

CPa9-HNE, A Novel Biomarker Of Neutrophil Activity Is Associated With Transmural Healing In Pediatric Crohn's Disease

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BACKGROUND

- Infiltration of neutrophils into intestinal tissue is a crucial component of the inflammatory response in Crohn's disease (CD).
- CPa9-HNE, a calprotectin fragment released by human neutrophil elastase during NETosis, has been shown to strongly correlate with endoscopic disease activity in adults with inflammatory bowel disease (IBD)
- CPa9-HNE also serves as an indicator of pharmacodynamic response.

Aim of the study

We aimed to investigate the association of CPa9-HNE with endoscopic disease activity and transmural healing in patients with pediatric CD.

METHODS

- The cohort included 174 children with CD (aged 2-18 years, 56% male) who underwent MRE and ileocolonoscopy as part of the ImageKids study (NCT01881490) with serum drawn at enrolment.
- Age- and sex-matched healthy subjects (HS) were included (n=82). CPa9-HNE, a human neutrophil elastase-derived fragment of calprotectin, was measured in serum by ELISA.
- Endoscopic disease activity was graded using the SES-CD score, and radiologic inflammation was assessed by MRE using the radiologist global assessment (RGA) of inflammation recorded on a 0-100 mm visual analog scale (VAS).
- Transmural healing was defined as endoscopic healing (SES-CD<3, EH) and RGA<10 mm. Spearman's rho correlations and one-way ANOVA with Dunn's correction were applied.

RESULTS

Summary of results:

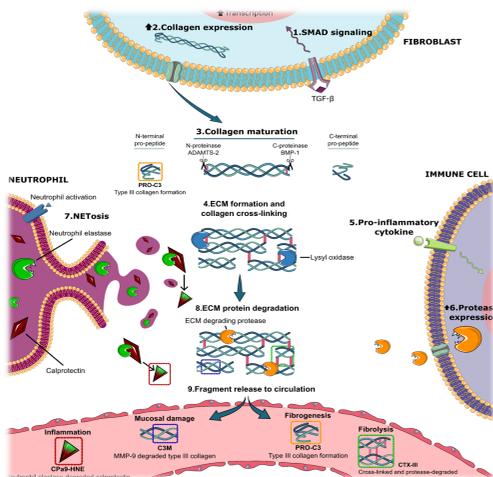
- CPa9-HNE showed a fair correlation with the SES-CD score ($\rho=0.30$, $p<0.001$).
- A positive correlation was also observed between CPa9-HNE and RGA of inflammation ($\rho=0.30$, $p<0.001$).
- For SES-CD, CPa9-HNE was significantly elevated in all subgroups compared with HS ($p<0.0001$ for all) and demonstrated a stepwise increase across disease severity groups.
- Patients with severe endoscopic disease had significantly higher levels of CPa9-HNE than those in remission (ng/ml [IQR]: 275.6 [182.4-461.9] vs. 158.1 [127.6-211.2], $p<0.001$).
- CPa9-HNE was able to significantly discern patients with transmural healing from patients with transmural disease activity (AUC [95%CI]: 0.80 [0.73-0.87]).

Table 1: Patient demographics

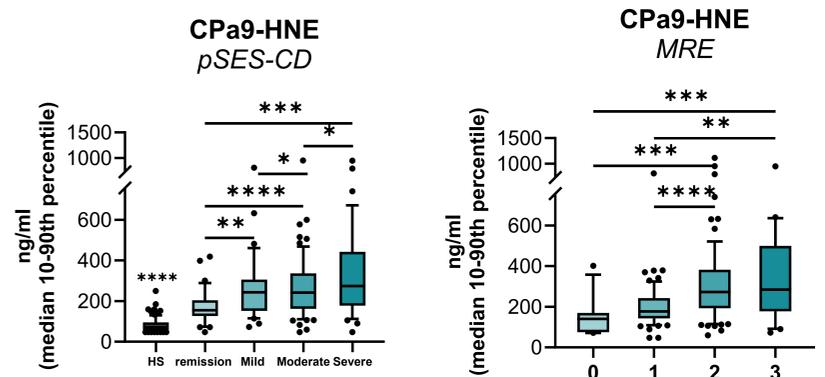
Gender, Male (%)	31 (62 %)
Age, median (range)	15 (11-18.5)
BMI, median (range)	19.6 (15.4-32.1)
Disease duration, median (range)	3.7 (0-13)
MRE damage VAS, median (range)	14 (0-100)
SES-CD, median (range)	8 (0-27)
pCAI, median (range)	20 (0-92.5)
History of resection, %	2 %

The Fibro-inflammatory Axis and related biomarkers

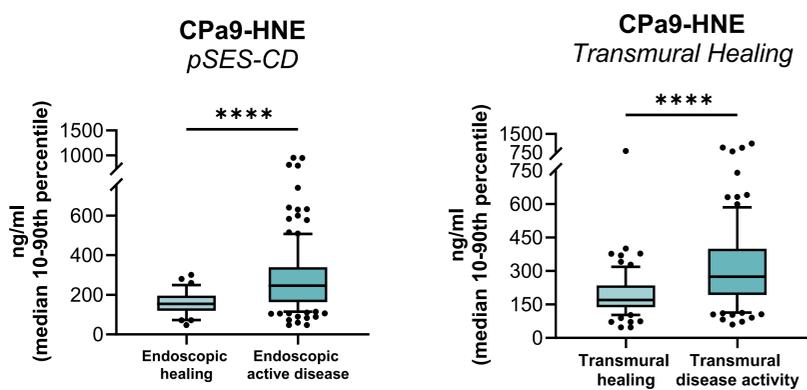
- How neo-epitopes are being generated through the fibro-inflammatory axis:
 - **Immune cell activity:** CPa9-HNE, VICM
 - **Mucosal damage:** C3M, C4M, C7M,
 - **Fibrogenesis:** PRO-C3, PRO-C6, PRO-C5
 - **Fibrolysis:** CTX-III



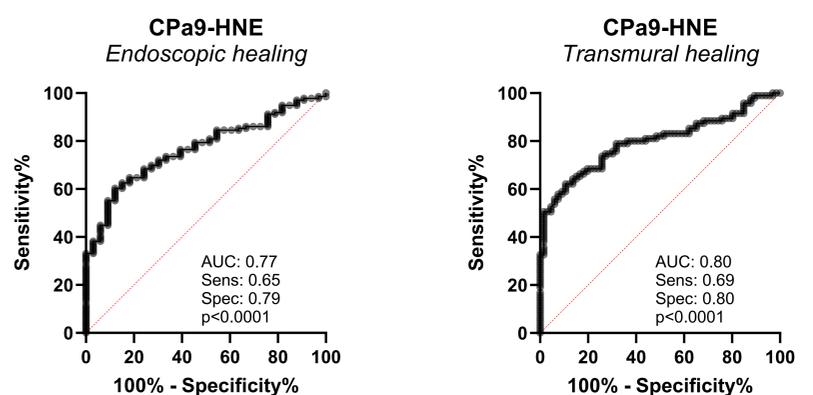
CPa9-HNE reflects disease activity in pediatric Crohn's disease based on pSES-CD and MRE



CPa9-HNE reflects Endoscopic healing and Transmural healing



CPa9-HNE diagnostic accuracy



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

NORDIC BIOSCIENCE



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CONCLUSION

- This study showed that CPa9-HNE, a biomarker of neutrophil activity, is associated with mucosal and radiologic mucosal damage in pediatric CD.
- These findings highlight the potential use of CPa9-HNE as a complementary tool for the endoscopic or radiographic assessment of intestinal mucosal damage/healing and provide an opportunity for further studies in children with CD.