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Tu1552

**PRESERVED SARS-CoV-2 VACCINE CELL-MEDIATED IMMUNOGENICITY IN INFLAMMATORY BOWEL DISEASE PATIENTS ON IMMUNE-MODULATING THERAPIES**

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**BACKGROUND:** Immune-modulating medications for inflammatory bowel diseases (IBD) have been associated with suboptimal vaccine responses. There is conflicting data with regards to SARS-CoV-2 vaccination.

**METHODS:** We measured SARS-CoV-2 vaccine immunogenicity at 2 weeks post 2nd mRNA vaccine in IBD patients as compared to normal healthy donors (NHD). We measured humoral immune responses to SARS-CoV-2: anti-sp immune globulin G (IgG) and anti-receptor binding domain (RBD) IgG were measured by ELISA, and neutralizing antibody titters were measured using recombinant, reporter SARS-CoV-2. Antigen specific memory B cells were measured using recombinant SARS-CoV-2 proteins. Activation induced marker T cell (AIM) assays were performed using SARS-CoV-2 spike magnetoplas. Immunophenotyping was performed by flow cytometry.

**RESULTS:** We enrolled 29 patients with IBD (19 with Crohn’s disease, 10 with ulcerative colitis) on infliximab (IFX) monotherapy (N=9), IFX combination therapy with a thiopurine (N=9), vedolizumab monotherapy (N=11) as compared to matched NHD (N=12). At 2 weeks post vaccination, all subjects made detectable anti-sp IgG and anti-RBD IgG. There were no differences in anti-sp IgG titers among the different groups. IBD patients on IFX monotherapy, but not IBD patients on IFX combination therapy or vedolizumab monotherapy, had lower anti-RBD and neutralization titers as compared to NHD (p-value: 0.041 and 0.023, respectively) (Fig. 1). There were no significant differences in the proportion of spike-specific or RBD-specific memory B cells in IBD patients as compared to NHD (Fig. 1). There were no differences in the proportion of spike-specific CD4+ or CD8+ T cells in all IBD patients as compared to NHDs (Fig. 2).

**CONCLUSIONS:** We demonstrate overall comparable and preserved cell-mediated immunity to SARS-CoV-2 vaccination in a small cohort of IBD patients treated with a range of different immune-modulating medications as compared to healthy controls. Larger numbers of patients are needed to validate these findings.

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**Figure 1**

Humoral Immune Responses to SARS-CoV-2 vaccine in IBD patients. (A) Spike IgG, (B) RBD IgG, (C) Nucleocapsid IgG titers by ELISA and (D) Pseudovirus neutralizing titers for IBD patients on infliximab (n=9), infliximab combination therapy (n=9), and vedolizumab (n=11) and normal healthy donors (NHD, n=12). There were no differences in the frequency of (E) spike-specific and (F) receptor binding domain (RBD)-specific memory B cells between IBD patients and normal healthy donors. Frequencies of post vaccine responses were compared between IBD patients on their respective biologies and NHDs using Mann-Whitney test. Red dots indicate recipients of mRNA-1273 (NHD-Moderna); blue dots indicate recipients of BNT 162b2 (Pfizer-BioNTech) vaccine. Dotted lines = Limit of Detection for Assay. Dashed Lines = Limit of Sensitivity for Assay. ETI = Endpoint titer.

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**Tu1553**

**SPECIFIC IMMUNOGLOBULIN A INDUCED BY THE PERSISTENT COLONIZATION OF ADHERENT-INVASIVE E. COLI LIMITS PATHOBIONT LOCALIZATION TO THE EPITHELIAL NICHE**

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**Introduction.** A new category of bacteria, called pathobionts, that promotes disease only when host genes or environmental conditions are altered, has been identified. A pathotype of Escherichia coli, namely adherent-invasive E. coli (AIEC), is known as a potential pathobiont associated with Crohn’s disease (CD). The colonization by AIEC exacerbates inflammatory inflammation and fibrosis in murine colitis models (Macalod Immunol. 2019,12(3):632).

**Methods:** Specific pathogen-free (SPF) mice were pre-treated with a cocktail of antibiotics and then colonized either by an AIEC strain LBF2 or a commensal E. coli strain HS. The induction of IgA was measured by ELISA. The specificity of IgA was evaluated by flowcytometry. LBF2 and HS AIEC, ΔoppA, and ΔoppC mutant strains were used to determine the antigen specificity of induced IgA. The function of IgA was assessed by in vitro bacterial invasion assay using a human colonic epithelial cell line Caco-2. Results: We found that AIEC, but not commensal E. coli, colonized induced IgA production in mice. The induced IgA selectively bound to AIEC strains but not to commensal E. coli strains. Induced IgA recognized surface antigen of AIEC LBF2, including fimbriae and outer membrane proteins. Also, we found that AIEC-specific IgA limits the invasion of the AIEC LBF2 to the colonic epithelial cells. Conclusion: These results suggested that IgA, induced by the persistent colonization by AIEC, interfered the protection to the host by inhibiting invasion of the pathobionts to the colonic epithelial cells.

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**Figure 2**

Cell-mediated Immune Responses to SARS-CoV-2 vaccine in IBD patients. Comparable frequencies of SARS-CoV-2 specific total (A) CD4+ and (B) CD8+ T cells in IBD patients and normal healthy donors (NHD, n=10). The dotted line represents the limit of detection (LOD) at 0.01%. Frequencies of post vaccine responses were compared between IBD patients on their respective biologics and normal healthy donors using Mann-Whitney test. Red dots indicate recipients of mRNA-1273 (NHD-Moderna); blue dots indicate recipients of BNT 162b2 (Pfizer-BioNTech) vaccine. Dotted lines = Limit of Detection for Assay.

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**Tu1554**

**A NOVEL METHOD FOR COLLECTING MICROBIOLOGICAL SPECIMENS**

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**Introduction.** Our current understanding of intestinal microbiota is limited due to inaccessibility and lack of appropriate methods for direct sampling and analysis. Microbiome composition varies along the gastrointestinal (GI) tract and microtube analysis through the fecal sample does not provide a completely accurate snapshot of the microbial composition in the more proximal regions due to the inclusion of dead organisms from the upper respiratory tract and the gut. Our Recoverable Sampling System (RSS) capsule successfully aspirates intestinal fluid samples autonomously and non-invasively while passing naturally through the GI tract. Armed with anatomical site recognition algorithms, a novel sampling mechanism, and a preservative formulation, our device provides a revolutionary method of live microbiome specimen acquisition not afforded by traditional methods of collection. Using this device, we have been able to achieve precise and site-specific sampling of microbiome in the intestine. Methods We performed a feasibility study of microbiome collection in the large intestine using our RSS capsule in 4 healthy subjects. Three of the subjects swallowed two capsules on two occasions several days apart while the fourth subject swallowed one capsule only. Capsules were recovered in their feces and sent to the laboratory along with a preserved fecal sample for analysis. Aspirated and preserved fluid from each capsule was extracted and processed for quantitative culture, 16s qPCR, and 16S microbiome sequencing. The self-collected fecal samples were also processed and analyzed via 16S sequencing. Results The results from quantitative culture and 16s qPCR showed significant correlation in microbial load between fecal versus capsule samples which indicates the functionality of proximal sampling and preservative formulation of the RSS. Beta diversity analysis showed a distinct separation between samples collected through RSS capsule vs. fecal samples (Figure 1). The population of microorganisms collected through the RSS Capsule also showed a unique signature to the intestinal microbiome compared to the subject’s fecal sample. Discussion Our RSS Capsule is an electromechanical device that can recognize anatomical sites within the GI tract and is pre-programmed to take a single sample of intestinal fluid at a targeted location, for example within the upper or lower GI. Fluid aspirate is collected in sampling chambers that contain an absorbent pad impregnated with a preservative formulation capable of keeping organisms viable for weeks. After ingestion and natural passage, the capsule is retrieved from the feces using a Capsule Recovery Kit. This study demonstrated that RSS capsule can successfully collect a site-specific sample in the intestine. This has enormous implications for the microbiome field as a non-invasive, anatomical site-specific, collection device.