Discussion: Patients with UC and response to therapy had a significantly different pre-treatment microbiome and methylation of genes related to intestinal barrier function, including BAG4ALNT1. Larger studies will be needed to validate these findings, but these results suggest the microbiome and DNA methylation changes may be effective biomarkers of response to therapy and warrant further study.

8

ROLE OF THE HOST IMMUNE RESPONSE TO ENTERIC PROKARYOTIC VIRUSES IN INFLAMMATORY BOWEL DISEASE
Julia Angkeow, Daniel Monaco, Scott Handley, H.B. Larman

Background: Gut microbiota comprise important environmental exposures that influence human immune systems and may alter the clinical course of inflammatory bowel disease (IBD). Little is known about the role of gut bacteriophages (viral components that infect prokaryotic bacteria) and their interactions with the host’s immune responses. We tested the hypotheses that (1) immune responses of individuals with IBD to phages differ from those without IBD and (2) immune responses to phages are associated with disease type (i.e. those with Crohn’s disease have different responses than those with ulcerative colitis).

Methods: We have constructed the first bacteriophage peptide library (“phageome”), based on sequencing of environmental phages and large-scale metagenomic sequencing of virus-like particles isolated from stool samples from IBD patients and their non-IBD household contacts. Using Phage ImmunoPrecipitation Sequencing (PhIP-Seq) technology, we generated complete serum antibody binding profiles of 48 IBD patients (16 ulcerative colitis, 11 Crohn’s, and 11 indeterminate), 9 of their non-IBD household contacts, and an independent non-IBD cohort of 674 volunteers collected by the Vaccine Research Center (VRC) at the National Institutes of Health. Antibody binding profiles were compared among groups using nonparametric statistics.

Results: IBD patients as a group had lower antibody responses to specific phages compared to both non-IBD household contacts and the non-IBD VRC controls; this difference was significant and remained after control for unequal sample sizes. Patients with Crohn’s disease compared to those with ulcerative colitis had similar antibody responses. Particularly for phages of the genera Phivelus, the immune responses of Crohn’s patients were significantly reduced compared to their non-IBD household contacts, while the immune responses of patients with ulcerative colitis did not significantly differ from non-IBD household contacts. IBD disease type comparisons to the VRC controls yielded similar results. Conclusion: PhIP-Seq with a phageome library can be used to study the relationship between immune responses and gut bacteriophages in IBD. Our results suggest that IBD patients may have lower antibody responses to specific phages compared to non-IBD individuals. Differential antibody reactivities in Crohn’s disease vs. ulcerative colitis compared to their household contacts and VRC controls suggest disease-specific response to the gut phageome that warrant further study.

10

THE ROLE OF DIETARY L-SERINE IN THE REGULATION OF INTESTINAL MUCUS BARRIER DURING INFLAMMATION
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Background: Recent accumulating evidence suggests that amino acids have crucial roles in the maintenance of intestinal homeostasis. In inflammatory bowel disease (IBD), amino acid metabolism is changed in both host and the gut microbiota. Among amino acids, L-serine plays a central role in several metabolic processes that are essential for the growth and survival of both mammalian and bacterial cells. However, the role of L-serine in intestinal homeostasis and IBD remains incompletely understood. In this study, we investigated the effect of dietary L-serine on intestinal inflammation in a murine model of colitis.

Methods: Specific pathogen-free (SPF) mice were fed either a control diet (amino acid-based diet) or an L-serine-deficient diet (SDD). Colitis was induced by the treatment of dextran sodium sulfate (DSS). The gut microbiome was analyzed by 16S rRNA sequencing. We also evaluated the effect of dietary L-serine in germ-free mice and gnotobiotic mice that were colonized by a consortium of non-mucolytic bacterial strains or the consortium plus mucolytic bacterial strains.

Results: We found that the SDD exacerbated experimental colitis in SPF mice. However, the severity of colitis in SDD-fed mice was comparable to control diet-fed mice in germ-free condition, suggesting that the gut microbiota is required for exacerbation of colitis caused by the restriction of dietary L-serine. The gut microbiome analysis revealed that dietary L-serine restriction fosters the bloom of a mucus-degrading bacterium Akkermansia muciniphila and adherent-invasive Escherichia coli in the inflamed gut. Consistent with the expansion of mucolytic bacteria, SDD-fed mice showed a loss of the intestinal mucus layer. Dysfunction of the mucus barrier resulted in increased intestinal permeability, thereby leading to bacterial translocation to the intestinal mucosa, which subsequently increased the severity of colitis. The increased intestinal permeability and subsequent bacterial translocation were observed in SDD-fed gnotobiotic mice that colonized by mucolytic bacteria. In contrast, dietary L-serine restriction did not alter intestinal barrier integrity in gnotobiotic mice that colonized only by non-mucolytic bacteria. Conclusion: Our results suggest that dietary L-serine regulates the integrity of the intestinal mucus barrier during inflammation by limiting the expansion of mucus degrading bacteria.

Natural History and Outcomes

P117

CONTENT VALIDITY OF THE SUBCUTANEOUS ADMINISTRATION ASSESSMENT QUESTIONNAIRE (SQA AQ) IN ADULT AND ADOLESCENT PATIENTS WITH MODERATE TO SEVERE CROHN’S DISEASE
Theresa Hunter, April Naegeli, Laura Delbecque, Tamara Al-Zubeidi, Hannah Pegram, Helen Kitchen

Background: Subcutaneous (SC) delivery of biologic therapies is typically via a prefilled syringe or an auto-injector designed to offer a more convenient and more consistent administration of drug product. There is currently no gold standard instrument that is used to assess the usability and patient confidence and preference for an injection device in Crohn’s disease (CD). The Subcutaneous Administration Assessment Questionnaire (SQA AQ) was developed to evaluate ease of use and confidence in SC administrations of therapy. The SQA AQ (Figure 1) features 12 items scored on a 7-point Likert scale (1 = Strongly Disagree to 7 = Strongly Agree). Higher scores indicate better usage experience. The recall period is immediately after patients auto-inject. This study aimed to establish evidence of the content validity of the SQA AQ among patients with moderate to severe CD.

Methods: A semi-structured interview guide was used to conduct face-to-face qualitative interviews with adult (18+ years) and adolescent (12–17 years) patients from the US with a clinician confirmed diagnosis of CD. Cognitive debriefing interviews were structured into sections that explored patients’ opinions, interpretation, and acceptance of the SQA AQ. Data were coded using Atlas.ti using a framework approach where pre-defined codes were applied to quotes that demonstrated patients’ understanding/interpretation, acceptance, and usage of the instructions, items, response scale/options, and recall period.

Figure 1. Violin plots showing antibody enrichments (hits) to four phage genera for each individual in the healthy control (VRC) cohort (n=674) compared to enrichments for each individual in the IBD cohort (n=48). Hits to these four phage genera showed the most statistically significant differences in immune responses between the VRC and IBD cohorts. Mann-Whitney statistics used for comparisons.

Figure 2. Violin plots showing antibody enrichments (hits) to three phage genera for each individual with Crohn’s disease (n=11) compared to each individual with ulcerative colitis (n=16) and each non-IBD household control (n=9). Hits to these three genera showed the most statistically significant differences in immune responses between these three cohorts. Kruskal-Wallis and Mann-Whitney statistics used for comparisons. * denotes p ≤ 0.05, while ** denotes p ≤ 0.01.
CONTENT VALIDITY OF THE SUBCUTANEOUS ADMINISTRATION ASSESSMENT QUESTIONNAIRE (SQAAQ) IN ADULT AND ADOLESCENT PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

April Naegele, Theresa Hunter, Laure Delbecque, Hayley Karn, Anne Skalicky

Background: Subcutaneous (SC) delivery of biologic therapies is typically self-administered via a prefilled syringe or an auto-injector. Auto-injector devices are designed to offer a more convenient and more consistent administration of the drug product. The Subcutaneous Administration Assessment Questionnaire (SQAAQ) is a novel, 12-item, self-administered questionnaire that assesses ease of use of SC delivery devices and patient confidence while using the device to administer an injection of drug. This study aimed to establish evidence of the content validity of the SQAAQ among patients with moderate to severe ulcerative colitis (UC).

Methods: A cross-sectional, US-based, qualitative study using a semi-structured discussion guide was conducted using online focus groups and one-on-one telephone interviews among adolescent (12–17 years) and adult (18 yrs+) participants with diagnosis of moderate-to-severely active UC recruited from clinical sites and patient panels. Cognitive debriefing of the SQAAQ instruction items, recall period, scoring algorithm, and response options was conducted to assess understanding and interpretation of the items. The SQAAQ instructs patients to evaluate the questions based on “to what extent do you agree that the device you just used has these features” on a 7-point Likert scale ranging from “strongly disagree” to “strongly agree”.

Results: Twenty-four patients (adults, n=16; adolescents, n=8) participated in the interviews. Thirteen adults and 3 adolescents experienced moderate disease severity (reported by clinicians). Adult and adolescent groups contained an equal proportion (50%) of male and female participants. Adults had a mean age 50.3 years (range 27.0–75.0), adolescents with mean age 15.6 years (range 14.0–17.0). Overall, two-thirds (n=16, 67%) of patients were white, and the mean duration for CD diagnosis was 8.0 years (range 1.0–23.7). Ten (42%) patients had been on SC treatment for a mean 4.5 years (range 0.2–16.9), all self-administered. Seven (29%) patients had been receiving intravenous treatment for a mean 2.1 years (range 0.2–5.4). The SQAAQ was found to be conceptually relevant, understandable and usable by adults and adolescents with CD. Notably the measurement concepts were confirmed as relevant by participants who currently used SC treatment devices. The patients with no SC experience (n=7, 29%), understood the item wording, response scales, and recall period and had few difficulties completing the measure.

Conclusion: Content validity of the SQAAQ was established in this sample of adolescent and adult patients with CD. The SQAAQ is appropriate for inclusion in CD clinical trials for SC treatment devices with adult and adolescent patients.

Figure 1. Features of the SQAAQ

- Easy for me to learn how to use
- Easy for me to unlock
- Easy to hold in my hand when I inject my dose
- Easy to inject my dose
- Easy to know that my dose is complete
- Easy to store the device in the refrigerator
- Easy to remove needle shield/cover
- Easy to pick up
- Overall, easy to use
- The device is stable against my skin during the injection
- I am confident in my ability to use the device
- I am confident my dose is complete

11 ENTERAL NUTRITION THERAPY IS ASSOCIATED WITH FEWER READMISSIONS AND DEATHS AMONG MALNOURISHED INPATIENTS WITH INFLAMMATORY BOWEL DISEASE

Wendi LeBrett, Jenny Sauk, Berkeley Limkakai

Background: Malnutrition is a common complication observed in hospitalized patients with inflammatory bowel disease (IBD). Enteral nutrition therapy can be used to support the nutritional needs of inpatients with IBD. However, evidence on the impact of inpatient enteral nutrition on clinical outcomes is equivocal. This study assesses post-hospitalization outcomes associated with enteral nutrition therapy amongst inpatients with IBD in a large nationwide database.

Methods: We conducted a retrospective propensity score-matched study among IBD inpatients diagnosed with protein-calorie malnutrition using the Nationwide Readmissions Database from 2010–2015. ICD9 codes associated with each admission were used to identify patients who received enteral nutrition. Using propensity score matching, patients who received inpatient enteral nutrition were matched with patients who did not receive enteral nutrition on the follow-up variables: age, sex, elective admission, patient income, teaching hospital, and hospital urban or rural locality. Primary endpoints included 30-day readmissions, 90-day readmissions, 30-day mortality and 90-day mortality.

Results: Among the 1,588 IBD patients (822 Crohn’s disease, 755 ulcerative colitis, 11 unclassified IBD) with protein-calorie malnutrition, patients who received enteral nutrition (n=794) had fewer 30-day readmissions (OR 0.8; 95% CI 0.55–0.96) and 90-day readmissions (OR 0.77; 95% CI 0.61–0.97). None of the patients (0%) in the enteral nutrition group died on a subsequent admission within 30 days of discharge, compared to 6 patients (0.8%) in the control group (p=0.027). Inpatient mortality within 90 days of discharge did not differ significantly between the two groups (0.8%, enteral nutrition vs. 1.6%, control; p=0.086).

Discussion: Enteral nutrition therapy amongst IBD inpatients with malnutrition was associated with lower odds of readmission and 30-day mortality, but not 90-day mortality. The findings of our study support the use of enteral nutrition in IBD inpatients and motivate the need for prospective studies assessing the impact of enteral nutritional support in IBD inpatients.