




## Curriculum Vitae

	<b>Name</b> (First Name, Middle Name Last Name)	<b>Eytan Wine</b>
	<b>Position</b>	Professor of Pediatrics and Physiology, Clinician Scientist, and Pediatric Gastroenterologist
	<b>Affiliation</b>	<b>University of Alberta</b>
	<b>Country</b>	Canada
	<b>Major Field</b>	Pediatric IBD; Host-microbe interactions; Microbiome

### Education Background

After Medical and Pediatric training in Israel, Dr. Wine completed a Pediatric Gastroenterology Fellowship at the Hospital for Sick Children in Toronto and earned his PhD in Cellular Microbiology at the University of Toronto in Philip Sherman's laboratory, followed by post-doctoral training.

### Professional Experience

Dr. Wine's clinical expertise is managing children with inflammatory bowel diseases with specific interest in diets, such as the Crohn disease exclusion diet (CDED). This interest fits well with his laboratory research focus on involvement of intestinal bacteria and nutrition in development of intestinal inflammation, enabling translational bench-to-bedside research. The Wine lab has diverse expertise in basic aspects of IBD, especially in children, using patient samples and disease models to investigate the roles of microbes, nutrition, the epithelial lining and barrier function, and inflammation in pathogenesis.

### Professional Organizations

Dr. Wine is a co-principal applicant on the CIHR-CHILD Foundation Canadian Children IBD Network, member of the Dietitians or ECCO (D-ECCO) Committee, and is on the Executive of the ESPGHAN Porto IBD Group.

### Scientific Publication

**Contributions to Science** [Selected from a total of 117 peer-review publications; trainees underlined; H index: 36; total citations: 5,035 (as per Google Scholar, May 2022)]; trainees are underlined.

**Complete List of Published Work:** <https://scholar.google.com/citations?user=ON9jPY4AAAAJ&hl=en>

1. **Host-microbe interactions in the gut:** the main focus of my lab is on how intestinal microbes, and the host response to them, impact human disease, with specific focus on pediatric IBD. To achieve this, I have developed a translational program, mostly using samples collected from patients. We utilize cell models, animal models, and patient-derived microbes to test our hypotheses. The focus of host-microbe interaction is the mucosal surface, where we have identified changes in the mucus layer and microbes. Some of these changes are mediated by the inflammasome, which is critical for controlling bacterial growth. I have also worked on how these interactions with the gut epithelium impacts IBD, and the critical role of these interactions and the inflammation they contribute to in development of cancer later in life.
  - a. H Armstrong, M Alipour, R Valcheva, M Bording-Jorgensen, J Jovel, D Zaidi, P Shah, Y Lou, C Ebeling, AL Mason, D Lafleur, J Jerasi, GKS Wong, K Madsen, MW Carroll, HQ Huynh, LA

Dieleman, **E Wine**. *Host Immunoglobulin G Selectively Identifies Pathosymbionts in Pediatric Inflammatory Bowel Diseases. Microbiome 2019;7:1.*

- b. **M Alipour, D Zaidi, R Valcheva, J Jovel, I Martinez, C Sergi, J Walter, AL Mason, GK Wong, LA Dieleman, MW Carroll, HQ Huynh, E Wine**. Mucosal barrier disruption and loss of bacterial diversity are primary abnormalities in paediatric ulcerative colitis. *Journal Crohn's & Colitis (JCC) 2016;10:462-71.*
- c. **M. Alipour, Y. Lou, M. Bording-Jorgensen, D. Zimmerman, C. Sergi, JJ. Liu, E. Wine**. A Balanced IL-1 $\beta$  Activity is Required for Host Response to *Citrobacter rodentium* Infection. *PLoS One 2013;8:e80656.*
- d. **E Wine, S Hussay, NL Jones**. Microbial Interactions with Gut Epithelium. Chapter 19. In: RE. Kleinman, IR. Sanderson, O. Goulet, PM. Sherman, G. Mieli-Vergani, BL. Shneider, eds. Walker's Pediatric Gastrointestinal Disease, 6<sup>th</sup> Ed. 2018. People's Medical Publishing House.
- e. **H Armstrong, M Bording-Jorgensen, E Wine**. *The multifaceted roles of diet, microbes, and metabolites in cancer. Cancers 2021;13:767*
- f. **H Armstrong, M Bording-Jorgensen, S Dijk, E Wine**. The complex interplay between chronic inflammation, the microbiome, and cancer: understanding disease progression and what we can do to prevent it. *Cancers 2018;10:83.*

2. **IBD microbiome and metabolome:** in addition to the functional role of the host-microbe interface, we have recognized the importance of using microbe and their metabolites as biomarkers in IBD. Our work showing the ability of microbial composition to predict failure of response to steroids and need for rescue therapy in children hospitalized with acute severe colitis (Michail & Wine, 2012), has been extensively cited (~250). Most of this work is currently underway, including a paper recently published, showing the ability of specific metabolites to impact bacterial invasion (Zaidi & Wine). We have laid the foundations for using metabolomics in the stool and intestinal washes for investigating IBD pathogenesis. A recent clinical study on antibiotics in IBD and other clinical studies I'm involved in, offer additional opportunities for similar studies, currently underway.

- a. S. Michail, M. Durbin, D. Turner, AM. Griffiths, D. Mack, J. Hyams, N. Leleiko, H. Kenche, A. Stolfi, **E. Wine**. *Alterations in the gut microbiome of children with severe ulcerative colitis. Inflammatory Bowel Diseases (IBD) 2012;18:1799-808.*
- b. **D Zaidi, H Huynh, M Carroll, R Mandal, D Wishart, E Wine**. *Gut microenvironment impacts bacterial invasion in pediatric inflammatory bowel diseases. Journal of Pediatric Gastroenterology and Nutrition (JPGN) 2020;71:624-32.*
- c. R Little, **E Wine**, BM Kamath, AM Griffiths, A Ricciuto. *Gut Microbiome in primary sclerosing cholangitis: A review. World Journal of Gastroenterology 2020;26:2678-80.*
- d. N Karu, L Deng, **M Slae, AC Guo, T Sajed, H Huynh, E Wine, DS Wishart**. *A Review on Human Fecal Metabolomics: Methods, Applications and the Human Fecal Metabolome Database. Analytica Chimica Acta 2018;1030:1-24.*
- e. J Jovel, LA Dieleman, D Kao, AL Mason, **E Wine**. *The Human Gut Microbiome in Health and Disease*. Chapter 10. In: Muniyandi Nagarajan, ed. *Metagenomics: Perspectives, Methods and Applications*. 2017. Elsevier Inc., pp 197-213.
- f. A Levine, M Kori, J Kierkus, R Sigall Boneh, M Sladek, J Escher, **E Wine**... D Turner. *Azithromycin and Metronidazole versus Metronidazole Based Therapy for Induction of Remission in Mild to Moderate Paediatric Crohn Disease: a Randomized Controlled Trial. Gut 2019;68:239-47.*
- g. D Sprockett, N Fischer, R Sigall Boneh, D Turner, J Kierkus, M Sladek, JC Escher, **E Wine**... A Levine, DA Relman. *Treatment-Specific Composition of Gut Microbiota is Associated with Disease Remission in a Pediatric Crohn's Disease Cohort. IBD 2019;25:1927-38.*
- h. C Bourdon, N Lelijveld, D Thompson, P Dalvi, GB Gonzales, D Wang, **M Alipour, E Wine, E Chimwezi, JC Wells, M Kerac, R Bandsma, MJ Nyirenda**. *Metabolomics in plasma of Malawian children 7 years after surviving severe acute malnutrition: "ChroSAM" a cohort study. EBioMedicine 2019;45:464-72.*

3. **Nutrition in clinical and translational pediatric IBD:** my interest in nutrition in IBD offers an important bridge between clinical IBD and disease pathogenesis, all very much related to microbes. Together with Dr. Levine, I have described mechanisms by which diet can contribute to IBD and/or offer a solution, through dietary therapy; most of these mechanisms relate to microbes, their metabolites, and responses to microbes. Some of these findings are already applied to clinical guidelines (through ECCO) while others are under active ongoing investigation [such as the Crohn's disease exclusion diet (CDED), for which I am analyzing the metabolomic profiles; I am co-senior author on the first diet RCT in IBD, using the CDED; *Gastroenterology* 2019; 258 citations]. On the clinical side, we have identified the barriers and opportunities for improving care with nutritional therapy in pediatric IBD.
- A Levine\*, **E Wine\***, A Assa... and J van Limbergen\*. *Crohn's Disease Exclusion Diet Plus Partial Enteral Induces Sustained Remission in a Randomized Controlled Trial*. \* co-senior authors. *Gastroenterology* 2019;157:440-50.
  - A Levine, R Sigall Boneh, **E Wine**. *The Evolving Role of Diet in the Pathogenesis and Treatment of Inflammatory Bowel Disease*. *Gut* 2018;67:1726-38.
  - A. Levine, **E. Wine**. *Effects of exclusive enteral nutrition on Crohn's disease: Clues to the impact of diet on disease pathogenesis*. *IBD* 2013;19:1322-9.
  - H Armstrong, I Mander, Z Zhang, D Armstrong, **E Wine**. *Not all fibres are born equal; variable response to dietary fibre subtypes in IBD*. *Frontiers in Pediatrics* 2021;8:620189.
  - M Lawley, JW Wu, VM Navas-López, HQ Huynh, MW Carroll, M Chen, P Medvedev, AS Day, S Hussey, R Sigall-Boneh, A Levine, **E Wine**. *Global Variation in Use of Enteral Nutrition for Pediatric Crohn Disease*. *JPGN* 2018;67:e22-29.
  - R Sigall Boneh, J Van Limbergen, **E Wine**... A Levine. *Dietary Therapies Induce Rapid Response and Remission in Pediatric Patients with Active Crohn's Disease*. *Clin Gastroenterol Hepatol* 2021;19:752-.
  - A Levine, JM Rhodes, JO Lindsay, MT Abreu, MA Kamm, P Gibson, C Gasche, MS Silverberg, U Mahadevan, R Sigall Boneh, **E Wine**... JD Lewis. *Dietary Guidance for Patients with Inflammatory Bowel Disease from the International Organization for the Study of Inflammatory Bowel Disease*. *Clin Gastroenterol Hepatol* 2020;18:1381-92.
4. **Cellular microbiology, host immune responses, and intestinal pathogens:** specific aspects of the host-microbe interface have become foci in the lab. This includes the immune recognition and response to intracellular microbes through the inflammasome. Work in my lab has delineated the mechanisms of inflammasome activation, leading to bacterial killing, and suggests that improving inflammasome response could reduce systemic inflammation. Related to this, we have focused on the NF- $\kappa$ B signalling pathway and its regulation through A20 as a key mediator of pediatric IBD. Some specific microbial pathways have also been explored.
- M Bording-Jorgensen, H Armstrong, M Wickenberg, P LaPointe, **E Wine**. *Macrophages and Epithelial Cells Mutually Interact Through NLRP3 to Clear Infection and Enhance the Gastrointestinal Barrier*. *Immuno* 2022;2:13-25.
  - H Armstrong, M Bording-Jorgensen, R Chan, **E Wine**. *Alternative activation of the NLRP3 inflammasome in Macrophages Increases Bacterial Killing*. *Frontiers in Immunology* 2019;10:2296.
  - M Bording-Jorgensen, M Alipour, G Danesh, **E Wine**. *ATP-induced inflammasome activation enhances *Citrobacter rodentium* clearance mediated by ROS*. *Cellular Physiology Biochemistry* 2017;41:193-204.
  - D Zaidi, HQ Huynh, M Carroll, S Baksh, **E Wine**. *Tumor necrosis factor  $\alpha$ -induced protein 3 (A20) is Dysregulated in Pediatric Crohn Disease*. *Clin Exp Gastroenterol* 2018;11:217-31.
  - D Zaidi, **E Wine**. *Regulation of Nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B) in Inflammatory Bowel Diseases*. *Frontiers in Pediatrics* 2018;6:317.

f. W Elhenawy, M Bording-Jorgensen, E Valguarnera, MF Haurat, **E Wine**, MF Feldman. *LPS Remodelling triggers formation of Outer Membrane Vesicles in Salmonella. mBio 2016;7:e00940.*

5. **Clinical/translational research in pediatric IBD:** although I am involved in clinical studies in pediatric IBD, my main interest (and papers selected below reflect this) is in more mechanistic studies, describing this unique patient population. Specifically, I've been interested in studying the uninvolved gut in IBD, as this most likely is less impacted by inflammation itself. We have described fundamental changes in the small bowel of children with ulcerative colitis (which is thought to be unaffected), including changes in the epithelial barrier and blood flow, using advanced imaging (confocal endomicroscopy). We have also shown a prognostic capacity for cytokine responses in acute severe colitis.

- a. PF van Rheen... **E Wine\***, FM Ruummele. \* Equal contribution. *The Medical Management of Paediatric Crohn's Disease: an ECCO-ESPGHAN Guideline Update. JCC 2021;15:171-94.*
- b. D Zaidi, M Bording-Jorgensen, HQ Huynh, M Carroll, JF Turcotte, C Sergi, JJ Liu, **E Wine**. *Increased epithelial gap density in the non-inflamed duodenum of children with inflammatory bowel diseases. JPGN, 2016;63:644-50.*
- c. D Zaidi, L Churchill, HQ Huynh, MW Carroll, R Persad, **E Wine**. *Capillary Flow Rates in the Duodenum of Pediatric Ulcerative Colitis Patients Are Increased and Unrelated to Inflammation. JPGN 2017;65:306-10; Featured on Journal Cover.*
- d. D Zaidi, HQ Huynh, M Carroll, **E Wine**. *Prognostic value of probe-based confocal laser endomicroscopy in pediatric inflammatory bowel diseases. J Gastroenterol Res 2018;2:77-87.*
- e. **E. Wine**, DR. Mack, J. Hyams, AR. Otley, J. Markowitz, WV. Crandall, N. Leleiko, AM. Muise, AM. Griffiths, D. Turner. *Interleukin-6 is associated with steroid resistance and reflects disease activity in pediatric severe ulcerative colitis. JCC 2013;7:916-22.*

### Honors & Awards

1999	Tel-Aviv University M.D. Thesis of the Year Award and Scholarship (\$2,000)
2006-2008	Hospital for Sick Children Research Training Competition (Ranked 1 <sup>st</sup> ; \$160,000. Declined)
2006-2009	Canadian Institutes of Health Research/Canadian Association of Gastroenterology/Industry (AstraZeneca) Research Initiative Award. (\$195,000 over 3 years)
2007-2011	Hospital for Sick Children Clinician Scientist Training Program (\$40,000; Declined after 1y)
2007-2009	Canadian Child Health Clinician Scientist Program (CCHCSP) CEP Award (\$10,000)
2011	Future Leaders in IBD (FLIBD) Preceptorship Travel Award: 1 week at the Alimentary Pharmabiotic Centre, Cork University, Ireland, with Prof. Fergus Shanahan.
2012	Young Investigator Travel Award for the WCPGHAN in Taiwan (US\$1,500)
2015	CIHR Nutrition, Metabolism and Diabetes New Investigator top ranked application. CAD\$5,000
2015	Top 10 teachers of the year undergraduate students teaching award.
2017	Department of Pediatrics 2017 Cooperation, Collaboration, and Teamwork Award to the Edmonton Pediatric IBD Clinic (EPIC); Team member.
2019	Annual Academic & Clinical Research Paper Author Award, Department of Pediatrics (for <i>Armstrong &amp; Wine, Microbiome, 2019</i> )
2021	Department of Pediatrics: Annual Teaching Award by Subspecialty Pediatric Residents