P138

Clinically validated markers of extracellular matrix remodeling are altered by anti-fibrotic compounds in a human skin ex vivo model

Cecilie Møller Hausgaard[1], Signe Holm Nielsen[1], Helena Port[1,2]

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

Introduction and Aim

Skin pathologies, such as hidradenitis suppurativa and scleroderma, are characterized by excessive extracellular matrix (ECM) remodeling. Clinically validated ECM neo-epitope biomarkers, related to progression, treatment response, and outcomes, may be useful for the evaluation of potential anti-inflammatory and anti-fibrotic effects.

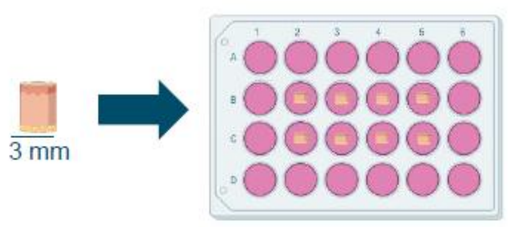
METHODS

1

Human skin samples were collected from two donors undergoing abdominoplasty.

2

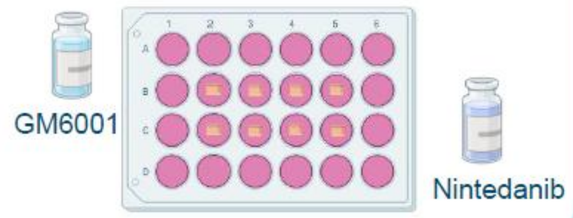
Within 24 hours, the skin was processed as 3mm full-thickness punch biopsies (epidermis, dermis and hypodermis.



3

Five biological replicates from each patient were cultured for 48 hours in serum-free medium with either:

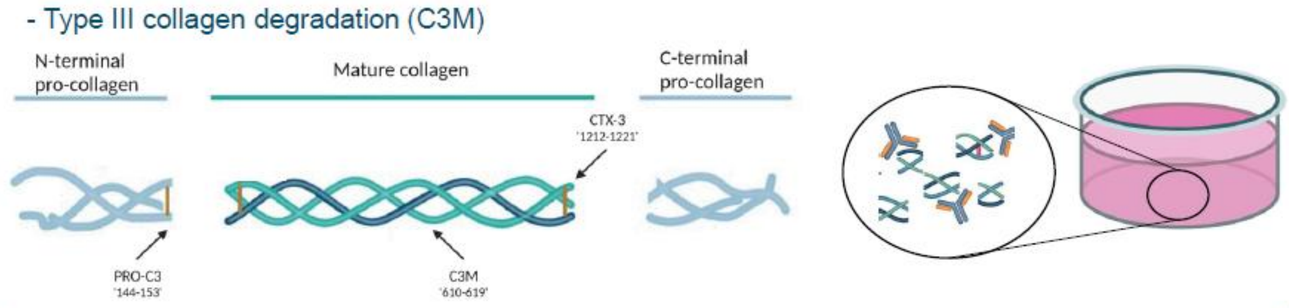
- GM6001 – an Matrix Metalloproteinase (MMP)-inhibitor
- Nintedanib – an anti-fibrotic compound



4

Biomarkers of type III collagen were evaluated in the supernatants using ELISA assays:

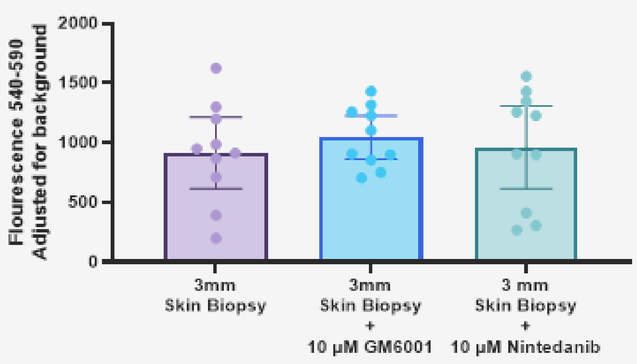
- Type III collagen formation (PRO-C3)
- Type III collagen degradation (C3M)



RESULTS

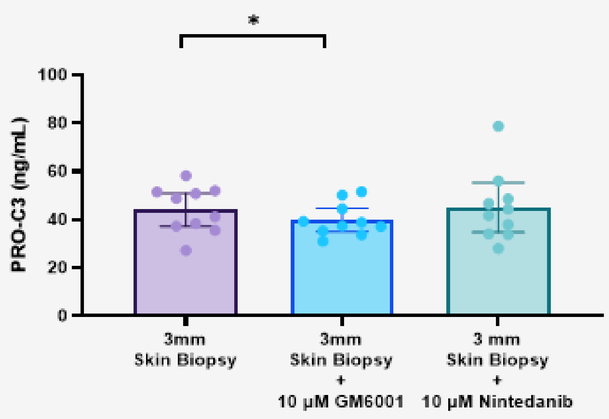
The tissue from both donors was responsive to Alamar blue, and no toxicity was seen with the selected compounds. C3M and PRO-C3 were significantly reduced by GM6001 (p=0.0001 and p=0.0305, respectively), while only C3M was reduced by Nintedanib (p=0.0240). Data varied dependent on donor.

Viability by Alamar Blue



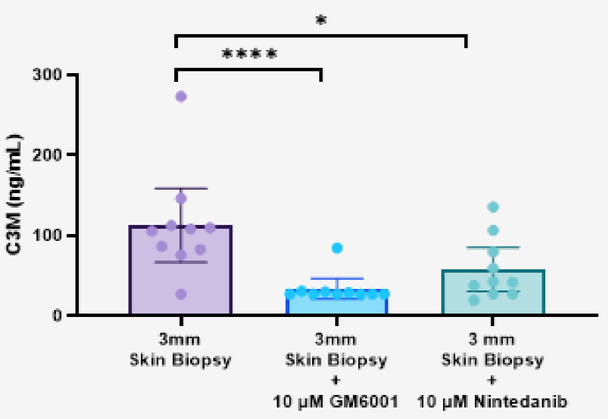
Kruskal Wallis test
Data is shown as mean with 95% CI

PRO-C3 levels are inhibited by GM6001



Kruskal Wallis test
Data is shown as mean with 95% CI

C3M levels are inhibited by GM6001 and Nintedanib



Kruskal Wallis test
Data is shown as mean with 95% CI

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

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Contact: Cecilie Møller Hausgaard, cmn@nordicbio.com
Disclosures: SHN, HP and CMH are employed at Nordic Bioscience and may be shareholders.

CONCLUSION

We found that an MMP-inhibitor and anti-fibrotic decreased biomarkers of ECM remodeling in a human skin ex vivo model and may potentially be used as a tool for evaluating anti-inflammatory and anti-fibrotic compounds in a 3D skin structure.