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## INTRODUCTION

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I am a physician-scientist with clinical expertise in inflammatory bowel disease and research expertise in clinical trial methodology and design, biomarker discovery, and multi-omic multi-dimensional data integration to study immune mediated inflammatory diseases. I completed my internal medicine residency and chief residency at Dartmouth where I was mentored by Corey Siegel, and subsequently I completed a 3-year NIH sponsored T32 research fellowship and a 1-year IBD clinical fellowship at the University of California San Diego under the mentorship of Bill Sandborn. I joined faculty at University of California San Diego in 2018, and during my first year as faculty I completed a clinical trials fellowship at Robarts Clinical Trials (now Alimentiv) where I worked closely with Geert D'Haens, Brian Feagan, and Vipul Jairath to study clinical trial design and methodology. During my NIH funded research fellowship and early years as faculty, I secured career development support from the American Gastroenterology Association and was co-mentored by Lucilla Ohno-Machado, a world-renowned expert in bioinformatics, data modeling, and distributed computing, and Rob Knight, a well-recognized pioneer in the field of microbiome research and high-throughput multi-dimensional data generation and computation. The totality of my training in clinical trials for IBD, end-point development, multi-omic data integration, and multi-level data modeling, has allowed me to embark into the field of human-translational research with a specific focus on integrating evolving technology and methodology to study immune-microbe interactions in the context of therapeutic interventions. My goal is to provide a growing framework for how we in the field of IBD can begin to develop and validate companion tools and/or biomarkers for disease prognosis, treatment prediction, and drug development programs.

During my training and early faculty years notable accomplishments, which are further outlined in detail in my Bibliography, include: 1) the completion of two phase 2 clinical trials for hyperbaric oxygen therapy in ulcerative colitis and the accompanying translational research to support the approval of a \$12 million NIH funded clinical trial across the United States with deep immune-microbe profiling using state of the art spatial profiling technology, 2) a patent related to the discovery of novel microbial proteases which can be targeted for treatment of inflammatory bowel disease which has now been license for further drug development, 3) development of novel end-points and disease activity assessment tools including a new patient reported outcome tool and the Prometheus Endoscopic Healing Index, 4) the creation of a large consortium across North America to generate real world evidence for small molecules and biologics (VICTORY and SUCCESS consortiums), and 5) the development and validation of prediction models and clinical decision support tools for personalized use of biologics which has now led to the development of a medical device in Europe for personalized use of vedolizumab. The totality of my work to date has led to my Sherman Emerging Leader Prize in 2022.

Within just the first 3 years as faculty at UC San Diego I was recommended for promotion to Associate Professor, and I was subsequently recruited to Northwestern University in the tenure track at the Feinberg School of Medicine where I serve as the Director of GI Clinical Trials and Precision Medicine, and I also oversee our GI biorepository for the Division of Gastroenterology and Hepatology. At Northwestern University my research program a robust infrastructure for both industry and investigator initiated clinical trials, as well as a wet lab that is fully equipped for human translational biobanking and high-throughput digital spatial profiling and single-cell sequencing of both immune cells and microbes at the tissue level. I am working to integrate this novel technology with my prior computational and bioinformatic training to bring forward spatial biology into drug development programs and translational research in IBD. This is demonstrated by my recent NIDDK funded R01 to study the spatial interactions of neutrophils and how they govern treatment resistance in IBD, and my role on several steering committees to lead the translational research programs for pharmaceutical companies.

**EDUCATION**

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2009	Medicine Bachelor and Bachelor of Surgery (MBBS) Dayanand Medical College - Ludhiana, Punjab; India
2012	Certificate Degree, Hyperbaric Medicine Medical University of South Carolina, Charleston, SC; USA
2021	Clinical Research Enhancement Through Supplemental Training (CREST) University of California San Diego, San Diego, CA; USA

**CLINICAL**

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**ACADEMIC APPOINTMENTS**

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Feb 1, 2022	– Current	Associate Professor of Medicine, Gastroenterology Feinberg School of Medicine Northwestern University
March 1, 2019	– Jan 18, 2022	Assistant Professor of Medicine, Gastroenterology University of California San Diego – San Diego, CA VA Medical Center – San Diego, CA
July 1, 2017	– Feb 28, 2019	Instructor of Medicine, Gastroenterology University of California San Diego – San Diego, CA
July 1, 2013	– June 30, 2014	Instructor of Medicine Geisel School of Medicine at Dartmouth – Hanover, NH

**POST GRADUATE TRAINING AND FELLOWSHIPS**

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July 1, 2018	– June 30, 2019	Fellowship in Inflammatory Bowel Disease Clinical Trials Robarts Clinical Trials (Alimentiv Inc) – San Diego, CA
July 1, 2017	– June 30, 2018	Clinical IBD Fellowship, Gastroenterology and Hepatology University of California San Diego – San Diego, CA
July 1, 2016	– June 30, 2017	Chief Clinical Fellow, Gastroenterology and Hepatology University of California San Diego – San Diego, CA
July 1, 2014	– June 30, 2016	NIH T32 Research Fellow, Gastroenterology and Hepatology University of California San Diego – San Diego, CA
July 1, 2013	– June 30, 2014	Chief Resident, Department of Medicine Dartmouth Hitchcock Medical Center – Lebanon, NH
June 26, 2010	– June 30, 2013	Internship and Residency, Internal Medicine Dartmouth Hitchcock Medical Center – Lebanon, NH

**EXAMINATIONS, CERTIFICATION AND LICENSURE**

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Feb. 8, 2013	USMLE Step 3	
June 1, 2009	USMLE Step 2 CS	
June 27, 2009	USMLE Step 2 CK	
July 7, 2006	USMLE Step 1	
Mar 1, 2010	ECFMG Certification (#07036593)	
June 5, 2013	– June 30, 2015	New Hampshire State Medical License (#16161)
May 14, 2014	– Sept 30, 2023	California State Medical License (#A130399)
Dec 1, 2021	– July 31, 2023	Illinois State Medical License (#036.158764)
Aug 21, 2013	– Aug 21, 2023	American Board of Internal Medicine Certification (#341584)
Nov 13, 2017	– Nov 13, 2027	ABIM, Gastroenterology & Hepatology Certification (#341584)

**AWARDS AND HONORS**


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Sherman Prize	Emerging Leader, 2022
UCSD Internal Medicine Dept.	Resident Teaching Award, 2019
ACG International Meeting	Top Poster Award, 2019
ACG International Meeting	Auxiliary Abstract Award, 2019 (top ranked abstract)
AGA Career Development Award	Research Scholar Award, 2019
ACG Career Development Award	Junior Faculty Development Grant, 2019
ECCO International Meeting	Best Abstract Presentation, 2018
Digestive Disease Week	Poster of Distinction, 2015, 2018, 2022, 2023
Digestive Disease Week	AGA Fellow Abstract of the Year, 2017
ACG National Meeting	Presidential poster award, 2012
New England Endoscopy Society	Research Award, 2012
Dartmouth Hitchcock GME	Thomas P. Almy Housestaff Award, 2012
A.P. Gold Humanism Society	Humanism and Excellence in Teaching Award, 2011
Dartmouth Hitchcock DOM	Excellence in Teaching Award, 2010

**EXTERNAL PROFESSIONAL SERVICES****EDITORIAL BOARD**


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Gastroenterology: 2020 to present  
 Inflammatory Bowel Disease: 2020 to present  
 Alimentary Pharmacology & Therapeutics: 2020 to present

**GRANTS AND RESEARCH SUPPORT****CURRENT****Hyperbaric Oxygen for Hospitalized UC Flares (mPI Dulai/Balmert)**


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NIDDK U01 DK126626-01 \$12,712,824 03/1/23 – 8/30/28

During this U01 we will conduct a multi-center, double-blind, sham-controlled trial for hyperbaric oxygen to treat ulcerative colitis patients hospitalized for moderate to severe flares. Aims 2 and 3 will focus on spatial transcriptomics, spatial proteomics, and multi-omic microbial profiling to define host-microbe interactions governing treatment response and adaptation to oxygen exposure in colonic mucosa.

**Neutrophil Mechanisms for Resistance to Biologics in Ulcerative Colitis (MPI; Sumagin/Dulai)**

NIDDK R01DK135620 \$2,727,248 8/1/23-5/31/27

The goal of this proposal is to define the mucosal spatial heterogeneity in neutrophils within the context of biologic and small molecule treatment response, and confirm with in-vivo and in-vitro experiments the mechanisms of how neutrophils promote resistance to advanced medical therapies in ulcerative colitis.

**PREVIOUS****AGA Research Scholar Award (PI)**


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7/1/19 – 4/30/23

Career Development Award \$300,000

This grant provides infrastructure support and protected time to build and integrate point of care prediction models and clinical decision support tools into a single user interface, and further refine them using machine learning. Skills gained during this grant included multi-dimensional data integration, data modeling, and machine learning methodology.

**San Diego Digestive Disease Center (Co-I; Schnabl/Eckmann MPI)**

4/1/19 – 1/18/22

NIDDK P30 DK120515 \$9,147,418

This is a P30 sponsored digestive disease center with 3 core facilities related to microbiomics/genomics, human translational sample biobanking, and animal facilities. As a Co-investigator in the Human Translational Core, my major research goal is to create a HIPPA compliant, encrypted, dataware house and multi-omic integrated data interface for human translational samples that can be used by center members and become a resource for future collaborative research projects.

**PATENTS**

1. Therapeutic Approach for Inflammatory Bowel Disease by Targeting Microbial Proteases (Gonzalez, Dulai, Mills; provisional patent approved, full patent pending; 62/927,621 and 62/971,148) – Licensed out for further drug development

**PUBLICATIONS**

Relevant peer-reviewed publications highlighted below. Full bibliography of citations available at: <https://www.ncbi.nlm.nih.gov/myncbi/1NawasFl-YCQ3/bibliography/public/>

**Hyperbaric Oxygen Therapy for Inflammatory Bowel Disease:** I led two phase 2 clinical trial programs to study the efficacy and safety of hyperbaric oxygen therapy for the treatment of ulcerative colitis patients hospitalized for moderate-severe flares. We demonstrated that the addition of oxygen therapy to intravenous steroids (compared to sham air with intravenous steroids) resulted in significantly higher rates of clinical response and remission within 5 days, and significantly lower rates for in-hospital progression to colectomy or need for rescue biologic therapy. Subsequently, using a multi-omic approach, we integrated bulkRNA sequencing, spatial transcriptomics and proteomics, mucosal tandem-mass tag proteomics, and microbial sequencing (16S, metagenomics, metabolomics, metagenomics, metaproteomics) to define mechanisms of treatment response and/or resistance. We identified and confirmed a central mechanism of response to oxygen therapy in colitis was neutrophil related degranulation and tissue injury via STAT3. We further identified that a central mechanism of resistance to hyperbaric oxygen therapy in colitis was *Akkermansia muciniphila* adaptation to oxygen exposure leading to persistent mucus degradation and mucosal inflammation. This work led to the funding of my NIDDK U01 clinical-translational research program for hyperbaric oxygen therapy in colitis.

- a. **Dulai PS**, Buckey JC Jr, Raffals LE, Swoger JM, Claus PL, O'Toole K, Ptak JA, Gleeson MW, Widjaja CE, Chang JT, Adler JM, Patel N, Skinner LA, Haren SP, Goldby-Reffner K, Thompson KD, Siegel CA. Hyperbaric oxygen therapy is well tolerated and effective for ulcerative colitis patients hospitalized for moderate-severe flares: a phase 2A pilot multi-center, randomized, double-blind, sham-controlled trial. *Am J Gastroenterol*. 2018 Oct;113(10):1516-1523. doi: 10.1038/s41395-018-0005-z. Epub 2018 Feb 16. PMID:29453383
- b. **Dulai PS**, Raffals LE, Hudesman D, Chiorean M, Cross R, Ahmed T, Winter M, Chang S, Fudman D, Sadler C, Chiu EL, Ross FL, Toups G, Murad MH, Sethuraman K, Holm JR, Guilliod R, Levine B, Buckey JC Jr, Siegel CA. A phase 2B randomised trial of hyperbaric oxygen therapy for ulcerative colitis patients hospitalised for moderate to severe flares. *Aliment Pharmacol Ther*. 2020 Sep;52(6):955-963. doi: 10.1111/apt.15984. Epub 2020 Aug 3. PMID:32745306
- c. **Dulai PS**, Jairath V. A Microsimulation Model to Project the 5-Year Impact of Using Hyperbaric Oxygen Therapy for Ulcerative Colitis Patients Hospitalized for Acute Flares. *Dig Dis Sci*. 2021 Nov;66(11):3740-3752. doi: 10.1007/s10620-020-06707-3. Epub 2020 Nov 13. PMID:3318578
- d. Gonzalez CG, Mills RH, Kordahi MC, Carrillo-Terrazas M, Secaira-Morocho H, Widjaja CE, Tsai MS, Mittal Y, Yee BA, Vargas F, Weldon K, Gauglitz JM, Delaroque C, Saucedo C, Rossitto LA, Ackermann G, Humphrey G, Swafford AD, Siegel CA, Buckey JC Jr, Raffals LE, Sadler C, Lindholm P, Fisch KM, Valaseck M, Suriawinata A, Yeo GW, Ghosh P, Chang JT, Chu H, Dorrestein P, Zhu Q, Chassaing B, Knight R, Gonzalez DJ, **Dulai PS**. The Host-Microbiome Response to Hyperbaric Oxygen Therapy in Ulcerative Colitis Patients. *Cell Mol Gastroenterol Hepatol*. 2022;14(1):35-53. doi: 10.1016/j.jcmgh.2022.03.008. Epub 2022 Apr 1. PMID: 35378331

**Host-Microbe Determinants and Drivers of Inflammatory Bowel Disease:** During my American Gastroenterology Association Research Scholar Award I worked closely with the lab of Rob Knight, my co-mentor, and other labs with expertise in metabolomics (Dorrestein lab) and proteomics (Gonzalez lab). We discovered a novel *Bacteroides Vulgatus* protease and demonstrated that this protease was a primary determinant of disease activity in ulcerative colitis. We further demonstrated that by targeting and

blocking this protease we could reverse epithelial damage and colitis in epithelial cell models and gnotobiotic mice. This led to a co-first author publication in *Nature Microbiology* and a patent for targeting microbial proteases in IBD (Gonzalez DJ, Dulai PS, Mills RH, US patent 62/971,148 and 62/927,621). The patent has been licensed for further drug development and I am currently guiding the industry partner on the phase 1 trial program in addition to the development of companion biomarkers. The training and expertise gained from this work supported the funding of the translational aims in my NIH/NIDDK U01.

- a. Mills RH<sup>#</sup>, **Dulai PS<sup>#</sup> (co-first authors)**, Vazquez-Baez Y, Ochoa MM, Zhu Q, Weldon K, Humphrey G, Carrillo-Terrazas M, Goldasich LD, Bryant M, Quinn RA, Gewirtz AT, Chassaing B, Chu H, Sandborn WJ, Dorrestein P, Knight R, Gonzalez D. Meta-omics Reveals Microbiome Driven Proteolysis as a Contributing Factor to Severity of Ulcerative Colitis Disease Activity. *Nature Microbiology* 2022 Feb;7(2):262-276
- b. Gonzalez CG, Mills RH, Zhu Q, Saucedo C, Knight R, **Dulai PS\* (co-corresponding/co-senior)**, Gonzalez DJ. Location-specific signatures of Crohn's disease at a multi-omics scale. *Microbiome* 2022 Aug 24;10(1):133

**End-point development for IBD:** I have worked to develop novel patient reported outcome, biomarker, and endoscopy-based indices for inflammatory bowel diseases. First, I led a multi-national prospective observational cohort study to develop a novel patient reported outcome tool which is now undergoing further evaluation and validation for use in FDA registration trials. Second, leveraging my prior work and expertise in multi-omic biomarker data integration, I provided scientific guidance and expertise to support the development and validation of a novel serum-based biomarker panel of disease activity in Crohn's disease is now commercially available through Prometheus Labs (EHI Index). Third, I provided oversight and guidance for the modeling work done which led to the development of a new endoscopic scoring index in Crohn's disease, which was demonstrated to be superior to existing indices in its prognostic and discriminative performance. Finally, I have now taken my prior work with end-point development to guide the identification of histological features associated with treatment resistance. This work, paired with my emerging work in spatial biology, led to the funding of my NIH/NIDDK R01 and has now allowed me to embark on pursuing tissue based multi-plexed biomarker panels for individualized treatment response stratification and prediction.

- a. **Dulai PS**, Jairath V, Khanna R, Ma C, McCarrier KP, Martin ML, Parker CE, Morris J, Feagan BG, Sandborn WJ. Development of the symptoms and impacts questionnaire for Crohn's disease and ulcerative colitis. *Aliment Pharmacol Ther.* 2020 Jun;51(11):1047-1066.
- b. D'Haens G, Kelly O, Battat R, Silverbeg MS, Laharie D, Louis E, Savarino E, Bodini G, Yarur A, Boland BS, Afif W, Li XJ, Hale M, Ho J, Kondragunta V, Huang B, Kuy C, Okada L, Hester KD, Bray KR, Mimms L, Jain A, Singh S, Collins A, Valasek MA, Sandborn WJ, Vermeire S<sup>#</sup>, **Dulai PS<sup>#</sup>(co-senior)**. Development and validation of a test to monitoring endoscopic activity in patients with Crohn's disease based on serum levels of proteins. *Gastroenterology* 2020, Feb;158(3):515-526
- c. Narula N, Wong ECL, Colombel JF, Sandborn WJ, Marshall JK, Daperno M, Reinisch W<sup>#</sup>, **Dulai PS<sup>#</sup> (co-senior)**. Prediction endoscopic remission in Crohn's disease by the modified multiplier SES-CD (MM-SES-CD). *Gut* 2021 Mar 25
- d. Narula N, Wong ECL, Colombel JF, Riddell R, Marshall JK, Reinisch W<sup>#</sup>, **Dulai PS<sup>#</sup> (co-senior)**. Early Change in Epithelial Neutrophilic Infiltrate Predicts Long-Term Response to Biologics in Ulcerative Colitis. *Clin Gastroenterol Hepatol* 2021 Jul 3;S1542-3565

**IBD Health Outcomes Consortium:** As the overall and primary coordinating PI, I led the development of a multi-national collaborative research consortium comprised of over 20 academic centers across North America. This includes the VICTORY consortium and SUCCESS consortium. I created a centralized data warehouse which served as a data repository for effectiveness and safety data on over 10,000 biologic treated IBD patients. This collaborative research group published over a dozen manuscripts utilizing this database and provided me with hands on experience and oversight for relational database management, data integration, and advanced analytic methodologies. I have leveraged this larger consortium to now

bring together data integration with endoscopic video recording to provide the framework and support for my NIDDK U01 pragmatic clinical trial for hyperbaric oxygen therapy in ulcerative colitis.

- a. **Dulai PS**, Singh S, Jiang X, Peerani F, Narula N, Chaudrey K, Whitehead D, Hudesman D, Lukin D, Swaminath A, Shmidt E, Wang S, Boland BS, Chang JT, Kane S, Siegel CA, Loftus EV, Sandborn WJ, Sands BE, Colombel JF. The Real-World Effectiveness and Safety of Vedolizumab for Moderate-Severe Crohn's Disease: Results from the US VICTORY Consortium. *Am J Gastroenterol*. 2016 Aug;111(8):1147-55.
- b. Narula N, Peerani F, Meserve J, Kochhar G, Chaudrey K, Hartke J, Chilukuri P, Koliani-Pace J, Winters A, Katta L, Shmidt E, Hirten R, Faleck D, Parikh MP, Whitehead D, Boland BS, Singh S, Sagi SV, Fischer M, Chang S, Barocas M, Luo M, Lasch K, Bohm M, Lukin D, Sultan K, Swaminath A, Hudesman D, Gupta N, Shen B, Kane S, Loftus EV, Siegel CA, Sands BE, Colombel JF, Sandborn WJ, **Dulai PS**. Vedolizumab for Ulcerative Colitis: Treatment Outcomes from the VICTORY Consortium. *Am J Gastroenterol*. 2018 Sep;113(9):1345-1354.
- c. Johnson AM, Barsky M, Ahmed W, Zullo S, Galati J, Jairath V, Narula N, Peerani F, Click BH, Coburn ES, Dang TT, Gold S, Agrawal M, Garg R, Aggarwal M, Mohammad D, Halloran B, Kochhar GS, Todorowski H, Ud Din NM, Izanec J, Teeple A, Gasink C, Muser E, Ding Z, Swaminath A, Lakhani K, Hogan D, Datta S, Ungaro RC, Boland BS, Bohm M, Fischer M, Sagi S, Afzali A, Ullman T, Lawlor G, Baumgart DC, Chang S, Hudesman D, Lukin D, Scherl EJ, Colombel JF, Sands BE, Siegel CA, Regueiro M, Sandborn WJ, Bruining D, Kane S, Loftus EV Jr, **Dulai PS** The Real-World Effectiveness and Safety of Ustekinumab in the Treatment of Crohn's Disease: Results From the SUCCESS Consortium. *Am J Gastroenterol*. 2023 Feb 1;118(2):317-328.

**Prognostic and predictive clinical decision support tools:** Leveraging my experience and training in clinical trials, and the collaborative research consortium built to study real-world outcomes for biologics, I led the development of novel drug specific prediction tools for vedolizumab, infliximab, and ustekinumab in Crohn's disease and ulcerative colitis. Using the training gained in advanced regression modeling and machine learning, I was able to combine these tools into an easy-to-use decision support tool which is freely available online for providers and endorsed by the American Gastroenterology Association ([www.CDSTforIBD.com](http://www.CDSTforIBD.com)). The vedolizumab clinical decision support for Crohn's disease is now going through EMA review as a medical device and will be marketed in Europe for guiding treatment selection and patient care decisions.

- a. **Dulai PS**, Boland BS, Singh S, Chaudrey K, Koliani-Pace JL, Kochhar G, Parikh MP, Shmidt E, Hartke J, Chilukuri P, Meserve J, Whitehead D, Hirten R, Winters AC, Katta LG, Peerani F, Narula N, Sultan K, Swaminath A, Bohm M, Lukin D, Hudesman D, Chang JT, Rivera-Nieves J, Jairath V, Zou GY, Feagan BG, Shen B, Siegel CA, Loftus EV Jr, Kane S, Sands BE, Colombel JF, Sandborn WJ, Lasch K, Cao C. Development and Validation of a Scoring System to Predict Outcomes of Vedolizumab Treatment in Patients With Crohn's Disease. *Gastroenterology*. 2018 Sep;155(3):687-695
- b. **Dulai PS**, Leonard G, Ma T, Jairath V, Singh S, Feagan BG, Gasink C, Pires A, Sandborn W. Clinical Prediction Model and Decision Support Tool for Ustekinumab in Crohn's Disease. *Am J Gastroenterol*. 2019 Oct; 114:S373
- c. **Dulai PS**, Singh S, VandeCastele N, Meserve J, Winters A, Chablaney S, Aniwani S, Shashi P, Kochhar G, Weiss A, Koliani-Pace J, Gao Y, Boland BS, Chang JT, Faleck D, Hirten R, Ungaro R, Lukin D, Sultan K, Hudesman D, Chang S, Bohm M, Varma S, Fischer M, Shmidt E, Swaminath A, Gupta N, Rosario M, Jairath V, Guizzetti L, Feagan BG, Siegel CA, Shen B, Kane S, Loftus EV, Sandborn WJ, Sands BE, Colombel JF, Lasch K, Cao C. Development and Validation of Clinical Scoring Tool to Predict Treatment Outcomes With Vedolizumab in Ulcerative Colitis *Clin Gastroenterol Hepatol*. 2020 Dec;18(13):2952-2961
- d. **Dulai PS**, Wong ECL, Reinish W, Narula N. Clinical Decision Support Tool for Infliximab in Crohn's Disease. *Clin Gastroenterol Hepatol*. 2021 Jun 30;S1542-3565