

# Saliva and serum inflammatory protein profiles in inflammatory bowel disease

Majster M<sup>1</sup>, Lira-Junior R<sup>1</sup>, Höög C<sup>2,3</sup>, Almer S<sup>2,4</sup>, Boström EA<sup>1</sup>

<sup>1</sup> Division of Oral Diseases, Department of Dental Medicine, Karolinska Institutet, Sweden.

<sup>2</sup> Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden.

<sup>3</sup> GHP Stockholm Gastro Center, Stockholm, Sweden.

<sup>4</sup> Division of Gastroenterology, Department of Gastroenterology, Dermatology and Rheumatology, Karolinska University Hospital, Stockholm, Sweden.

**Aim:** Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, causes chronic inflammation of the gut. IBD can manifest itself both macroscopically and microscopically in the oral cavity however, little is yet known of salivary changes in IBD. Therefore, this study aimed to assess the saliva and serum protein profiles to identify potential salivary markers reflecting presence/activity of IBD.

**Methods:** We measured 92 known inflammatory proteins in serum, unstimulated and stimulated whole saliva samples from IBD patients with active intestinal inflammation (n=21) and matched controls (n=22) by proximity extension assay. Fifteen of the IBD patients returned 10-12 weeks after treatment escalation for re-sampling.

**Results:** Seventy-four proteins were detectable in  $\geq 20\%$  of the samples of the three fluids. Five were unique to serum, IL-22RA1 to unstimulated saliva, IL-1 $\alpha$  to saliva in general, and five proteins were detected only in serum and unstimulated saliva. IL-24 was significantly less detected in serum and stimulated saliva, IL-13, GDNF, and IL-33 more frequently in serum/stimulated saliva from controls compared to IBD patients. Twenty-one inflammatory proteins were significantly increased, and four were significantly decreased in serum of IBD patients compared to controls. Two of the increased serum proteins, IL-6 and MMP-10, were also significantly increased in stimulated saliva of IBD patients and correlated positively to their respective abundance in serum. None of the proteins were significantly altered by IBD treatment in serum nor saliva.

**Conclusions:** The majority of inflammatory proteins detected in serum are detected in saliva as well. The results from our discovery cohort suggest IL-6 and MMP-10 in stimulated saliva as potential salivary markers of IBD, which deserve further investigation and validation.