Evaluating Cancer-Associated Fibroblasts Activity and Collagen Expression Profiles Using Clinically Validated Biomarkers

Annika Hettich[1,2], Morten Karsdal[2], Nicholas Willumsen[2]

[1]Nordic Bioscience, Herlev, Denmark
[2]University of Copenhagen, Copenhagen, Denmark

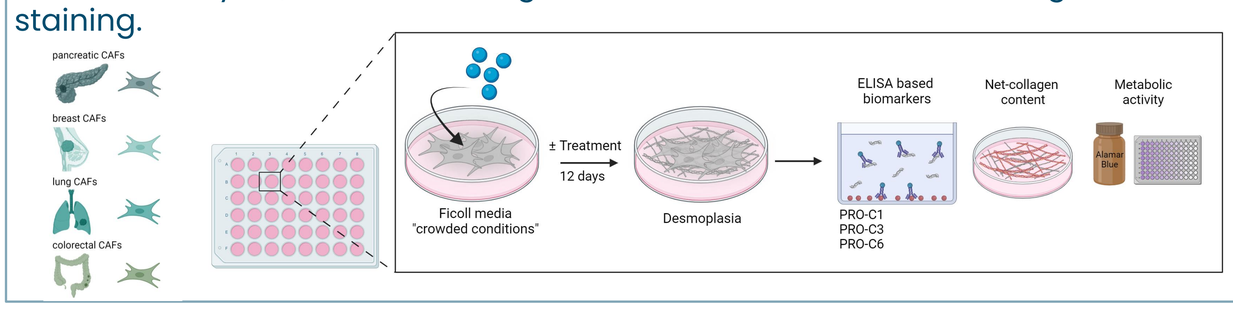
BACKGROUND

- Cancer-associated fibroblasts (CAFs) are pivotal orchestrators of tumor progression through their modulation of the extracellular matrix (ECM), particularly via the deposition of collagen.
- Different stimuli (e.g. TGF-β, PDGF-AB, IL-1α) can activate fibroblasts and induce phenotypic alterations in CAFs, promoting a pro-tumorigenic microenvironment characterized by enhanced ECM synthesis and remodeling.
- Known for their heterogeneity across tumors, their collagen expression and fibrotic activity patterns remain unclear.

This study aims to elucidate differences in collagen production among various CAF subtypes from different cancer tissues, using non-invasive biomarkers to identify distinct expression profiles and fibrotic activity levels.

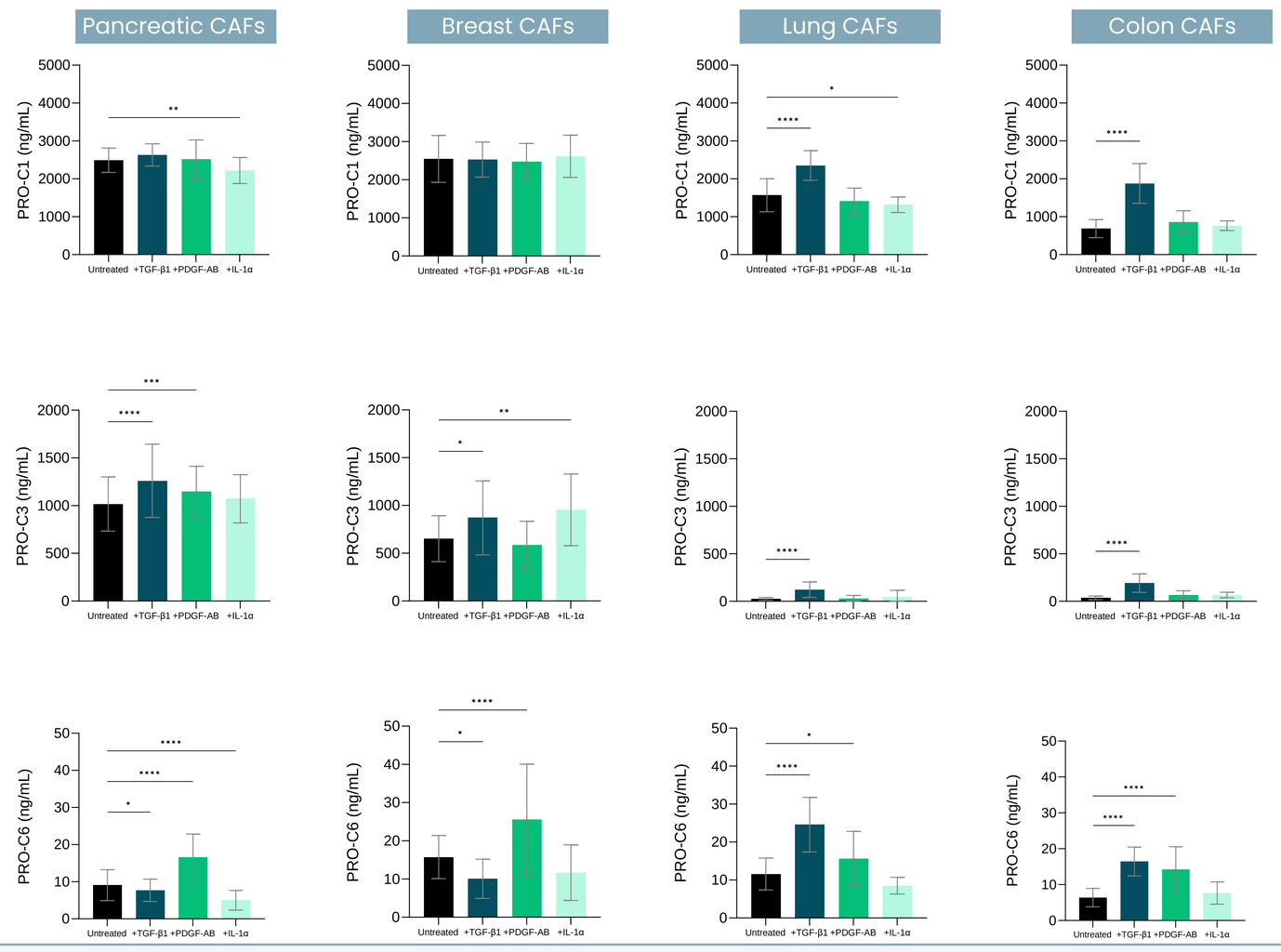
METHODS

Primary CAFs were isolated from patients with breast (n=1), pancreatic (n=1), colorectal (n=1), and lung cancer (n=1). These cells were cultured over a 12-day period in ficoll-based media, either unstimulated or stimulated with pro-fibrotic compounds (TGF-β1 (1 ng/ml), PDGF-AB (100 ng/ml), IL-1α (10 ng/ml)). Collagen synthesis (PRO-C1 for collagen I, PRO-C3 for collagen III, and PRO-C6 for collagen VI) was assessed in the cell supernatant on days 3, 6, 9, and 12 using competitive ELISA. On day 12, the net collagen content was evaluated using Sirius Red staining.

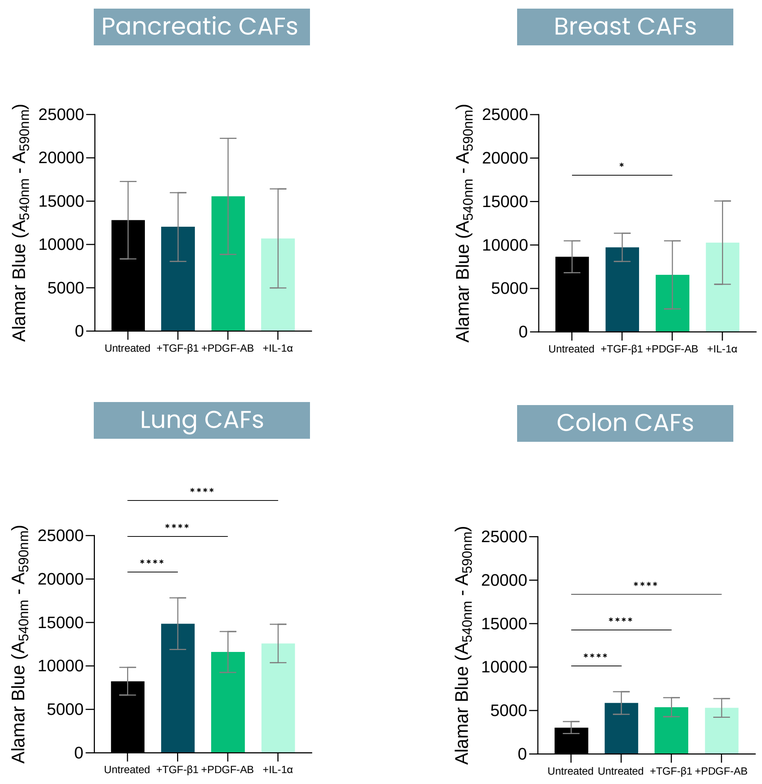


RESULTS

Distinct collagen profiles can be detected in CAFs across cancer indications following stimulation with pro-fibrotic compounds

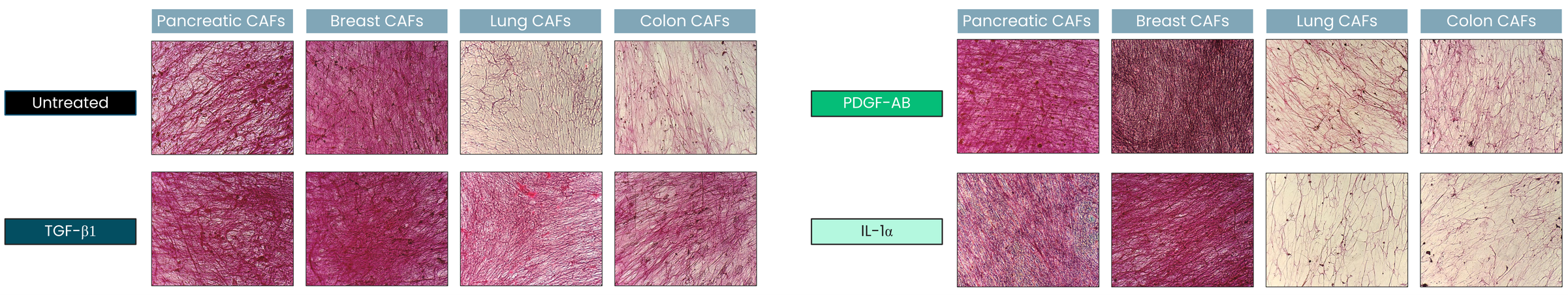


Metabolic activity of distinct CAFs



* p<0.05 ; ** p<0.01; *** p<0.001; **** p<0.0001

The net-collagen content of distinct CAFs is reflecting the collagen-based biomarker measurements



CONCLUSION

- These findings underscore the heterogeneity in collagen production and fibrotic activity among CAFs from different indications, providing valuable insights into the ECM dynamics within distinct TMEs.
- Collagen-based non-invasive biomarkers demonstrate the capability to differentiate between the fibrotic activity of CAFs isolated from different tissues.

Contact: Annika Hettich, anhe@nordicbio.com
Disclosures: MK and NW are employed at Nordic Bioscience and may be shareholders.