



Diarrhea in IBD

Pejman Rohani MD

Associate Professor

Head of Pediatric Gastroenterology and Hepatology

Research Center

ESPGHAN Member

PIBD SIG of ESPGHAN

CF and Pancreatic SIG of ESPGHAN

PSC SIG of ESPGHAN

Pediatric Center of Excellence, Children's Medical Center



ORIGINAL ARTICLE

INTESTINAL
RESEARCH

pISSN 1598-9100 • eISSN 2288-1956
https://doi.org/10.5217/ir.2025.00061
Intest Res, Published online December 12, 2025

Preventive and therapeutic effects of co-administration of *Bacteroides thetaiotaomicron* and infliximab on dextran sodium sulfate-induced colitis in mice

Sara Ahmadi Badi^{1,2*}, Hamid Reza Moradi^{3*}, Ahmad Berimipour⁴, Shima Shojaie¹, Arian Kariman¹, Hananeh Tavakoli Aval², Seyed Amirhesam Seyedi², Mehdi Davari⁵, Mohammad Hassan Sohoul¹, Shohreh Khatami², Seyed Davar Siadat^{5,6}, Pejman Rohani¹

¹Pediatric Gastroenterology and Hepatology Research Center, Pediatrics Center of Excellence, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran; ²Department of Biochemistry, Pasteur Institute of Iran, Tehran, Iran; ³Department of Basic Sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran; ⁴Department of Biological Sciences and BioDiscovery Institute, University of North Texas, Denton, TX, USA; ⁵Department of Mycobacteriology and Pulmonary Research, Pasteur Institute of Iran, Tehran, Iran; ⁶Microbiology Research Center, Pasteur Institute of Iran, Tehran, Iran



www.nature.com/pr



CLINICAL RESEARCH ARTICLE

Clinical and genomic features of Iranian patients with very early onset IBD

Mahya Haghipanah¹, Pejman Rohani², Meino Rohlf³, Shabnam Shahrokh⁴, Fatemeh Farahmand², Maryam Sotoudeh Anvari², Maximilian Witzel³, Shokoufeh Ahmadipour⁵, Mohammadhassan Sohoul², Seyed Mohsen Dehghani⁶, Christoph Klein^{3,7}, Daniel Kotlarz^{3,8,9}, Bahram M. Soltani^{1,9} and Mehdi Totonchi^{4,9,10}

© The Author(s), under exclusive licence to the International Pediatric Research Foundation, Inc 2026

Ghorbanpour et al. *Molecular Medicine* (2026) 32:26
https://doi.org/10.1186/s10020-026-01424-5

Molecular Medicine

REVIEW

Open Access



Monogenic forms of inflammatory bowel disease: Genetic mechanisms, models, and clinical implications

Amirhossein Ghorbanpour¹, Pejman Rohani², Shabnam Shahrokh³, Georges Dimitrov⁴, Mehdi Totonchi^{3,5,6*} and Stefan Dimitrov^{5,7*}

FEASIBILITY STUDY

Establishment of an NGS-Based Clinical Genomics Diagnostic Laboratory

Whole Exome Sequencing (WES) with IBD-Focused Panel-Based Clinical Reporting

Proposed Investigators:

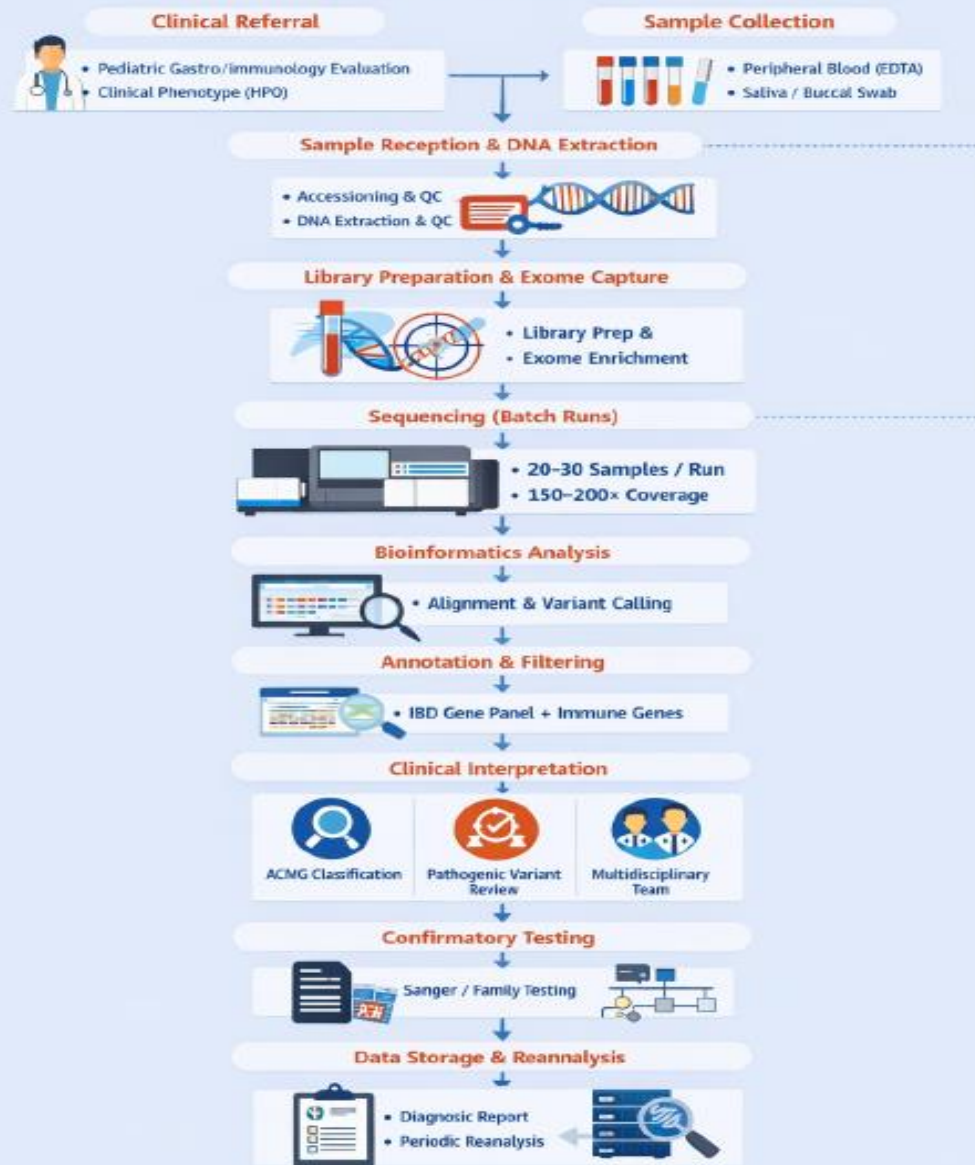
Dr Pejman Rohani,

Children's Medical Center Hospital, Medical University of Tehran,

Dr Mehdi Totonchi,

University of Campania Luigi Vanvitelli, Naples, Italy.

Genomics Workflow for Pediatric IBD Diagnostics



Genomic Diagnostics Laboratory Layout

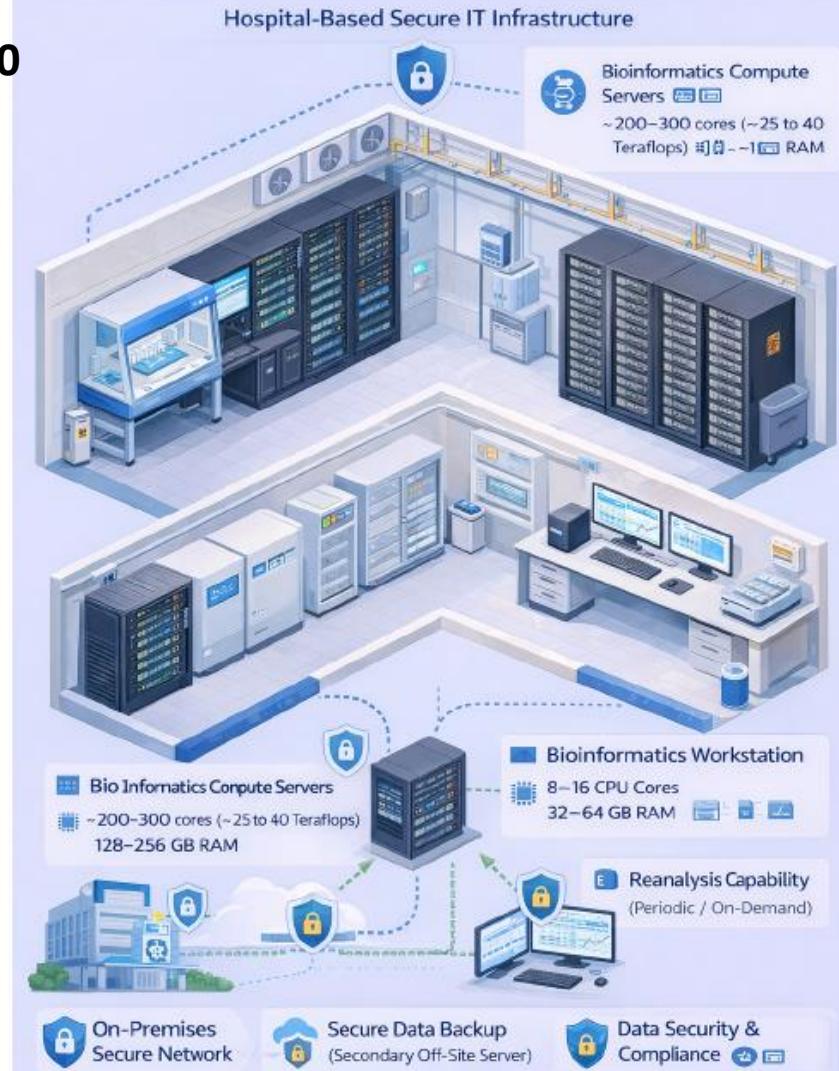


Don't forget to mention control with intensive presence of staff.
Ensure potent panel separation for sample preservation.

Equipment & Infrastructure
Estimated Total: 650,000 USD

Expected Annual Operating Cost Range: 200,000 USD per year.

Bioinformatics Infrastructure Requirements for Pediatric IBD Genomics (~100 WES Cases/Month)



Diarrhea is the hallmark symptom associated with IBD and is seen in almost 80% of the cases.

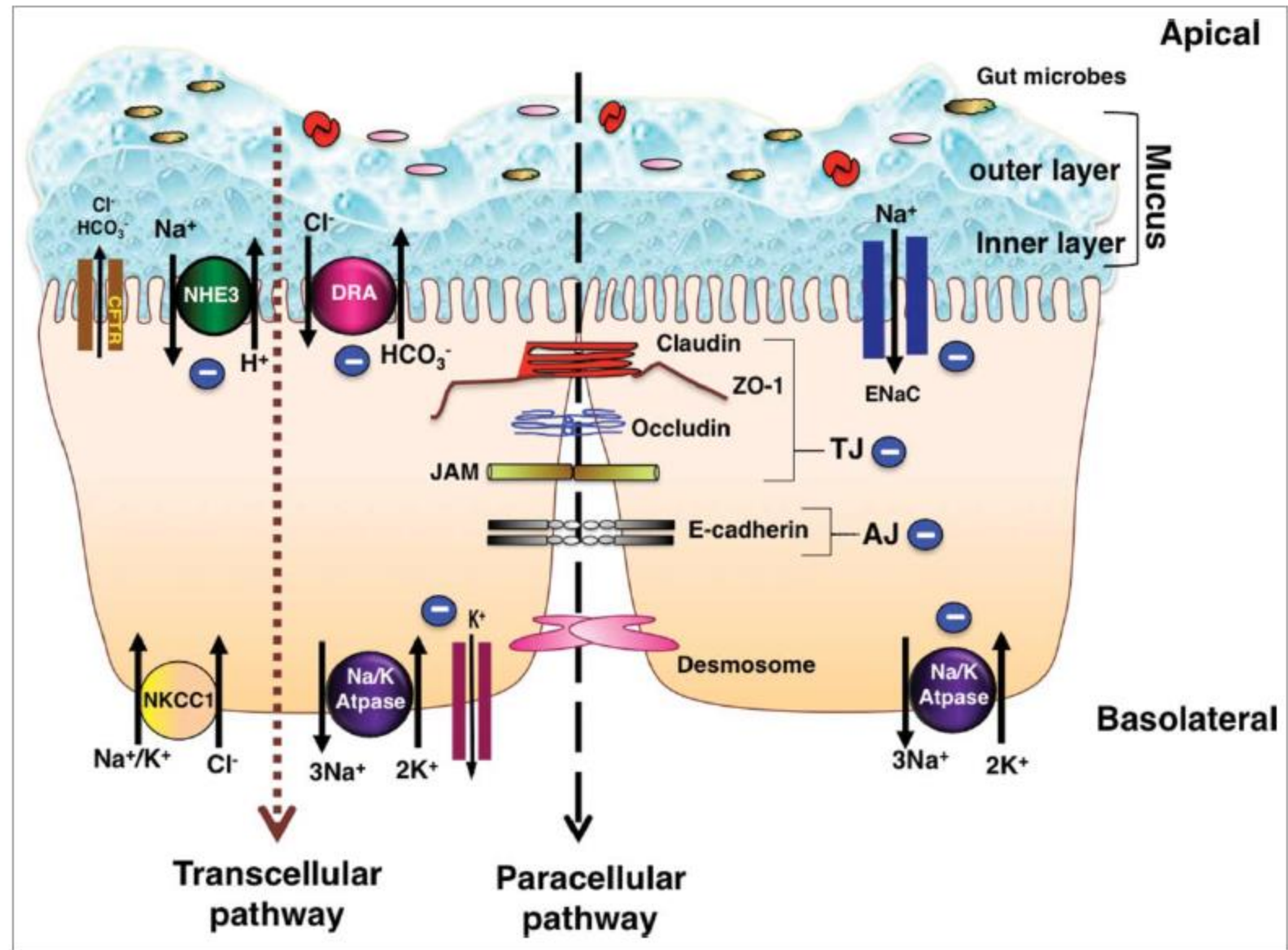
Depending upon the site and magnitude of intestinal inflammation the severity of diarrhea varies in IBD patients, ranging from increased bowel frequency to chronic diarrhea requiring electrolyte supplementation and hospitalization.

The severity of diarrhea (stool frequency and consistency) is thus considered as an important determinant of the disease activity index.

Predominant mechanism of diarrhea in IBD involves impairment of electroneutral NaCl absorption accompanied with dysfunctional ENaC and NaC/KC-ATPase, with very little role if any played by anion secretion.

Negative sign indicates the downregulation in function and/or expression of NHE3, DRA, ENaC and NaC/KC-ATPase in IBD.

Negative sign indicates the downregulation in function and/or expression of TJ and AJ proteins in IBD. Breakdown of barrier function in IBD results in diarrhea via leak-flux mechanism.



IBD and altered NaC absorption in the intestine

So far 11 NHE isoforms (NHE1-11) have been identified in mammals each having a different cellular localization and tissue distribution. In the intestinal epithelium, NHE2, NHE3 and NHE8 are present on the apical membrane and NHE1 is located on the basolateral membrane

Among the four isoforms that are present in the intestine, the direct involvement of NHE1 (SLC9A1) and NHE2 (SLC9A2) in IBD associated diarrhea is not evident.

Interestingly, CSD patients also carry mutations in guanylate cyclase C (GUCY2C) where deficiency in NaC absorption has been attributed to elevated cGMP levels resulting from gain-of-function mutations in GUCY2C.

Alterations in NHE3 function and/or expression observed in IBD patients have further substantiated that NHE3 dysfunction contributes to IBD associated diarrhea. However, the mechanism of NHE3 inhibition is controversial and is attributed to either i) decreased NHE3 activity as seen in human UC biopsies with unaltered protein, mRNA and surface expression or ii) decreased NHE3 protein levels observed in both UC and CD patient biopsies with reduced NHE3 mRNA observed only in CD biopsies

Recent report by Janecke et al,[47](#) identified loss-of-function mutations in the SLC9A3 gene in 9 CSD (Congenital Sodium Diarrhea) patients. Interestingly, among this subset of 9 patients with mutated NHE3, 2 patients developed IBD implicating the deficiency of NHE3 in the pathophysiology of diarrhea in IBD.

Aberrant epithelial barrier and leak-flux diarrhea

Enhanced intestinal permeability associated with disrupted paracellular barrier is observed in both CD and UC patients.

Two major consequences of compromised epithelial barrier in IBD are a) increased translocation of luminal antigens resulting in activation of mucosal immune system and perpetuation of inflammation and b) back flow of absorbed solutes and water via the paracellular pathway into the luminal compartment leading to “leak-flux” diarrhea

It has been noticed that the first-degree relatives of CD patients demonstrate increased intestinal permeability and are at increased risk for developing IBD.

Reduction in depth of TJ meshwork, number of TJ strands together with strand breaks and discontinuous strand architecture are identified as possible causes of barrier dysfunction in both CD and UC.

In this regard, investigations in patients with CD revealed unaltered expression for claudins-1 and 4, decrease in protein expression of occludin, claudins- 3, 5, 7, 8 and JAM-A.

Comparable changes in TJs were also seen in UC patients with contradictory reports for claudins-1, 4 and elevation in claudin- 2 protein levels

Sodium potassium ATPase (NaC/KC-ATPase) and IBD associated diarrhea

A number of in vivo and in vitro studies have indicated that pro-inflammatory cytokines such as IFN- γ , TNF α and IL-1 β are responsible for NaC/KC-ATPase dysfunction in IBD.

Several studies have shown that the activity of NaC/KC-ATPase was significantly down regulated in the inflamed mucosa of UC and CD patients

Chloride bicarbonate exchangers and diarrhea

Down Regulated in Adenoma (DRA or SLC26A3) and Putative Anion Transporter-1 (PAT-1 or SLC26A6) belong to SLC26 gene family and are the two main transporters involved in apical Cl⁻/HCO₃⁻ exchange in the mammalian intestine. DRA and PAT-1 exhibit an inverse pattern of expression along the length of the intestine.

DRA appears to be critical in the development of IBD associated diarrhea.

Causality of this correlation is not completely known but can be attributed (a) primarily to pro-inflammatory mediators and oxidative stress prevalent in IBD that can affect DRA transcriptionally and post-translationally, respectively and (b) secondarily to lost or reduced DRA function resulting in aberrant mucus barrier.