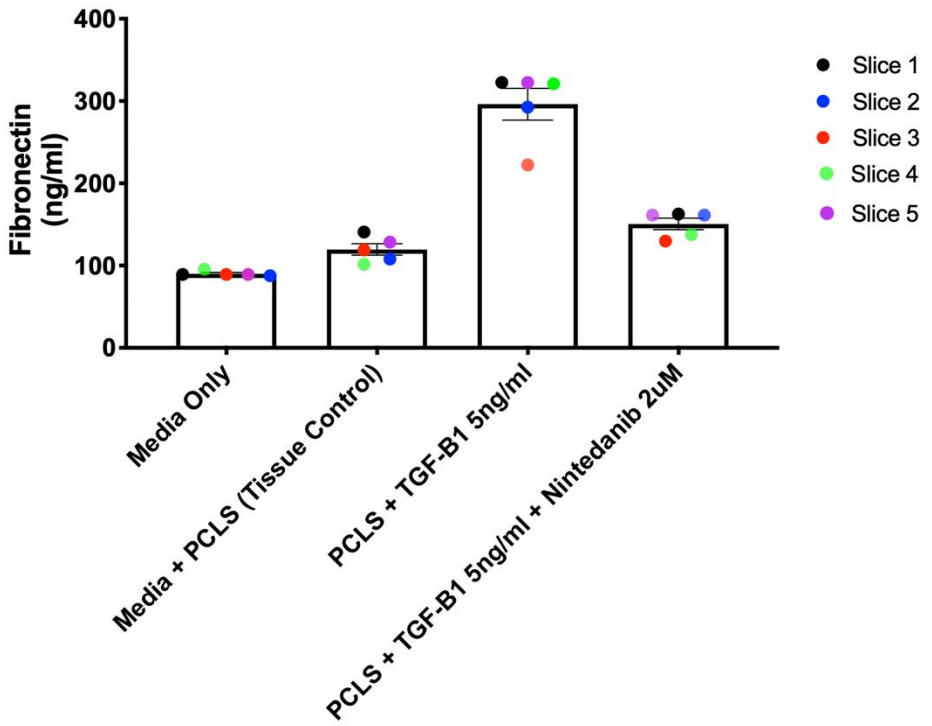
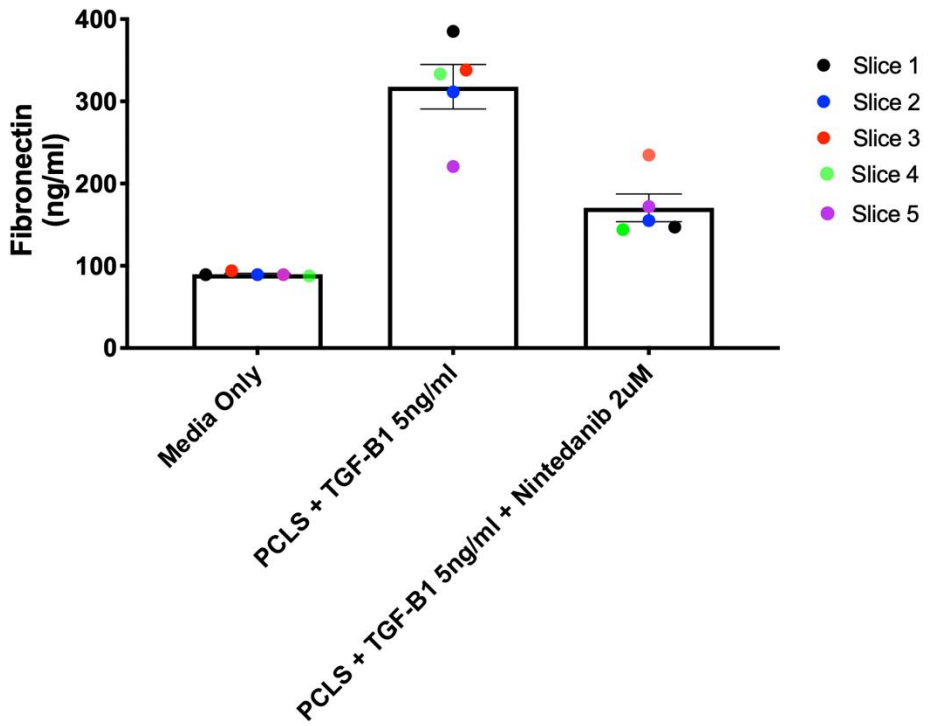
Nintedanib 尼达尼布调节TGF-β1诱导的纤维连接蛋白（Fibronectin）水平升高
正常供体 - 人肺精准切割组织切片（PCLS）培养上清液 - 处理5天

供体 1



供体 2



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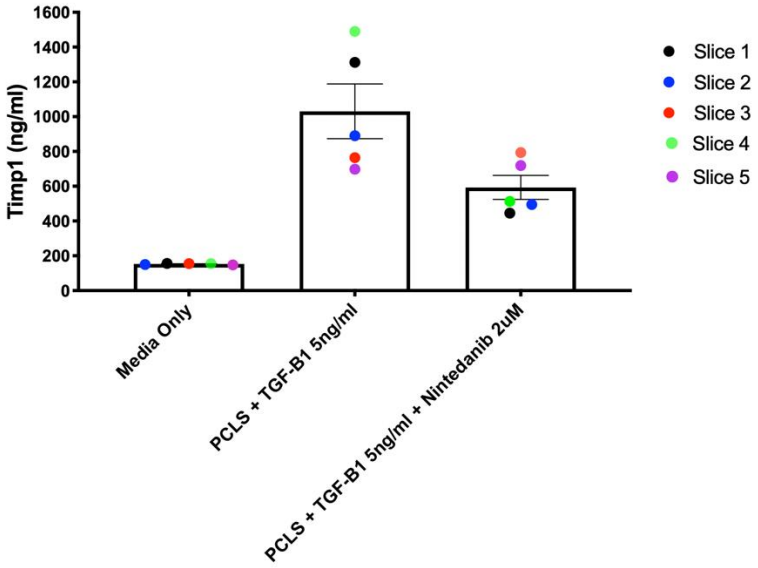
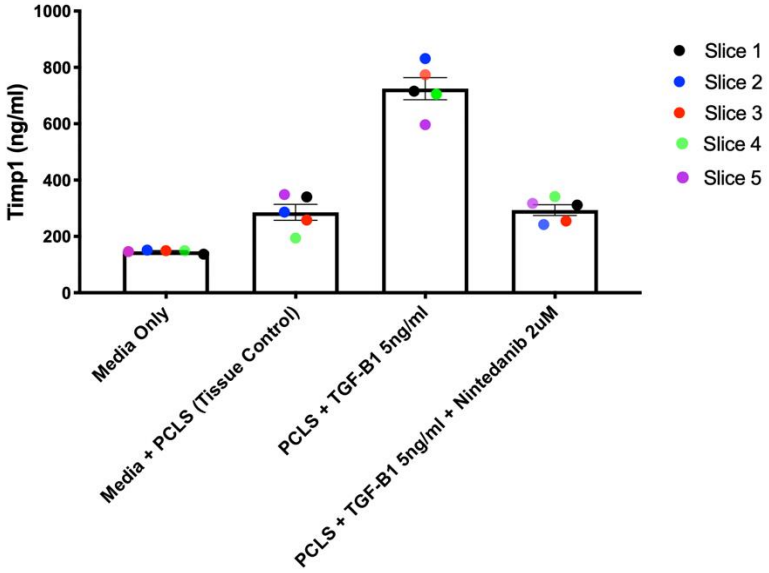
Nintedanib 尼达尼布调节TGF-β1诱导的Timp1水平升高
正常供体 – 人肺精准切割组织切片（PCLS）培养上清液 – 处理5天

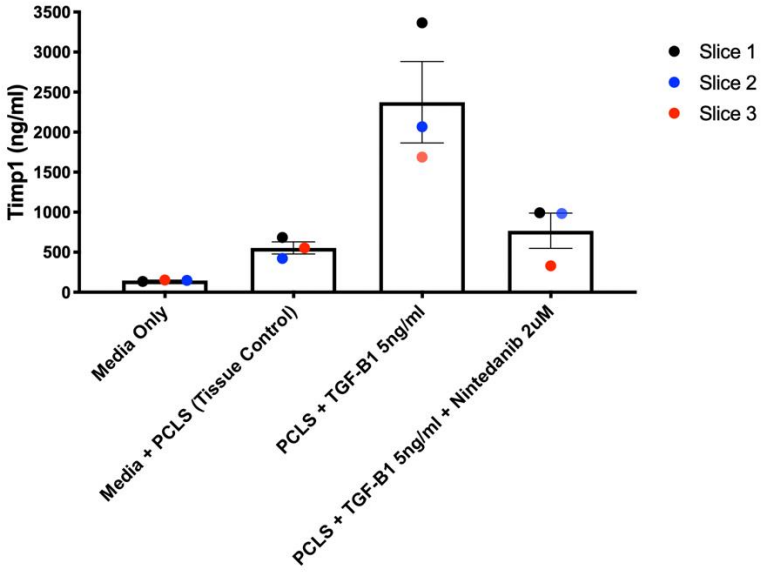
供体 1



供体 2

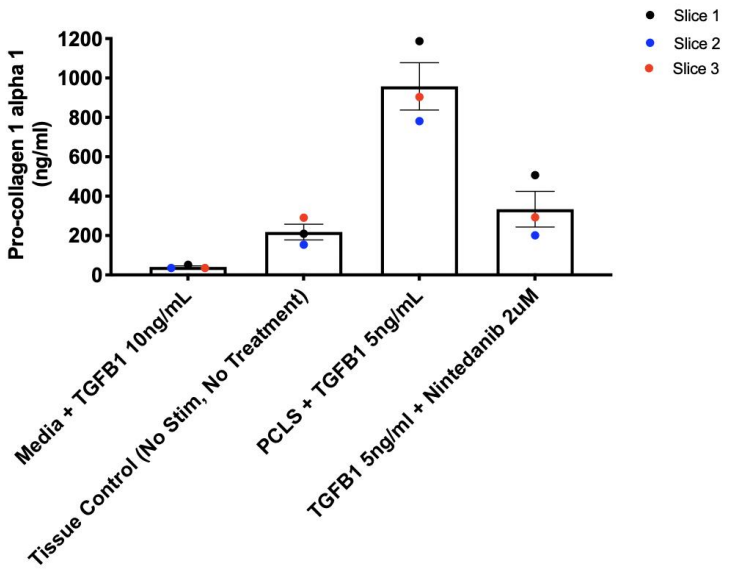


供体 3

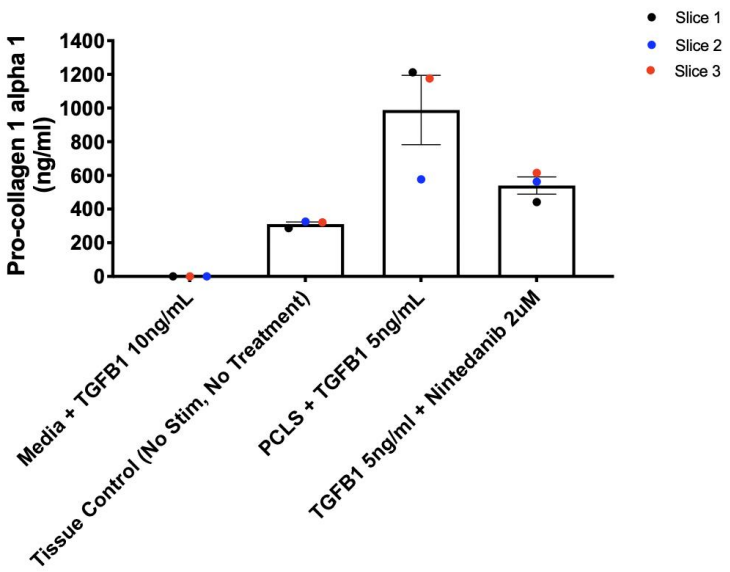


尼达尼布调节TGF-β1诱导的胶原蛋白1α1水平升高
正常供体 - 运输但未冷冻保存 的人肺精准切割组织切片（PCLS）培养上清液 - 处理5天 （本地运输而已）

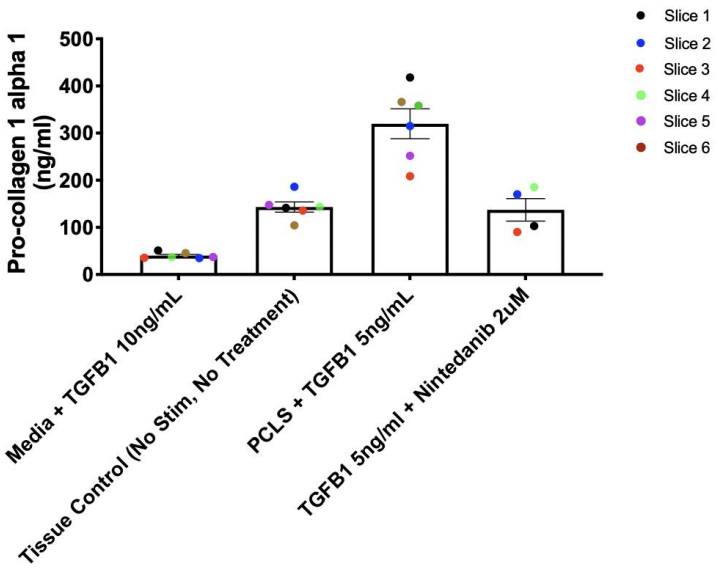
供体1 – 圣地亚哥 / 佛罗里达航班



供体1 – 圣地亚哥 / 芝加哥航班

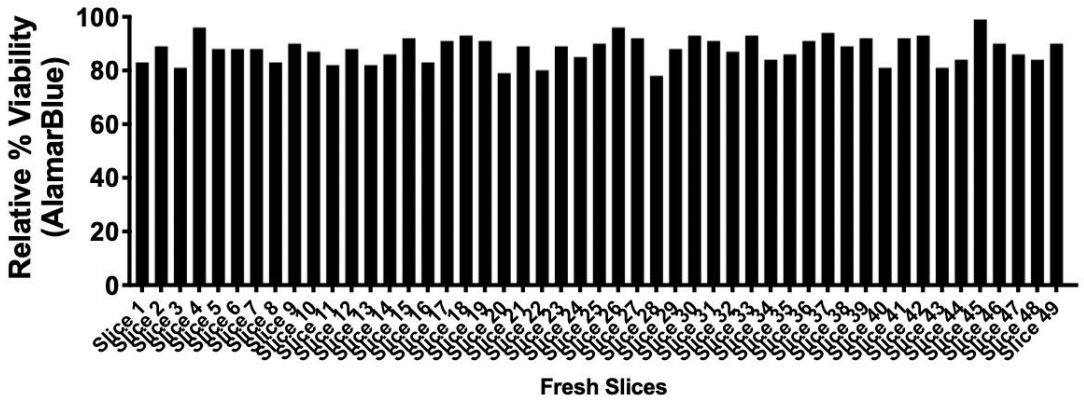


供体2 – 圣地亚哥 / 芝加哥航班

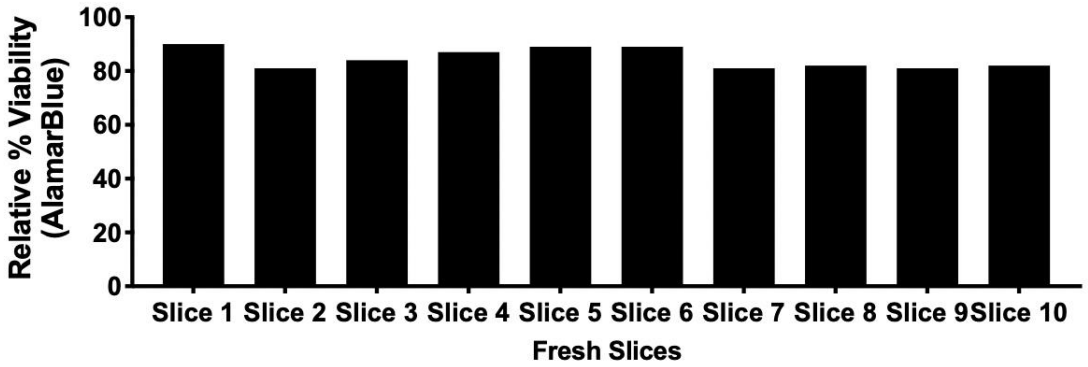


运输但未冷冻保存的组织保持高活性
正常供体 – 运送前后活性评估

Pre-Shipment Test

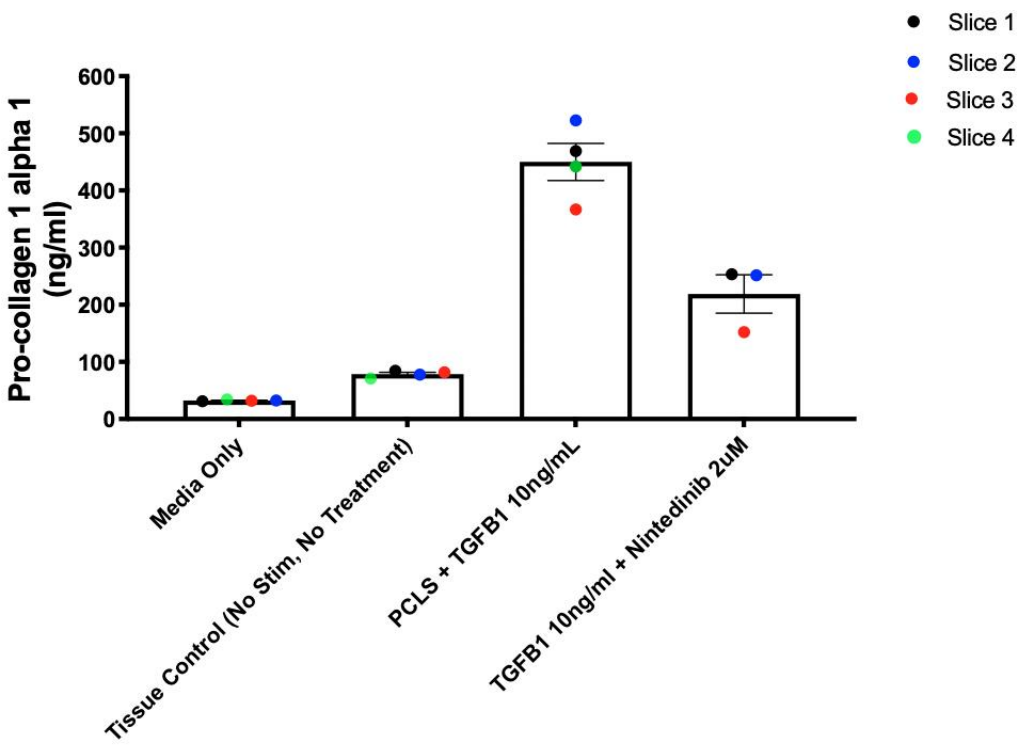


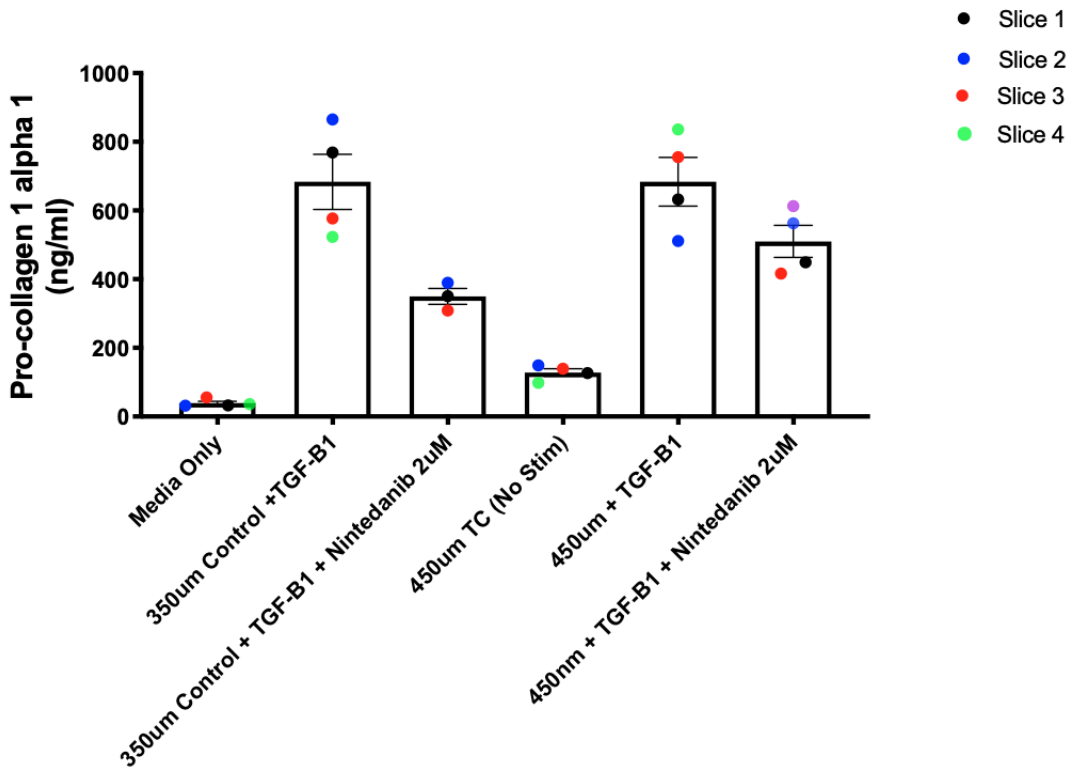
Post-Shipment Test



AnaBios
Early Human Insights

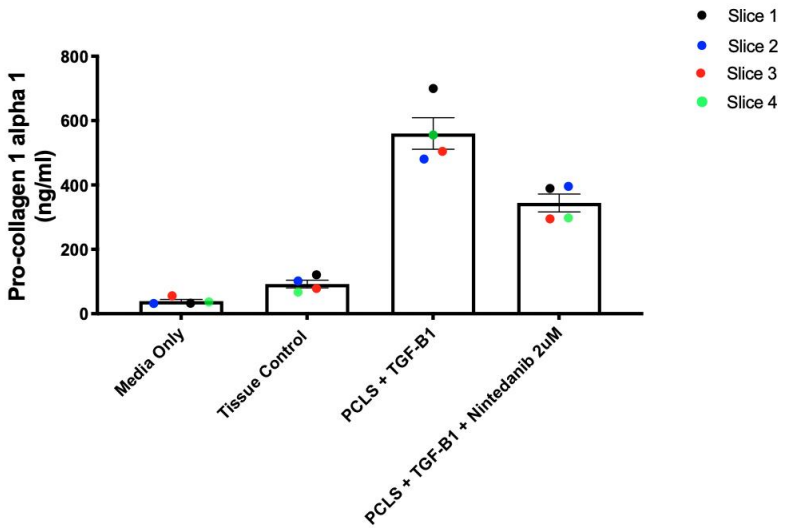
Nintedanib 尼达尼布调节TGF-β1诱导的胶原蛋白1α1水平升高
正常供体 – 450微米 人肺精准切割组织切片（PCLS）培养上清液 – 处理5天

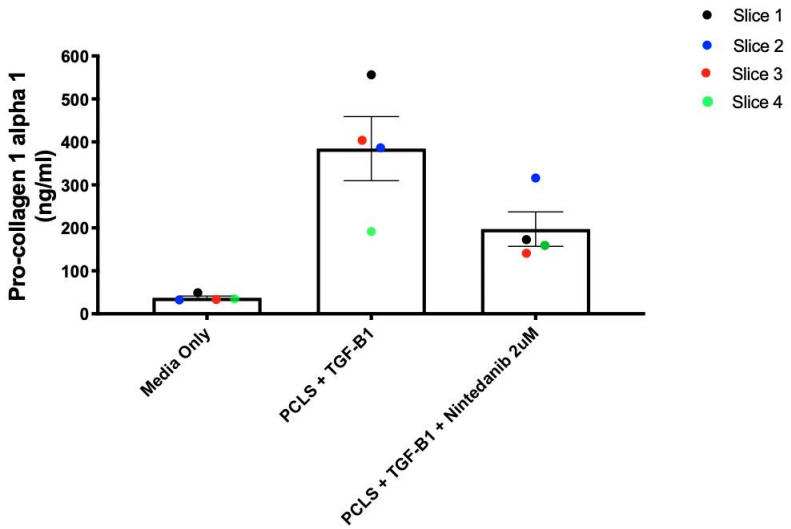


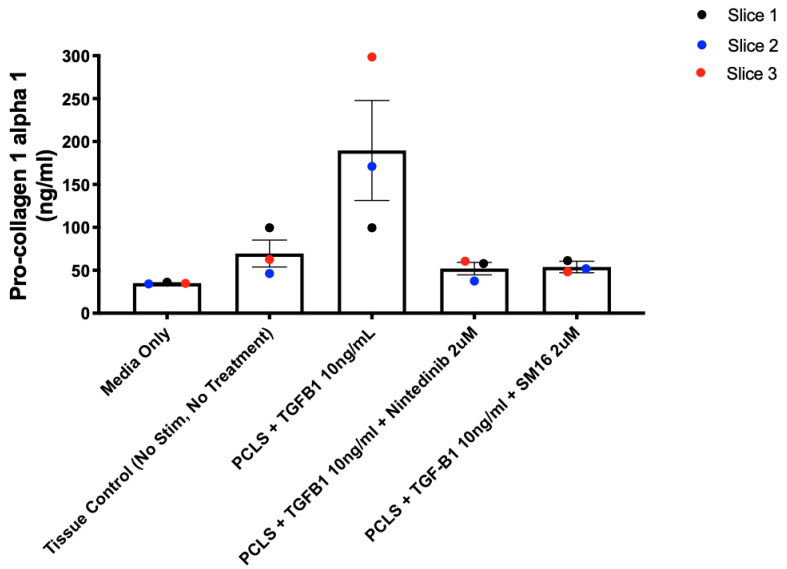


AnaBios
Early Human Insights

Nintedanib 尼达尼布调节TGF-β1诱导的胶原蛋白1α1水平升高
正常供体 – 抗生素处理 的人肺精准切割组织切片（PCLS）培养上清液 – 处理5天

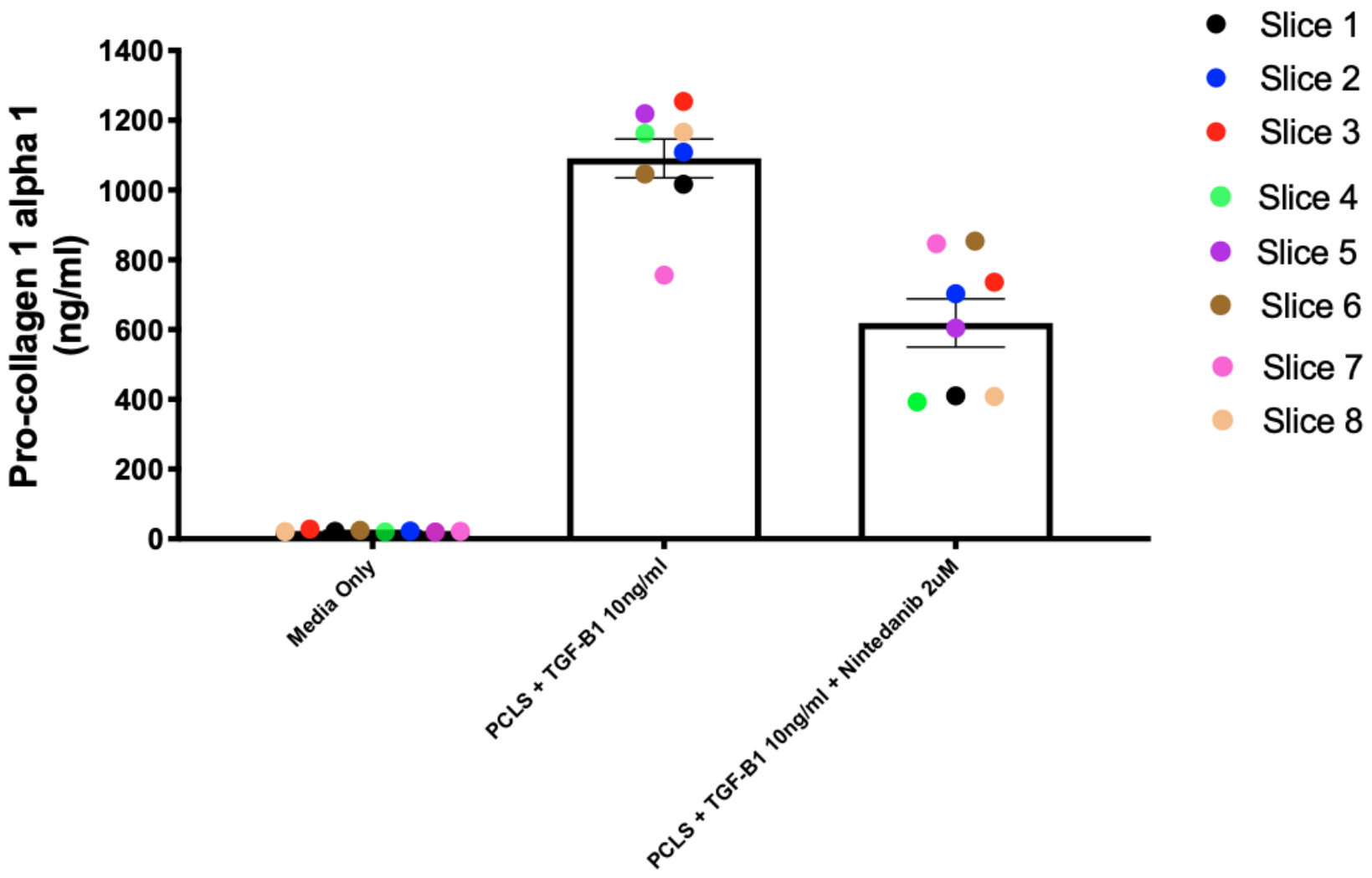






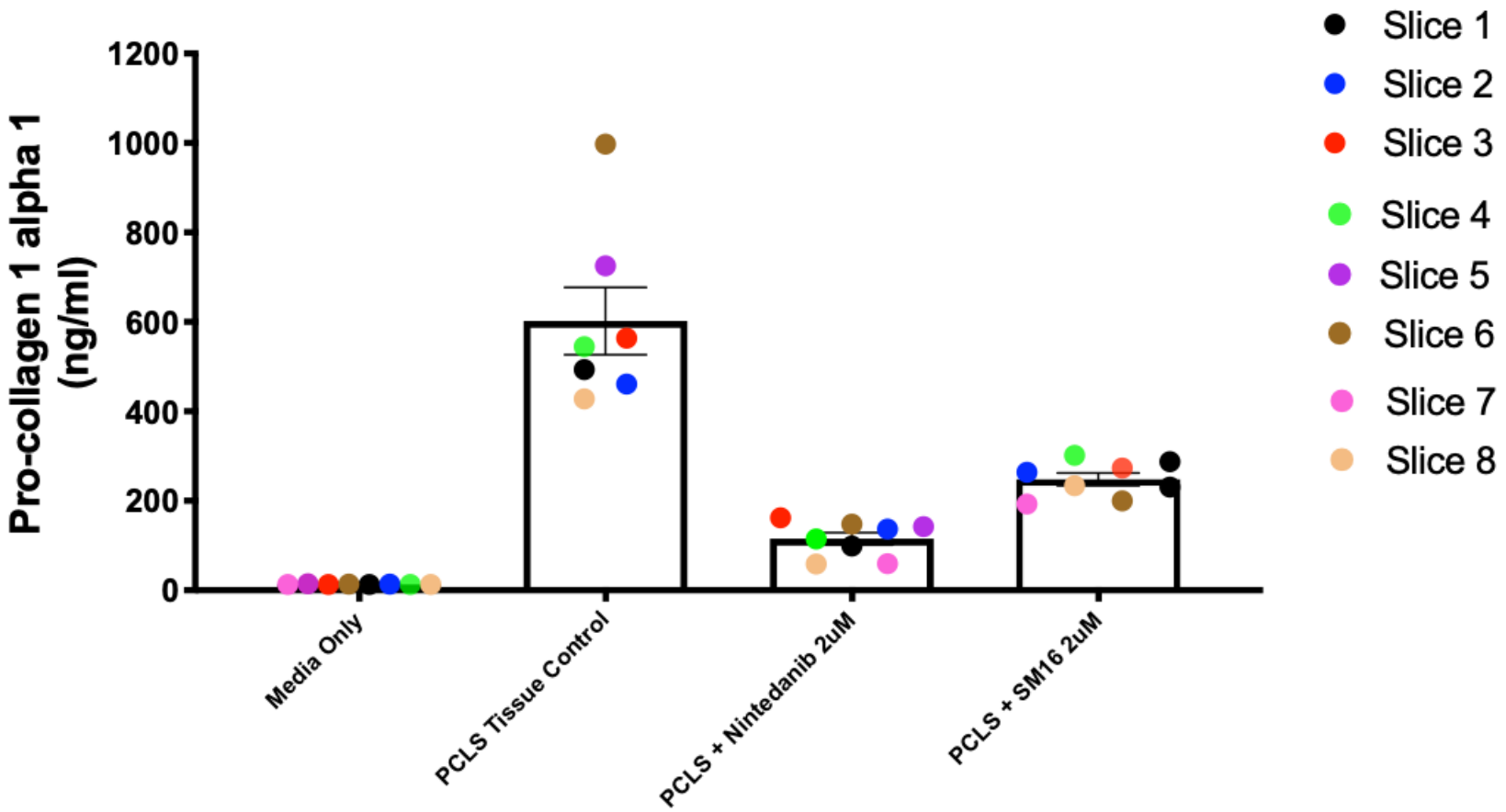
AnaBios
Early Human Insights

尼达尼布调节TGF-β1诱导的胶原蛋白1α1水平升高
5毫米直径尺寸 – 96孔板 正常人肺精准切割组织切片（PCLS）培养上清液 – 处理5天



AnaBios
Early Human Insights

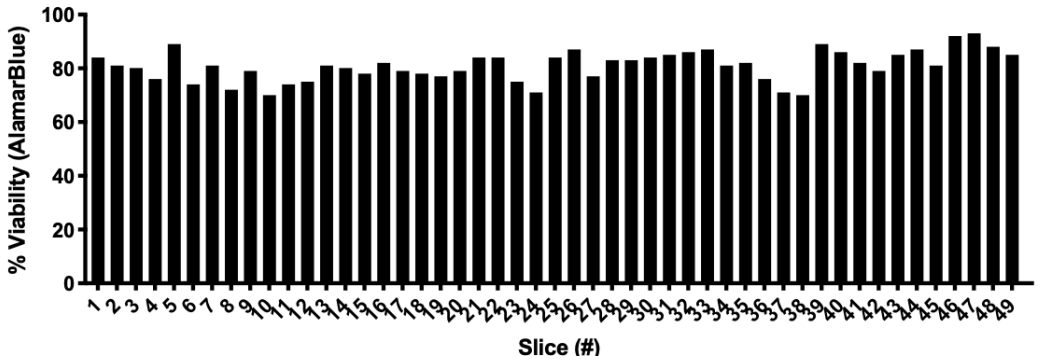
尼达尼布调节TGF-β1诱导的胶原蛋白1α1水平升高
5毫米直径尺寸 – 96孔板 IPF人肺精准切割组织切片（PCLS）培养上清液 – 处理5天



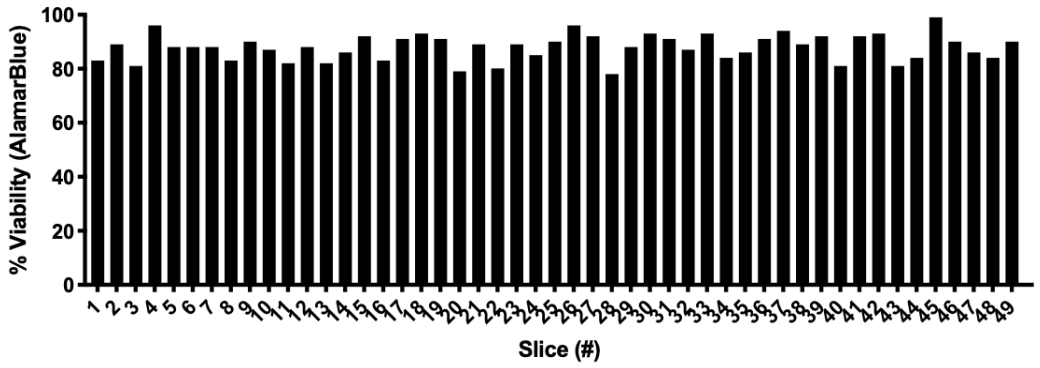
AnaBios
Early Human Insights

观察到的效应来源于治疗本身，而非切片健康受损
正常供体 – 实验前后活性评估

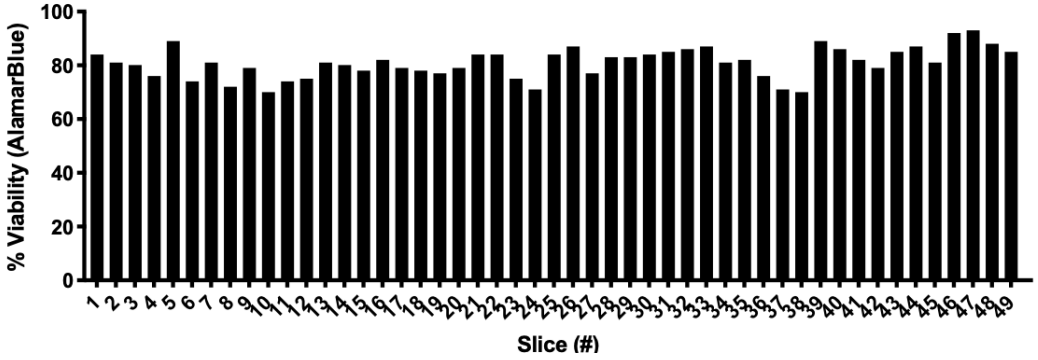
Donor 1
Pre-Screen



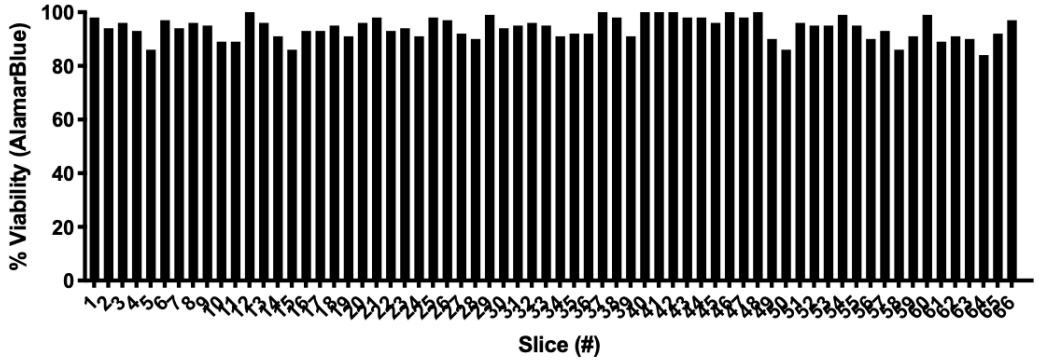
Donor 2
Pre-Screen



Donor 1
Post-Treatment



Donor 2
Post-Treatment

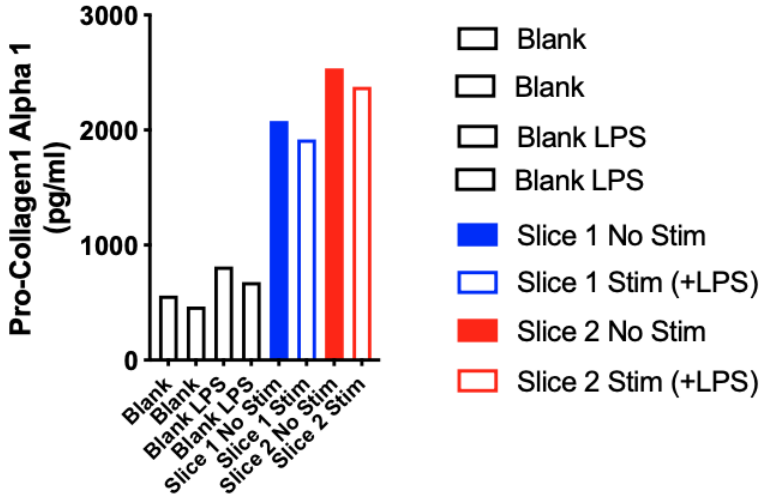


The PCLS model can be reliably used to screen drug effects

AnaBios
Early Human Insights

IPF供体肺组织中前胶原蛋白1α1水平显著升高
特发性肺纤维化（IPF）供体 - 人肺PCLS - 5天培养上清液

Donor 1



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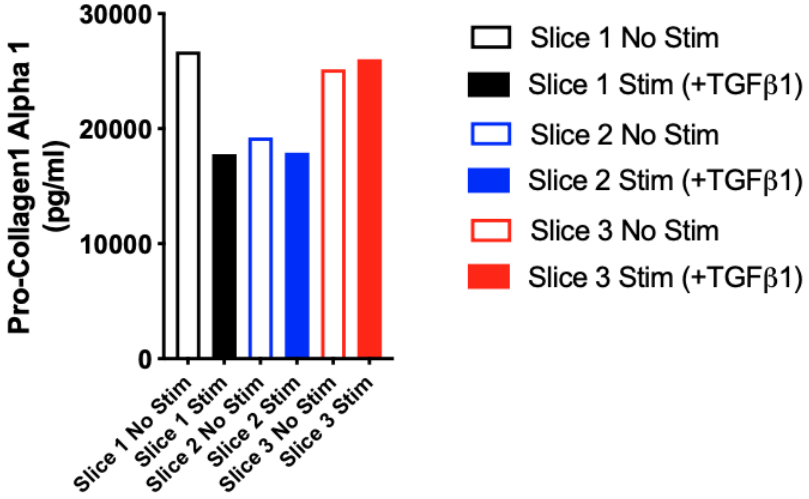

IPF切片： 无需额外刺激即可评估新疗法的抗纤维化潜力

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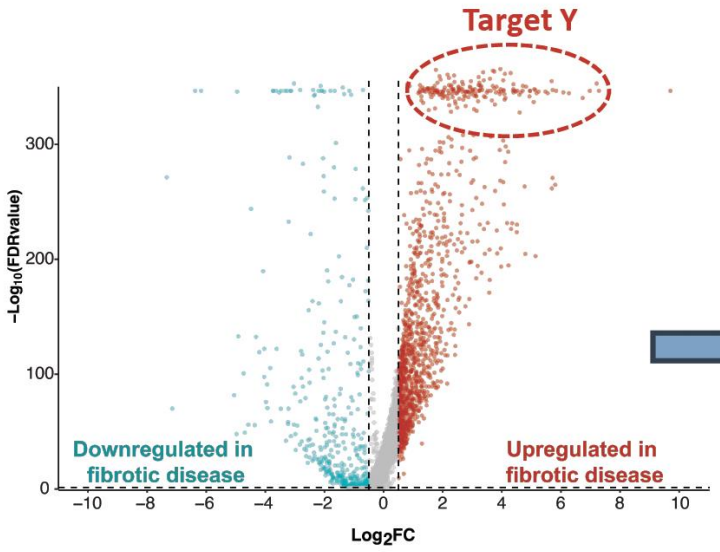
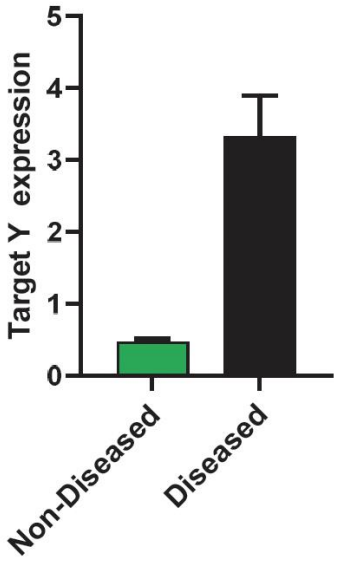
Early Human Insights

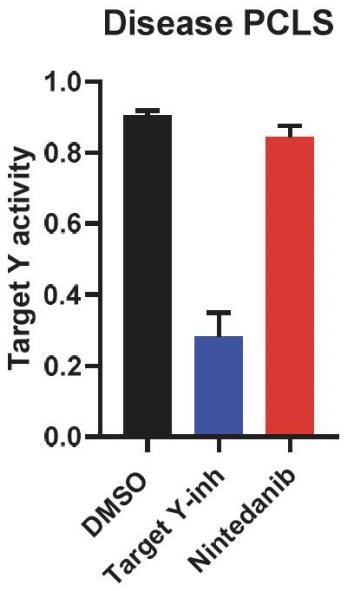
在人体PCLS中进行靶点识别、结合和验证

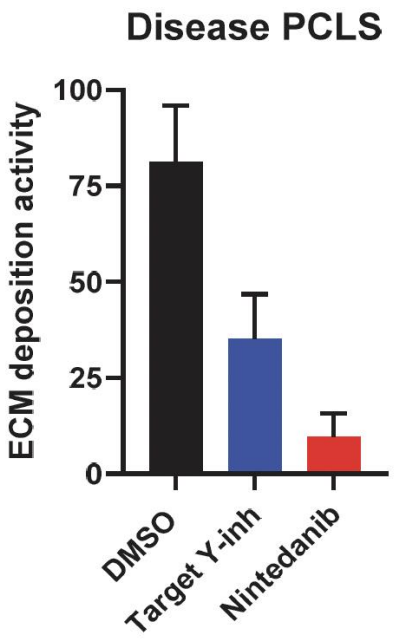


Collagen-producing lung cell atlas identifies multiple subsets with distinct localization and relevance to fibrosis GSE132771

Tsukui, T., Sun, KH., Wetter, J.B. *et al. Nat Commun, 2020*







纤维化疾病组织中的靶点识别

PCLS中的靶点识别

PCLS中的靶点结合

PCLS中的治疗反应

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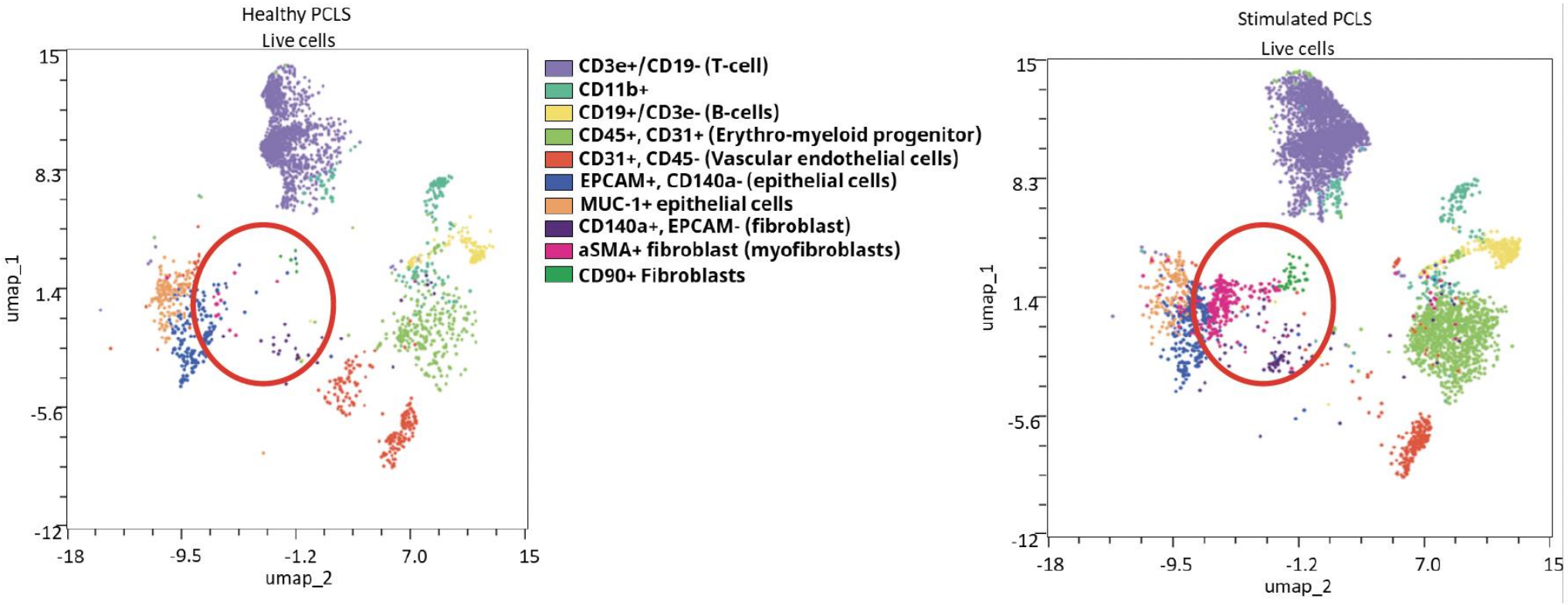
Early Human Insights

abbvie

PCLS作为基于人体组织的药物发现平台



对PCLS的单细胞分析可提供关于驱动疾病的细胞与分子机制的高分辨率洞察

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Early Human Insights

abbvie

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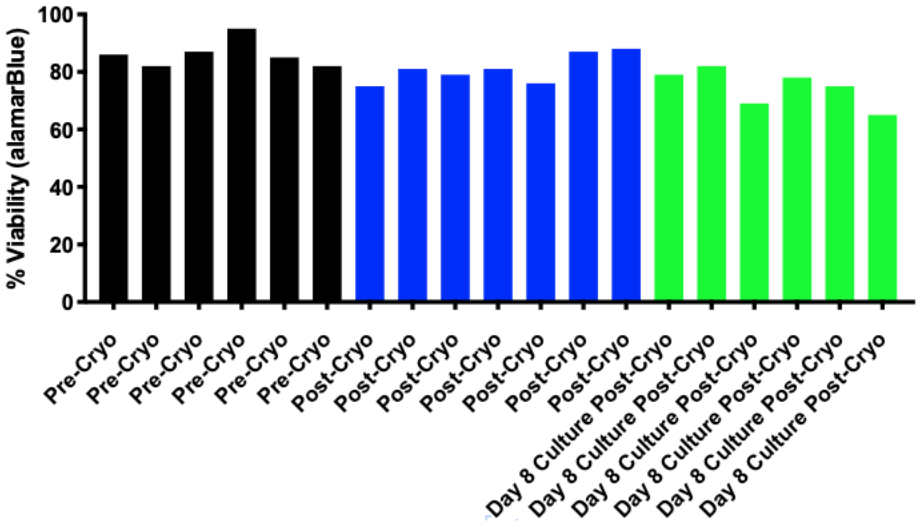
Early Human Insights

Human Precision-Cut Kidney Slice Model

长期人类PCKS活性评估 – AnaBios培养基 alamarBlue™ 细胞活力数据

Donor 1



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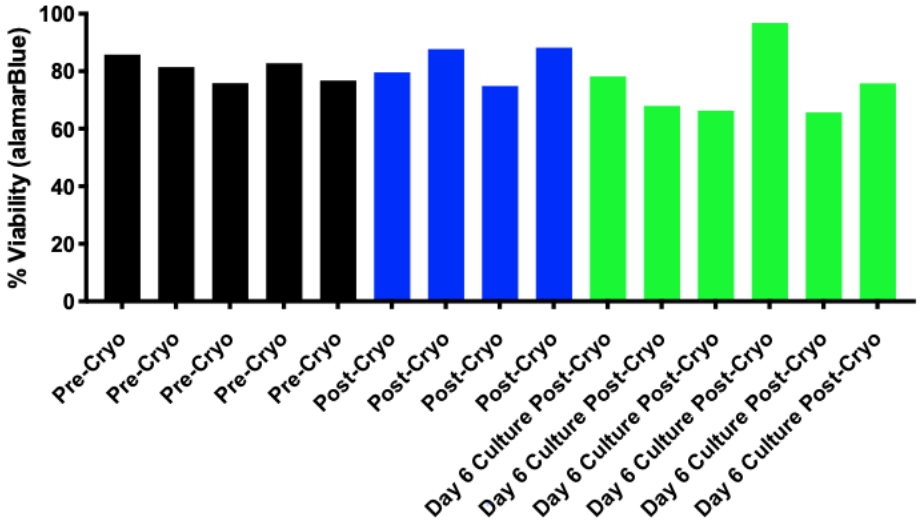

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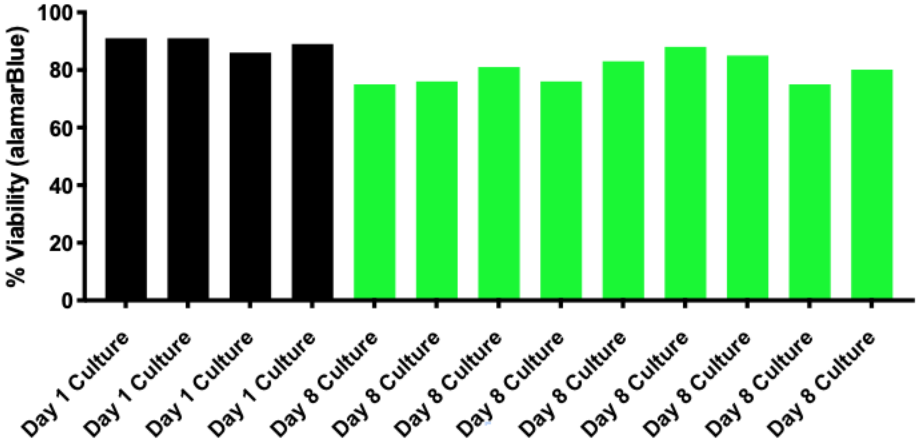

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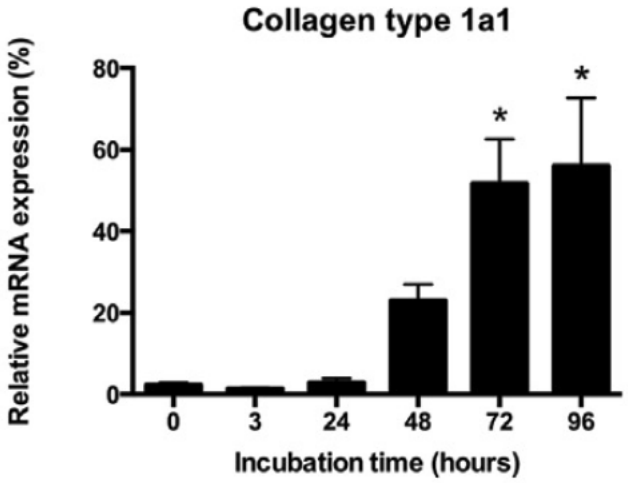
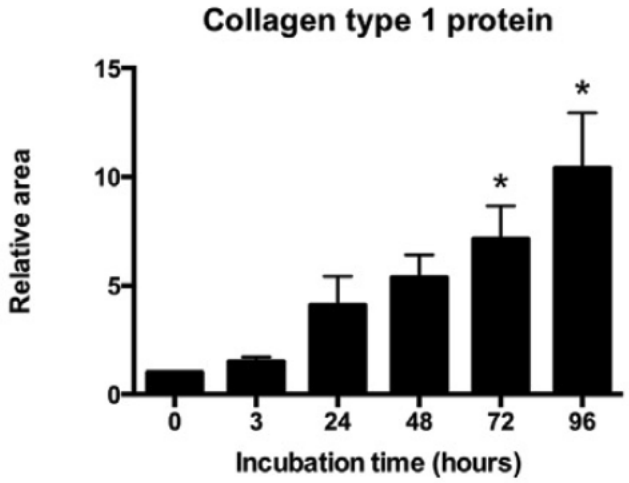
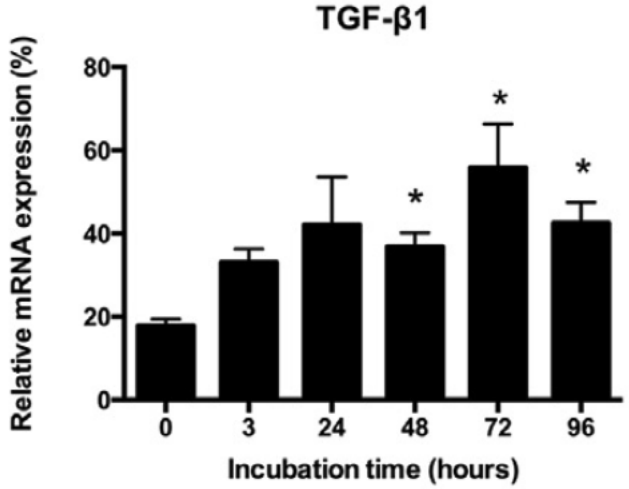
Early Human Insights

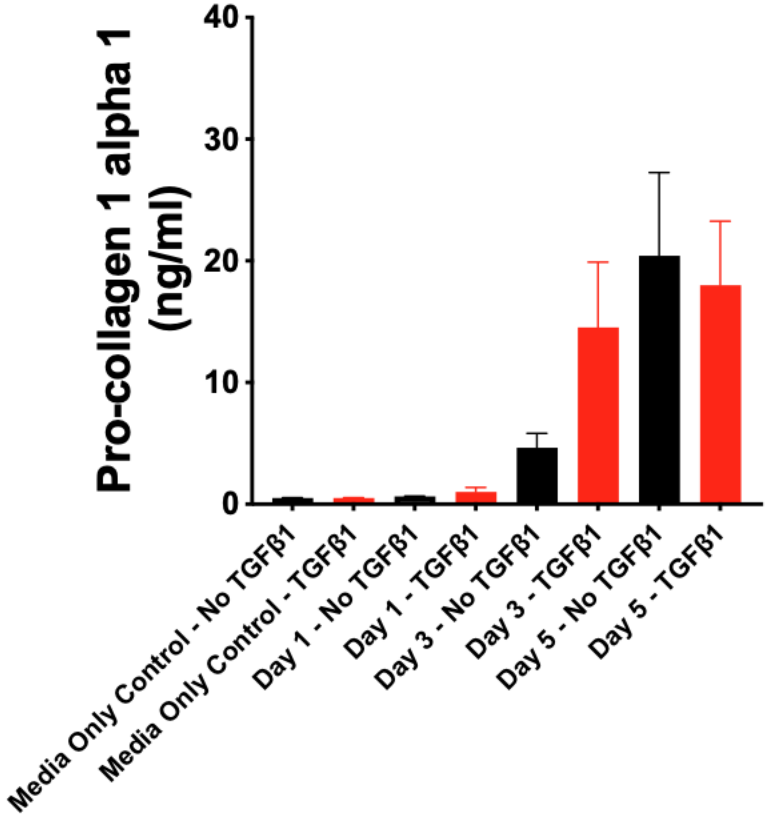
测试自发性和TGF-β1诱导的纤维化模型
正常供体 - 人肾PCKS培养上清液 – 多日培养







Stribos EGD et al., 2016
http://dx.doi.org/10.1016/j.trsl.2015.11.007



PCKS中的纤维化反应可以是自发的，也可以是诱导的

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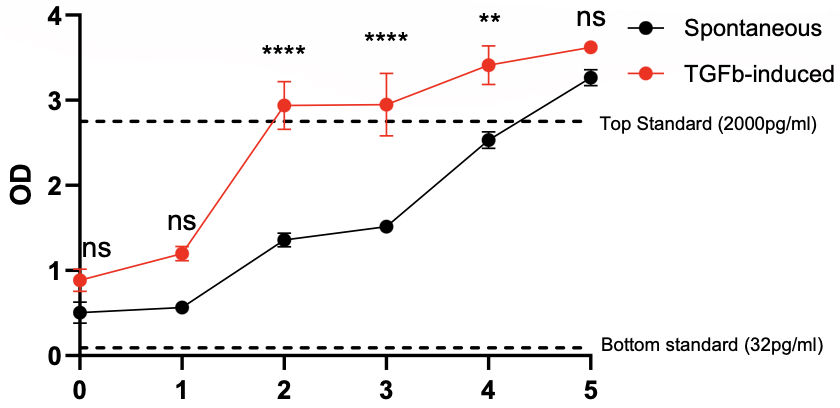
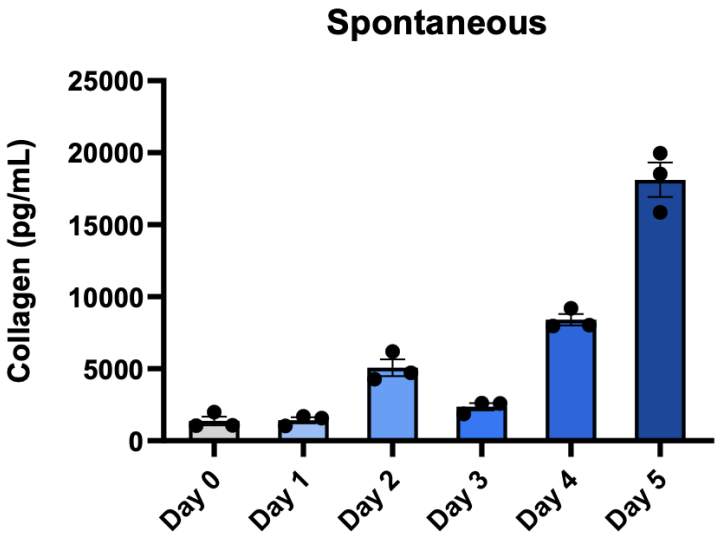
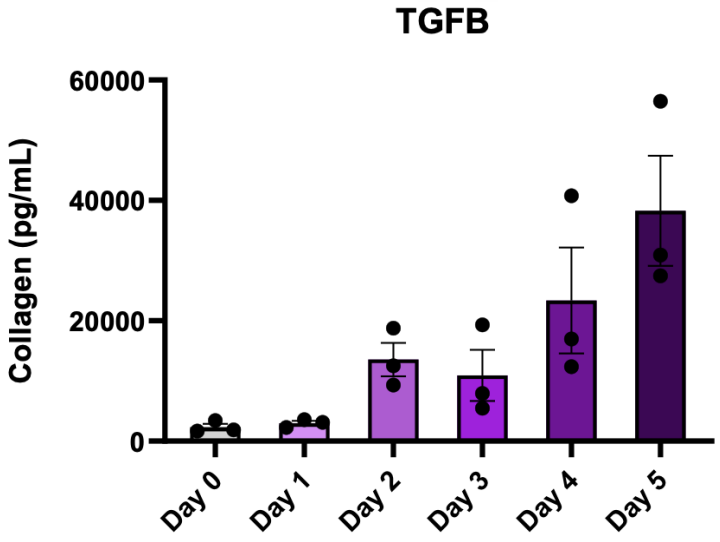
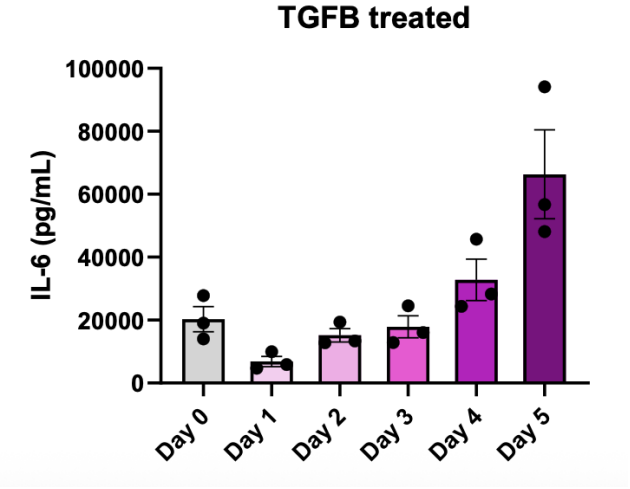
Early Human Insights

测试自发性和TGF-β1诱导的模型
正常供体 - 人肾PCKS培养上清液 – 多日培养 – 与制药公司合作









PCKS中的纤维化反应可以是自发的，也可以是诱导的

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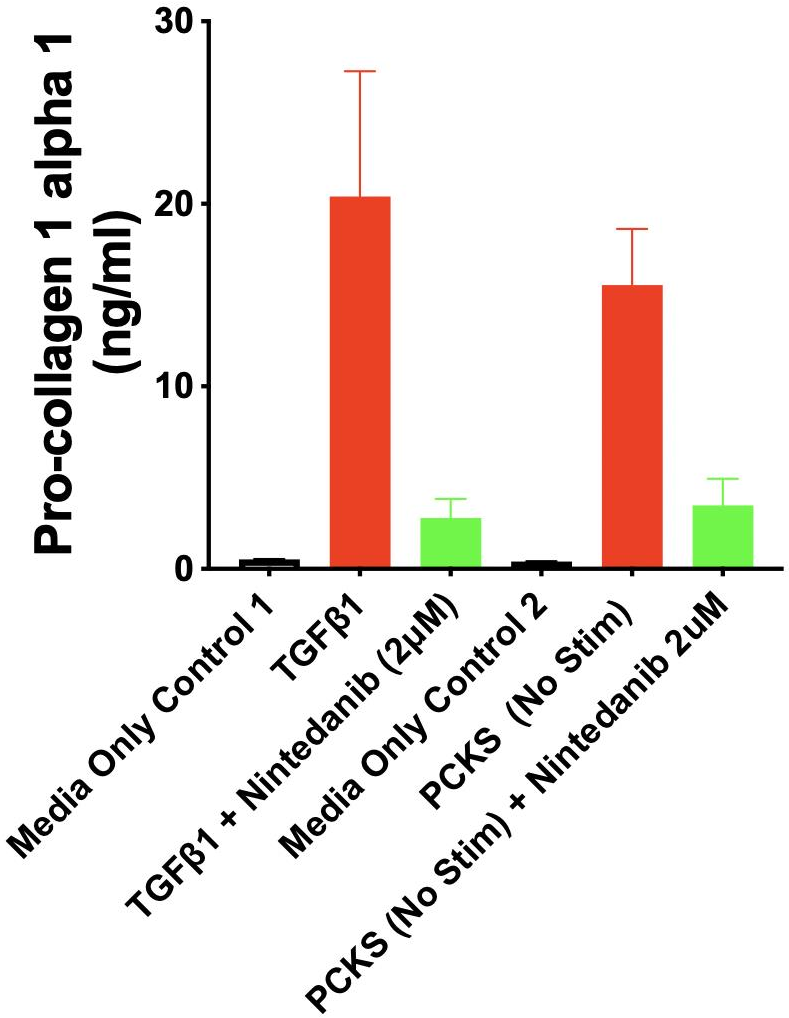
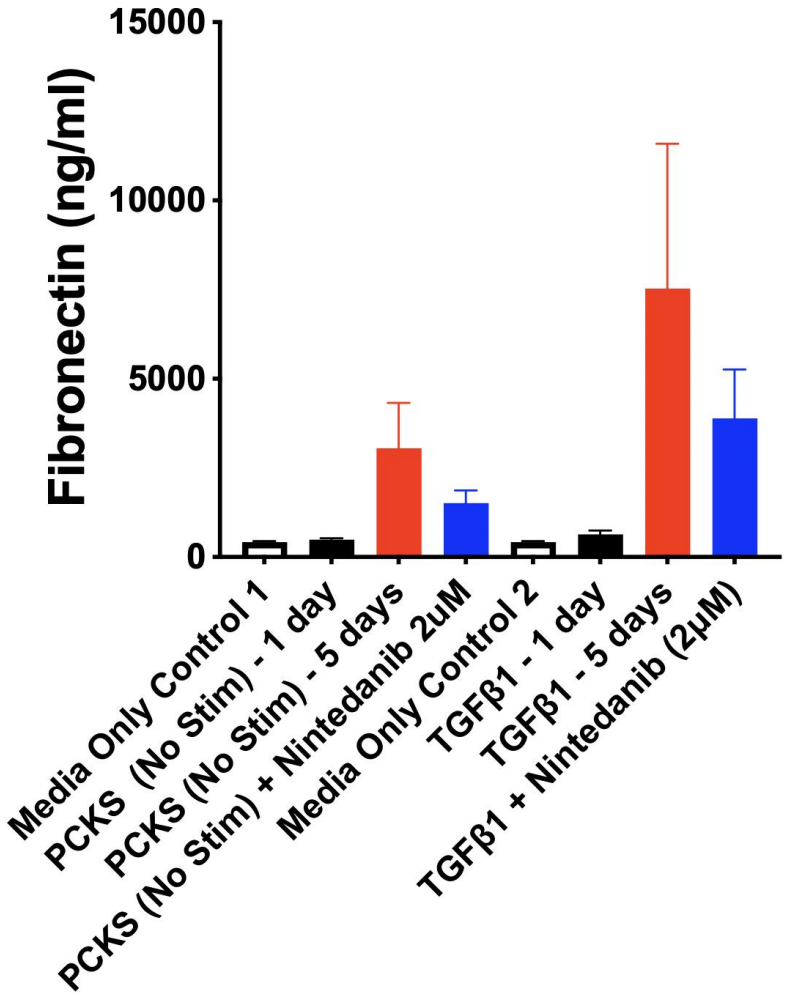
Early Human Insights

Nintedanib 尼达尼布调节自发性和TGF-β1诱导的纤维化反应
人肾PCKS培养上清液 – 处理5天

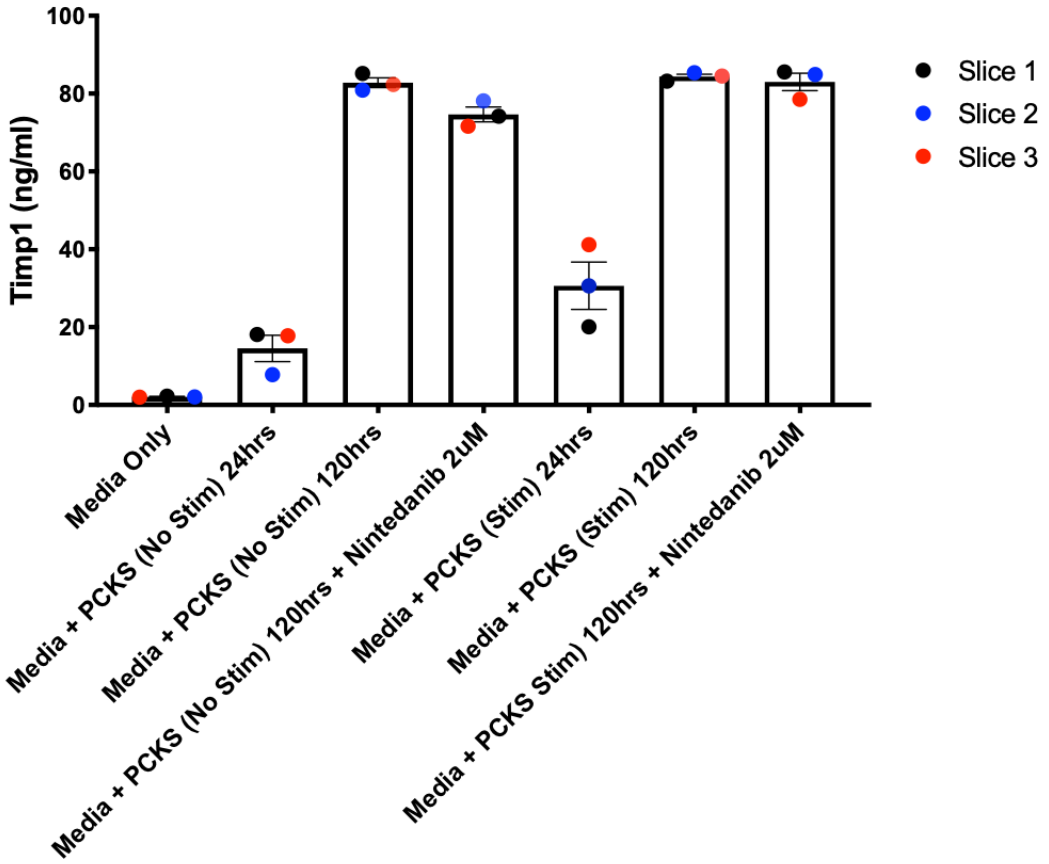


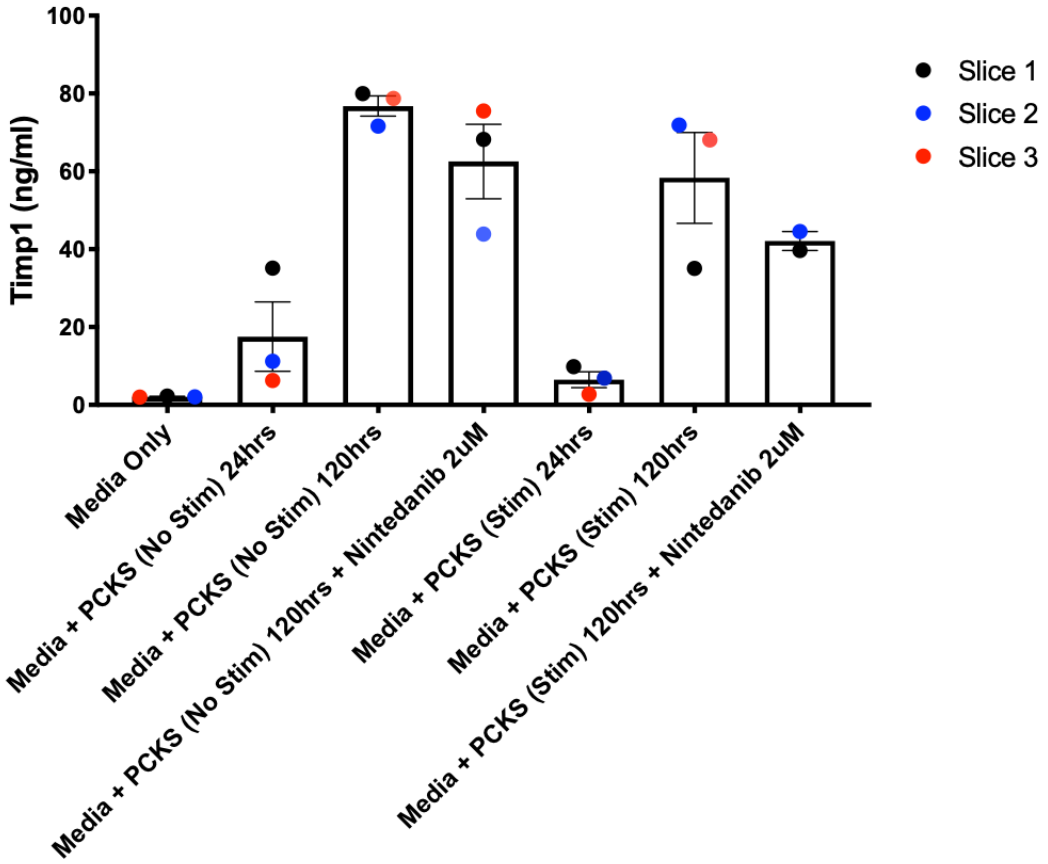


PCKS可用于评估新疗法的抗纤维化潜力

AnaBios
Early Human Insights

Nintedanib 尼达尼布不调节自发性和TGF-β1诱导的Timp1反应
人肾PCKS培养上清液 – 处理5天





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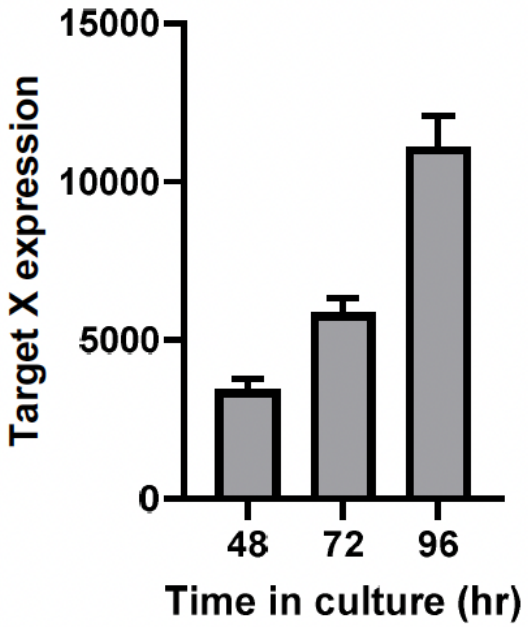
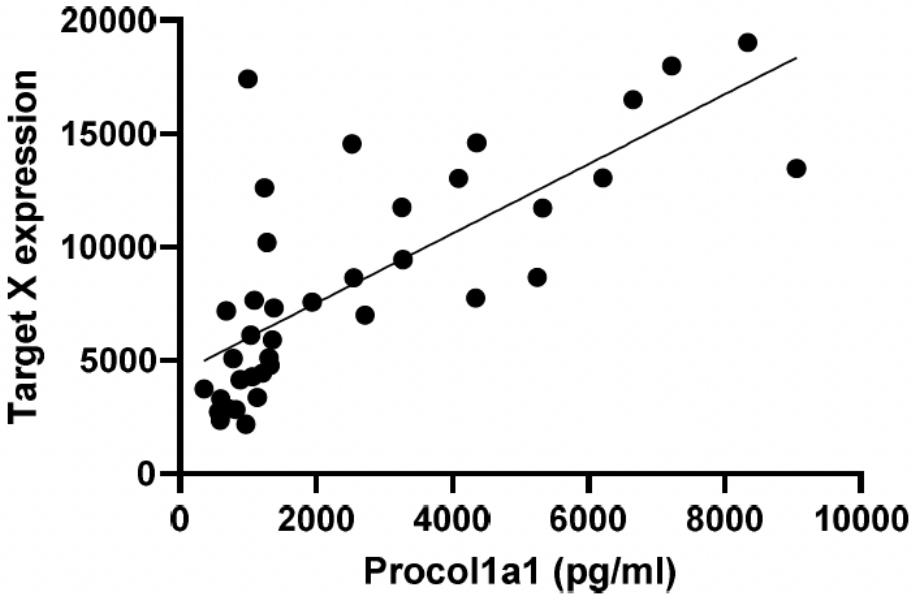
Early Human Insights

人肾PCKS作为肾纤维化研究平台 – 与艾伯维（AbbVie）合作
靶点X表达上调，与细胞外基质（ECM）沉积呈正相关





Various gene therapy approaches can be used to validate targets for the treatment of renal fibrosis

用于纤维化研究的精准切割组织切片

Advantages and Limitations

优势：

- 保留组织结构与细胞组成
- 保持肺功能、ECM修复及气道反应
- 模拟健康及病变组织
- 可进行刺激与药物处理
- 支持成像/IHC/单细胞分析
- 可用于药物筛选

局限性：

- 只能提供疾病的静态快照
- 来自异质性病变组织
- 肺组织缺乏呼吸运动与气体交换
- 肾组织无流动导致肾小球塌陷
- 给药方式受限

精准切割组织切片（PCTS）模型

重点总结

总结

- 强大的模型系统，支持研究正常与疾病相关的人体生物学
- 可预测平台，用于评估新药的疗效与安全性

AnaBios将出席2025年CPHI深圳大会

CPHI
Shenzhen China

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