Utilizing Plasma Proteomics to Predict Anti-TNF Treatment Response in Children with Crohn’s Disease

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Background: Inflammatory Bowel Disease (IBD), consisting of Crohn’s disease (CD) and ulcerative colitis (UC), is an inflammatory disorder of the intestinal tract. Biologics, such as monoclonal antibodies targeting tumor necrosis factor-alpha (TNF), are currently first line in CD. Our aim was to identify novel protein biomarkers predictive of primary anti-TNF response and validate large-scale proteomic results with (1) ELISA and (2) intestinal expression of selected proteins. We hypothesized that the SOMAscan measurement of plasma protein abundance would directly correlate with the plasma proteins abundance using ELISA.

Methods: Patients were previously enrolled in a longitudinal CD cohort (anti-TNF naïve) with blood obtained prior to the first infusion of infliximab. Treatment response was determined by reduction of baseline fecal calprotectin by >50% at 4th infusion. Plasma proteins were measured using SOMAscan (SomaLogic, LLC), a commercial assay measuring relative abundance of 1300 plasma proteins. C-reactive protein and albumin were measured by the CCHMC laboratory and Mannan-Binding Lectin Serine Peptidase 1 (MASP1) with an ELISA (LSBio). Ileal/rectal mRNA was an additional predictor to be determined from formalin, fixed paraffin-embedded (FFPE) blocks in CD patients with SOMAscan.

Results. Forty-six patients were analyzed with SOMAscan prior to anti-TNF (baseline) with 30/46 analyzed prior to fourth infusion. We found baseline median (IQR) CRP was 1 (0.29-2) mg/dL, mean albumin 3.4 (SD 0.5) g/dL with median fecal calprotectin of 1578 (533-2501) mcg/ml. The Spearman correlation coefficient compared CRP [r=0.72, p<0.001 (n=44)] and albumin [r=0.76, p<0.001 (n=35)] to the SOMAscan. As MASP1 was strongly predictive of bioresponse, the Spearman correlation was conducted between MASP1 from the ELISA and SomaLogic [r=0.23, p=0.16 (n=40)]. Additional proteins will be quantified and correlated with SOMAscan. We have performed DNA/RNA from 20 FFPE samples and NANO drop was used to test integrity and quantity of extracted RNA. RT-PCR will be used to determine TREM-1 and OSM evaluated as predictors of infliximab response.

Conclusions: Preliminary results demonstrated CRP and albumin correlated well to SOMAlogic proteomic platform. No correlation was found with additional proteins tested to date (MASP1, FCGR1A). The goal of the ongoing analysis is to test plasma and tissue expression of the proteins identified to predict response.

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