In IBD cases, microbiota close to mucosa, which differs from luminal microbiota, has so far received less attention, yet it is very close to inflammatory process. The composition of the mucosal and mid stream/faecal microflora has been shown to be significantly different. Intestinal epithelium forms a tight barrier and it has been commonly assumed that, in the absence of physical disruption, interactions between host cells and luminal bacteria occur exclusively with epithelial cells. Disruption of the intestinal epithelium induces a marked inflammatory response in the mucosa that includes induction of inflammatory cytokines. Mucosal immune responses to resident intestinal microflora require precise control and an immuno-sensory capacity for distinguishing commensal bacteria from the pathogenic ones. If the microbial sensors like Nod1 are defective and not able to function properly that may responsible for the unregulated immune response leads to the epithelial damage in intestine.

During the period of our study we recorded that the composition of predominating mucosal flora - Bacteroides, Bifidobacteria, Ruminococcus and Lactobacilli significantly altered in both UC and CD patients compared to controls. Significant increase in Eubacterium and Peptostreptococcus productus population in CD patients indicate the role of these bacteria in the pathogenesis of CD but not in UC thereby confirming that the subset of bacteria participating in the pathogenesis of UC and CD may be different. High rate of incidence as well as increased concentration of hydrogen sulfide bacteria in IBD patients indicate their role in colonic injury leading to the pathogenesis of the disease. The changes observed in mucosa-associated bacterial flora in these patients, showing either a predominance of some potentially harmful bacteria groups or a decrease in beneficial bacterial species. Thus localized dysbiosis of the mucosa associated intestinal microflora may be closely related to the disease.

During host pathogen interaction, innate immunity is initiated via the recognition of microbial products by pattern recognition receptors and the subsequent activation of transcription factors that upregulate proinflammatory genes. The Nod1 proteins recognize peptidoglycan (PGN), a component of bacterial cell walls, and are mainly expressed by two cell types that are exposed to this component under physiological conditions:
antigen-presenting cells (APCs) and also in various non-professional immune cells including epithelial and endothelial cells. Nod1 is upregulated by interferon-γ (IFNγ). Nod1 is further responsible for the upregulation of proinflammatory cytokine genes. We observed an increase in mucosal expression of innate immunity genes like NOD1, NOD2, IFNγ and TNFα in the inflamed colon of UC patients. Our result show the high expression of both IL-17 and IL-23 in all the disease conditions in UC and CD. Our data show IL-10 mRNA expression low compared to controls during different stages of UC. In our studies level of IL-13 in patients with CD are significantly decreased (p = 0.021) and are correlated with disease activity but concentration of IL-13 remained significantly high in remission condition (p = 0.002). Our results show significant decrease in another anti-inflammatory cytokine IL-11 expression level in active disease conditions both in UC and CD (p = 0.019, p = 0.006) patients.

Genetic variations in innate immunity genes have been reported to be associated with a range of inflammatory disorders. Screening of samples for genetic variation analysis was done by DHPLC technique. It was less time consuming in analyzing large number of patients samples. This high-throughput genotyping technique is particularly suitable for routine diagnosis of SNPs. We detected few existing and few new SNPs using this technique. We also confirmed association of three SNPs to ulcerative colitis. Significant mutations observed in ATP (W219R, p = 0.002) and Mg2+ (L370R, p = 0.039 and L349P, p = 0.002) binding domains of Exon 6 of NOD1 gene may lead to a defective oligomerization of protein which subsequently may lead to a ‘loss of function’ by preventing the recognition of MDP that is necessary for subsequent NF-κB activation. Deletion of G at 4773 position causing a frame-shift mutation observed in few Ulcerative colitis patients though not in a significant population. This can be predicted as a potential locus that give rise to a pre-termination codon at 295 position of the amino acid encoding a truncated protein that may affect the function of NOD1 gene considerably. We observed five statistically significant mutations in intron 9 associated with the disease that showed a strong association of the genotype with the severity of the disease. We observed high frequency of mutations that well correlate with the severity of disease.
activity in case of 11438A>G and 11421A>G reaching a value of 0.388 and in 11585C>T, attaining a value of 0.444. The data of 11438A>G and 11421A>G mutations also correlated well with the extent of disease in the rectum region of the patients, where the values were 0.409 and 0.484 respectively. We carried out a Haplotype analysis of the polymorphisms observed in the exon 6 and intron 9 loci of the NOD1 gene to assess any risk factors associated with the disease. GTTG haplotype was found to be significantly over represented in UC patients as compared to controls (P=3.3726E-6).

3D model generated by Homology modeling of NBD domain of NOD1 protein. The residues in active site of 3-D NBD domain of NOD1 protein structure as Gly (202), Gly (205), Gly (207) and Lys (208) were of hydrophobic nature. 3D model represents the walker A motif which consists of the characteristics consensus pattern GxxGKT/S where the Lysine residue directly interacts with a phosphate moiety of ATP. Observed SNPs in the NBD domain E266K SNP is lying on the surface of the protein, S355C, both serine and cysteine are hydrophilic amino acid they are present at the side of the active site, and L370R mutation is present on the exposed residue. They might change the position of the cleft which is involved in the oligomerisation of Nod1.
**Conclusion**

The great progress that took place in recent years in the field of mucosal immunology has resulted in an abundance of incoming information regarding the immunopathogenesis of Ulcerative colitis. At the same time, however, translating research information into therapeutic benefit has proven a challenging and largely unfulfilled task. Perhaps the term “Ulcerative colitis” encompasses a number of disorders that may all be present with chronic intestinal inflammation but differ in their etiology.

In human conditions, it is already indicated by genetic studies as the number of IBD susceptibility loci have reached 99 -71 for CD and 47 for UC with one third shared by both. (Lees et al, 2011). It is expected that in the near future, well-defined immunological pathways will be added to these genetic signatures. This approach will help in the identification of sub-groups of patients with well-defined clinical, genetic and immunological phenotypes. Such a sub-classification of UC eventually will lead to individualized, pathway-targeted treatments that will offer the maximum benefits to the patients.