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Inflammatory bowel disease (IBD) is a group of pathological conditions mainly concerned with the gastrointestinal tract of the human body. IBD encompasses a variety of disorders, of which, Ulcerative colitis (UC) and Crohn’s disease (CD) are the most significant ones. IBD deals with the inflammation of the intestine due to an autoimmune failure. UC and CD present a host of symptoms with specific pathological and clinical signs including periods of disease remission and with intermittent exacerbations of symptoms. IBD typically occurs in individuals belonging to the age group of 20 to 40 years, with many of the affected individuals progressing to a relapse and chronic disease. Amongst the families of the IBD patients, First-degree relatives have a greater relative risk. A pattern of rising incidence in the past one to two decades, is seen in many of the developing world countries with historically low rates of occurrence of IBD, pointing towards the involvement of environmental factors also.

UC is an inflammatory disorder of the mucosal lining of the intestines which is limited to the rectum and the colon, with its source at the rectum and developing into the upper intestinal tract at different distances. The disease is divided into various subtypes. When the inflammation is restricted at the rectum, it is known as Ulcerative proctitis. If the inflammation progresses to the splenic flexure it is referred to as left sided colitis and if it spreads beyond the splenic flexure, the condition is named as pancolitis. Infrequent involvement of the cecum or the terminal ileum in terms of inflammation, is called as “backwash ileitis”. UC is thus a relapsing disorder causing inflammation of the colon. Patients typically present with abdominal cramping causing bowel movements and bloody diarrhea along with passage of mucus. Left-sided colitis and proctitis show symptoms with lesser severity.

CD is a transmural inflammatory disorder of the lining of the mucous membrane with a relapsing nature, that may present itself in the entire GI tract. The symptoms of CD may be observed from the rectum all the way up to the mouth of the affected individual. Classical symptoms of CD are the intermittent involvement of different sections of the GI tract presenting complications including blisters, pus filled abscesses, or fistulised membranes. CD can be differentiated from other related diseases by focal, transmural, irregular, and frequently blistering inflammation that may engulf the entire GI tract.
The pathophysiology of IBD is highly intricate and hence is yet not entirely known. However, three different theories are proposed to explain its occurrence, including defects in the intestinal mucosal barrier, a genetic predisposition that leads to faulty regulation of immune cells, and a vulnerability to environmental factors that include patient’s commensal luminal bacteria or other specific antigens as well. Mutations in the NOD2 and CARD15 genes can result in defects in vital immunoregulatory proteins. Due to this, uncontrolled inflammation may be caused as a result of systemic responses. Mutations in the NOD2 and CARD15 genes may be instrumental in indicating prognostic evidence such as signs of early onset of the disorder, ileal disease and fistulisation.

The intestinal epithelium functions to facilitate interaction between the mucosal layer and the immune system and it also acts as a barrier to selectively separate the intestinal lumen from its content. Derangement of this barrier leads to enhanced permeability, further leading to the exclusion of water and micronutrients and finally entry of macromolecules and antigens. Anti Neutrophil Cytoplasmic Antibodies (ANCA) aid in the diagnosis of many autoimmune diseases. Typical ANCA are directed against Proteinase 3 (PR3-ANCA) and Myeloperoxidase (MPO-ANCA) antigens present in the human neutrophils. PR3 acts as a seromarker for Wegener’s Granulomatosis (WG) and MPO for Microscopic Polyangiitis (MPA). ANCA have not attained comparable immunodiagnostic value in IBD, primarily because the corresponding target antigens have not been elucidated and the non-specificity of the diagnostic tests available in the market. This has prompted us to develop enhanced assays to utilise the full potential of ANCA antibodies specific for Ulcerative Colitis and exploit its use as a serological biomarker for diagnosis, prognosis and surveillance of UC.

The etiology has not yet been completely elucidated despite years of ongoing research. This disease is mainly seen in the northern part of America and Europe. But it is also being reported in greater proportions in other unrelated areas over the globe as they migrate into a “Westernized Culture.” The rate of prevalence for CD varies between 26 to 199 cases per 1 lakh people in North parts of America, and for UC it is from 37 to 246 cases per 1 lakh people. Based upon the research being carried out all over the globe it is evident that discovery of new IBD biomarkers which will be able to
predict the disease occurrence and help in the diagnosis of the disease is a growing subject of interest. Biomarkers can be proteins present in biological fluids such as plasma, serum, and other cellular components, or a genetic testing component. The gold standard recommended for diagnosis of UC and CD histology of the biopsy specimens collected during endoscopy or colonoscopy along with other clinical evidence.

Serological biomarkers are a swiftly growing list of non-invasive assays for early detection, rapid diagnosis, calculation of the prognosis and clinical surveillance of IBD. The diagnostic industry relies on serological, imaging and fecal biomarkers, as well as genetically predisposed gene polymorphisms to aid the diagnosis of IBD. However, as of today, none of the available serological biomarkers can be marketed as a gold standard diagnostic assay for detection of IBD and can only be recommended as an aide to endoscopy in diagnosing IBD. Taking the fact into account that endoscopy is a cumbersome, expensive and painful process (involving invasive, expensive and laborious colonoscopic procedures), new non-invasive biomarkers for IBD are in great need.

Based upon the current diagnostic scenario, this project aims to enhance the knowledge in the field of biomarkers and immunoassays for early detection of UC. It describes the development and validation of a diagnostic algorithm for systematic analysis of UC in India aimed at reducing the large amount of expenses incurred by the patients for performing various diagnostic tests and to save upon the precious time wasted during the diagnosis phase due to which treatment gets delayed. This project also aims to develop novel, time efficient and cost effective Indirect Immunofluorescence (IIF) based assays for the detection of ANCA biomarker and diagnose UC in the Indian population. The diagnostic algorithm and in-house developed assays are poised to help doctors in recommending the minimal number of tests to the patients suspected of suffering from UC and thus aid in correctly diagnosing UC in the shortest amount of time and incurring the least possible expenses. Thus we hope that this project will dramatically change the diagnostic scenario with reference to UC diagnosis in India and other developing countries.