Underlying Processes leading to Inflammatory Bowel Disease

1. Hyper-immune reaction to normal gut commensals
2. Hypo-immune reaction resulting in insufficient clearance of bacteria and chronic low-grade inflammation
3. Loss of epithelial barrier function (primary genetic or secondary to inflammation) resulting in bacteria invasion
4. Abnormal and sustained auto-inflammatory process directed against host cells

Role of HLA variation in inflammatory process

1. HLA variants may promote specific (commensal) bacterial and viral epitope binding leading to immune activation
2. Molecular mimicry- specific HLA genotypes may recognise host peptides that are similar to bacterial/viral epitopes and trigger host immune response against self

Normal adaptive immune response to pathogen

Epitope derived from bacteria or virus

Inflammatory cell recruitment and infiltration (neutrophils and macrophages)

Tissue Damage and Chronic Inflammation

Molecular mimicry
Abnormal adaptive immune response to host-derived antigen resembling pathogenic epitope

Epitope derived from host

Bacteria- pathogenic or commensal

Intestinal epithelial cell- ileal or colonic

Epithelial and mucus barrier breakdown and bacterial invasion into mucosa and submucosa

Pro-inflammatory cytokines (TNF-α, IL-1, IL-6) +/- auto-antibodies

T-Cell

MHC II

APC

T-Cell

Pro-inflammatory cytokines (TNF-α, IL-1, IL-6) +/- auto-antibodies

T-Cell