Serum biomarkers of proteolytic tissue destruction, formation and macrophage activity can discern patients with IBD according to infliximab treatment non-response or response

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1) BACKGROUND

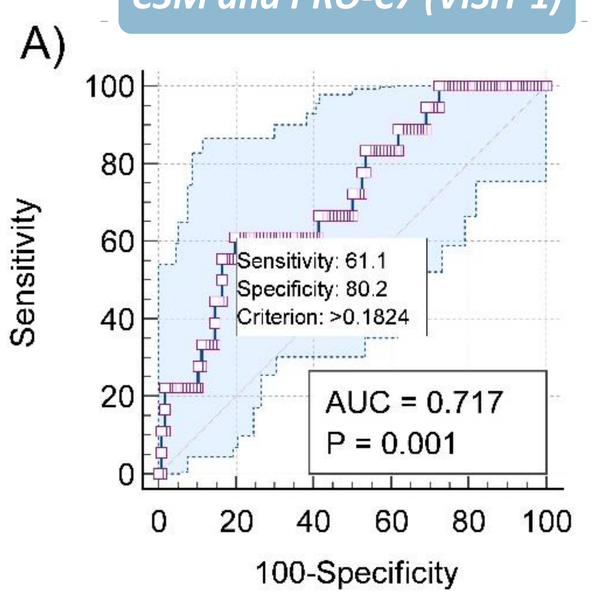
- Characterized by chronic inflammation, patients with Inflammatory Bowel Disease (IBD) experience detrimental remodeling of their intestinal extracellular matrix (ECM).
- Treatment with anti-inflammatory drugs can reduce inflammation, leading to remission and tissue healing.
- However, adequate monitoring of patients is critical to ensure and maintain treatment response. As potential surrogate markers of ECM remodeling, we investigated blood-based biomarkers of type III and -VII collagen and posttranslational modifications of vimentin in patients with IBD.

3) AIM

We aimed to determine the value of the C3M, PRO-C7, and VICM biomarkers for identifying and monitoring response to infliximab (IFX).

4) RESULTS

C3M and PRO-C7 (VISIT 1)



VICM (VISIT 2)

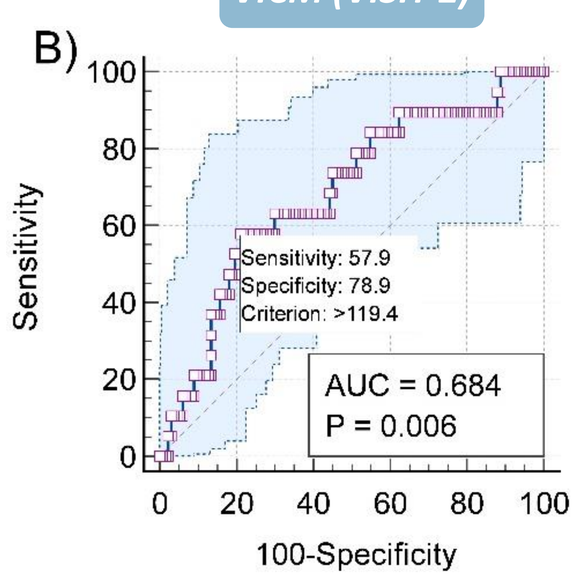


Figure 1. A) Using logistical regression, the combination of serum C3M and PRO-C7 measured at visit 1 could discern non-responders and responders with an AUC of 0.717 (p=0.001, sens: 61.1%, and spec: 80.2%). **B)** At visit 2, serum VICM provided an AUC of 0.684 (p=0.006, sens: 57.9%, and spec: 78.9%)

While all three biomarkers were evaluated at visits 1 and 2, the combination of quantifying mucosal damage and type VII collagen formation identified responders at visit 1 whereas the quantification of macrophage activity at visit 2 identified the responders to IFX treatment.

C3M (VISIT 3)

PRO-C7 (Visit 1) + VICM (Visit 2) + C3M (Visit 3)

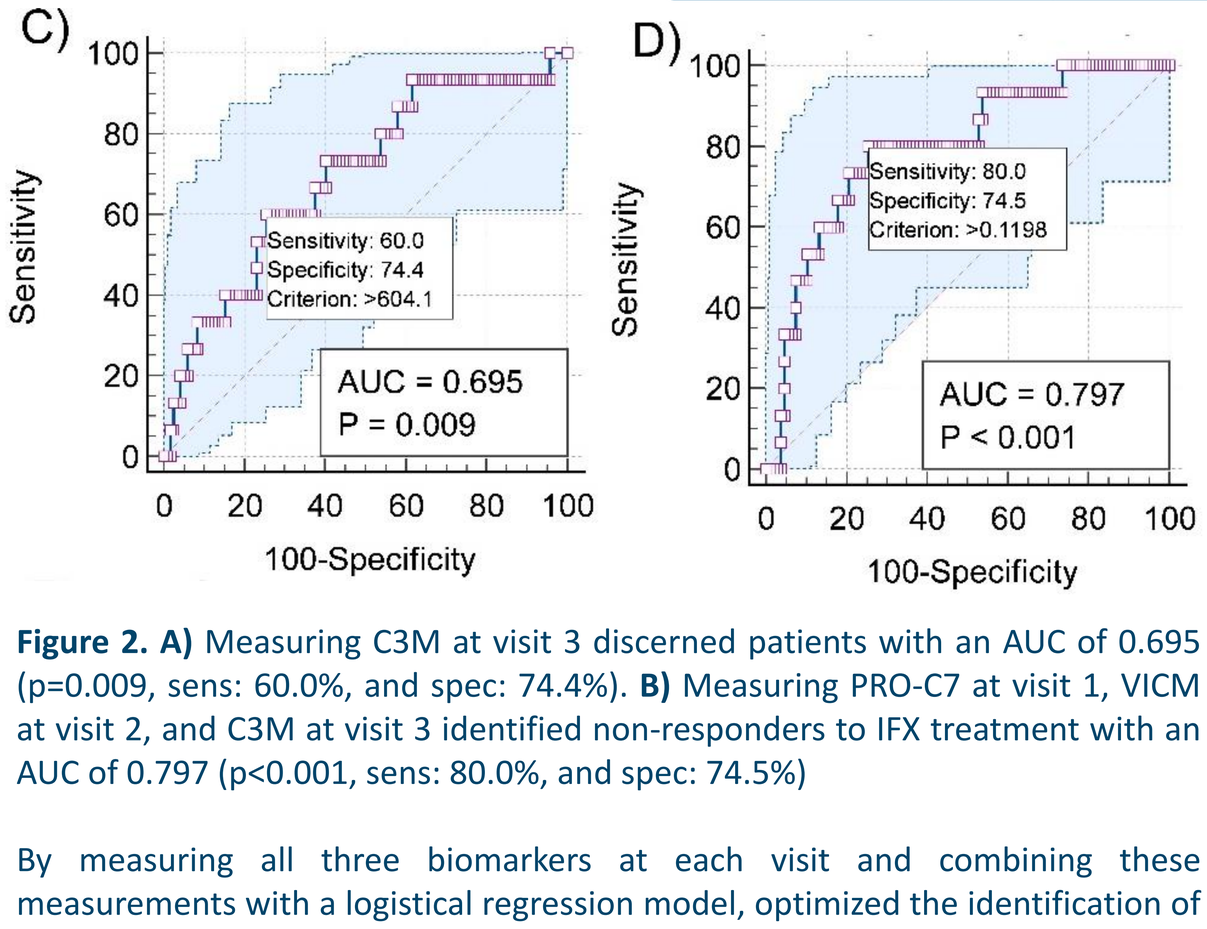
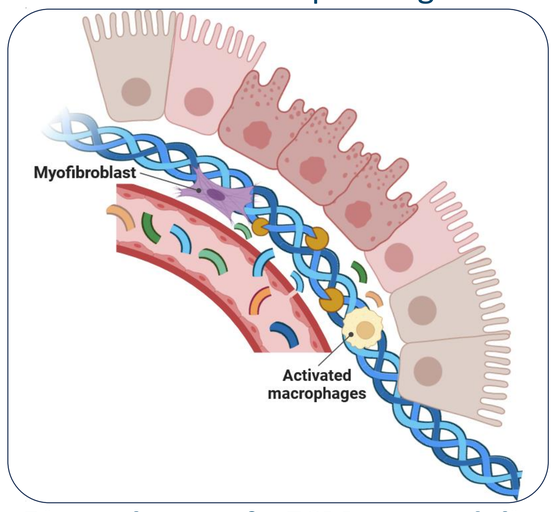


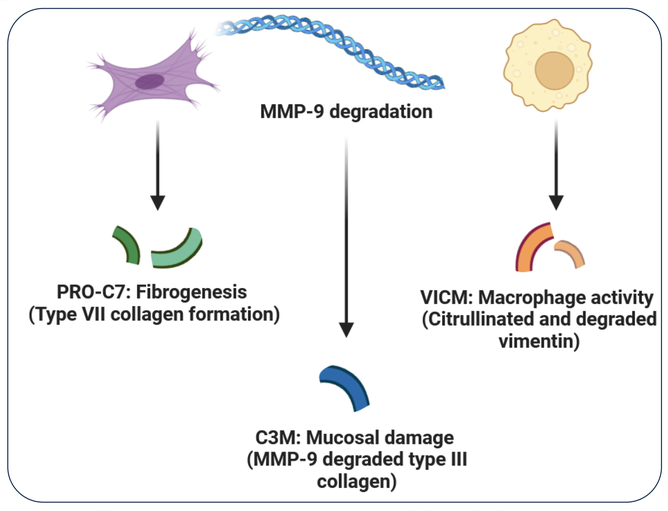
Figure 2. A) Measuring C3M at visit 3 discerned patients with an AUC of 0.695 (p=0.009, sens: 60.0%, and spec: 74.4%). **B)** Measuring PRO-C7 at visit 1, VICM at visit 2, and C3M at visit 3 identified non-responders to IFX treatment with an AUC of 0.797 (p<0.001, sens: 80.0%, and spec: 74.5%)

By measuring all three biomarkers at each visit and combining these measurements with a logistical regression model, optimized the identification of IFX treatment responders compared to measuring at only one visit.

2) METHODS

- Enzyme-linked immunosorbent assays where utilized to quantify MMP-9 degraded (**C3M: Mucosal damage**), type VII collagen formation (**PRO-C7: Fibrogenesis)**, and citrullinated and degraded vimentin (**VICM: Macrophage activity)**.
- The biomarkers, C3M, PRO-C7, and VICM were measured in the serum of 160 patients with IBD.
- Infliximab (IFX) treatment were initiated at Visit 1, with blood drawn at Visits 1, 2, and 3. Treatment response was determined at Visit 3 according to the Physicians Global Assessment (PGA) = 0.
- The biomarker levels between responders and non-responders were statistically assessed using a stepwise logistical regression model and DeLong et al. receiver operating characteristics.





Biomarkers of ECM remodeling in the intestine. Myofibroblasts drive fibrogenesis by release of collagens, including type VII collagen (PRO-C7), where as MMP-9 catalyzed degradation of type III collagen in the interstitial matrix results in the release the C3M (Mucosal degradation). Upon activation, macrophages catalyze the generation of the VICM biomarker, quantifying macrophage activity. Using these biomarkers allow for quantification of ECM remodeling in IBD patients.

Patient demographics

Patients, n	162
Responders, n (%)	147 (90.7%)
Nonresponders, n (%)	15 (9.3%)

Responders to IFX treatment were defined as having a score of 0 according to the Physicians Global Assessment determined at Visit 3.

Additional patient demographical data is pending.

5) CONCLUSION

- **Quantifying a combination of non-invasive biomarkers of ECM remodeling and macrophage activity provided AUCs of 0.684 to 0.797 identifying responders to IFX treatment.**
- **Each biomarker provided value at the three different visits (Visit 1, 2, and 3).**
- **Combining all three biomarkers measured at each visit resulted in an AUC of 0.797 identifying responders to IFX treatment.**

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