PRO-C11 AND PRO-C16 ARE MARKERS OF INTESTINAL FIBROSIS AND ARE ASSOCIATED WITH MRE-CONFIRMED INTESTINAL STRICTURES – RESULTS FROM THE IMAGEKIDS STUDY

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BACKGROUND

- Intestinal fibrosis and strictures is one of the most challenging complications in patients with Crohn's disease (CD).
- There is an urgent medical need for non-invasive serological biomarkers for intestinal fibrosis, as magnetic resonance enterography (MRE) is not a feasible tool for repeated monitoring.
- Here we wanted to investigate the role of the minor collagens; fibrillar type XI collagen and the Fibril-Associated Collagens with Interrupted Triple Helices (FACIT) type XVI collagen in relation to intestinal fibrosis.
- Therefore, we quantified the biomarkers PRO-C11 (formation of type XI collagen) and PRO-C16 (formation of type XVI collagen) in serum from pediatric CD (pCD).

HYPOTHESIS AND AIMS

- In this study, we investigated Protein Fingerprint Assays (PFA) biomarkers of collagen formation, PRO-C11 (formation of type XI collagen), and PRO-C16 (formation of type XVI collagen) in serum from pediatric CD (pCD).

MAJOR FINDINGS AND CONCLUSION

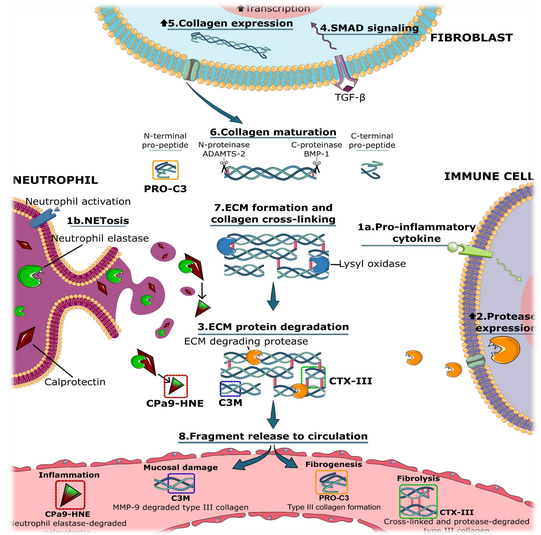
Based on these biomarker data from the ImageKids study, PRO-C11 and PRO-C16 demonstrate potential as important non-invasive biomarkers reflecting intestinal fibrosis and stenosis.

METHODS

Study Description

We enrolled children with CD who underwent MRE in the ImageKids study. (ImageKids study: NCT01881490).

- Serum samples were collected at enrolment (n=203), and from healthy age- and gender-matched healthy subjects (HS) (n=82).
- The Nordic PFA biomarkers of tissue fibrosis PRO-C11 and PRO-C16 were measured.
- Intestinal fibrosis and stenosis were determined by MRE, and VAS score was applied to assess severity of intestinal fibrosis.
- Pearson-r correlation, students t-test and one-way-ANOVA with false discovery rate correction were applied for statistical analysis.



Biomarkers	Description
PRO-C16	Formation of type XVI collagen
PRO-C11	Formation of type XXI collagen

Patient demographics

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 intestinal fibrosis VAS, median (range)	20 (0-100)
SES-CD, median (range)	8 (0-27)
pCDAI, median (range)	20 (0-92.5)
History of resection, %	2 %

Summary of results

- The sample size of the different groups were as follows, no fibrosis [n=138]: VAS=0, mild fibrosis [n=55]: VAS=1-44, moderate/severe [n=17]: VAS>44). PRO-C11 (r=0.20, p=0.01) and PRO-C16 (r=0.20, p=0.01) correlated with the MRE VAS score.
- **Both PRO-C11** (with fibrosis: median 26.4 ng/mL [IQR: 13.25-39.53 ng/mL]) and without fibrosis: median 20.6 ng/mL IQR 11.3-28.8 ng/mL) and **PRO-C16** (with fibrosis: median 2990 ng/mL IQR: 2093-3884 ng/mL, and without fibrosis: median 2548 ng/mL [IQR: 1579-3286 ng/mL]) were significantly elevated in those with fibrosis compared to without fibrosis MRE-confirmed stenosis (p<0.01).
- **Serum PRO-C11** levels were significantly elevated in patients with moderate/severe intestinal fibrosis (median 32.2 ng/mL [IQR: 19.5-46.7 ng/mL]) as judged by VAS compared to patients with mild intestinal fibrosis (p<0.05, median 28.8 ng/mL [IQR: 12.6-37.3 ng/mL]), with no intestinal fibrosis (p<0.01) and HS (p<0.0001, median 8.3 ng/mL [IQR: 7.0-12.5 ng/mL]).
- **Serum PRO-C16** was significantly elevated in patients with moderate/severe intestinal fibrosis (median 3567 ng/mL [IQR: 2287-4608 ng/mL]) compared to patients with mild intestinal fibrosis (p<0.05, (median 2791 ng/mL [IQR: 1970-3670 ng/mL]), with no intestinal fibrosis (p<0.001, (median 2548 ng/mL [IQR: 1579-3286 ng/mL]) and HS (p<0.0001, (median 1456 ng/mL [IQR: 1072-1804 ng/mL])

Biomarker correlation to intestinal fibrosis

Table 2: PFA biomarkers correlation to SES-CD

PFA BIOMARKERS	RHO	P-VALUE
Immune Cell Activity Biomarker Panel		
PRO-C11	0.20	<0.01
PRO-C16	0.20	<0.01

RESULTS

MRE confirmed fibrosis

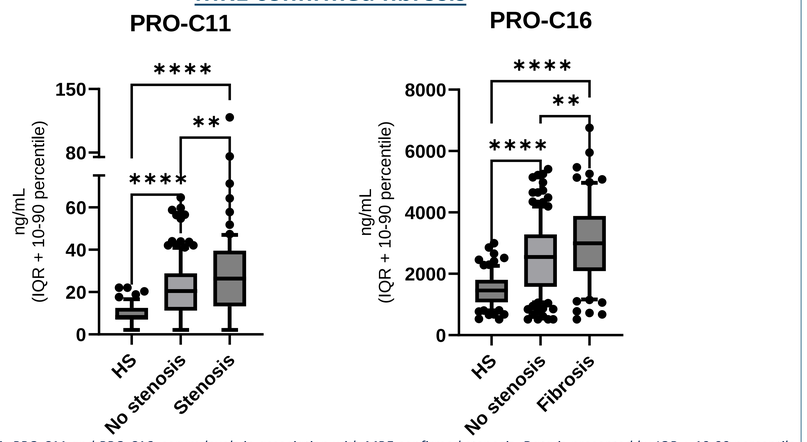


Figure 1: *PRO-C11 and PRO-C16 serum levels in association with MRE-confirmed stenosis. Data is presented by IQR + 10-90 percentile. Asterisks (*) represents statistical differences: *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001*

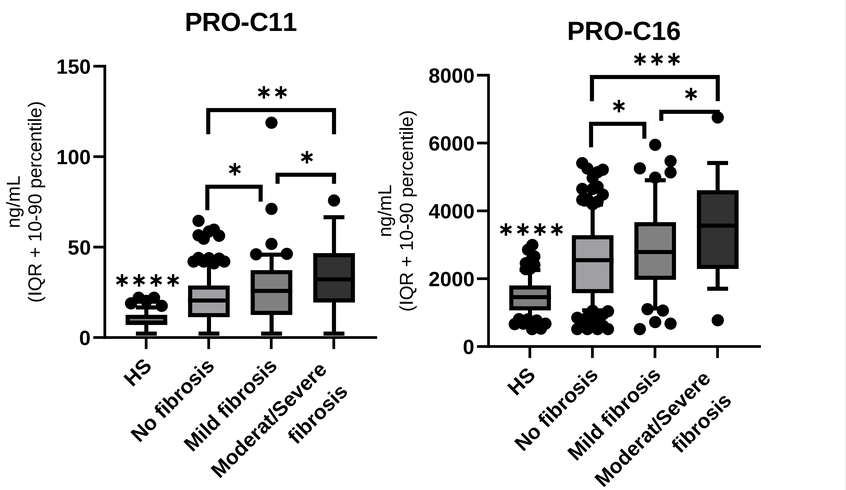


Figure 2: *PRO-C11 and PRO-C16 serum levels in association with the severity of MRE-confirmed stenosis. Data is presented by IQR + 10-90 percentile. Asterisks (*) represents statistical differences: *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001*

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Author disclosures:
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