Mucosal immune system markers

Your in-depth guide to mucosal immune system markers.

We've pulled together the key markers for inflammatory bowel disease, asthma, and allergy from recent literature, so you can quickly choose the right markers to study the mucosal immune system.

Contents

An introduction to the mucosal immune system

The mucosal immune system protects the internal surfaces of the body, including those of intestinal, respiratory and urogenital tracts. The mucosal surfaces are permeable barriers to the inner part of the body, which makes them especially vulnerable to the entry of pathogenic microorganisms and other antigens that can cause infections and inflammatory diseases [1-3]. To prevent the entry of unwanted antigens, mucosal surfaces are lined by a mucus-secreting epithelium which represents our first line of defense.

To protect us while creating tolerance to symbiotic microbiota, the mucosal immune system has evolved very sophisticated mechanisms where specialized CD4+ T cells, CD8+ T cells (including intraepithelial lymphocytes-IELs), Innate Lymphoid cells (ILC), Ig-secreting plasma cells, macrophages and dendritic cells compromise between suppression and activation of an immune response [1-5]. If this fine balance is disrupted, inflammatory conditions can arise. A clear example of this balance disruption is seen in inflammatory disorders in the gut in patients with inflammatory bowel disease or in the lung in allergic diseases.

Inflammatory bowel disease (IBD) markers

Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tract that includes Crohn's disease and ulcerative colitis and is characterized by severe epithelium damage and intestinal inflammation.

Jump to: Disease-associated genes | Antimicrobial molecules and bacterial recognition | Pro-inflammatory cytokines | Anti-inflammatory cytokines | Chemokines | Inflammasomes | microRNA

Disease-associated genes

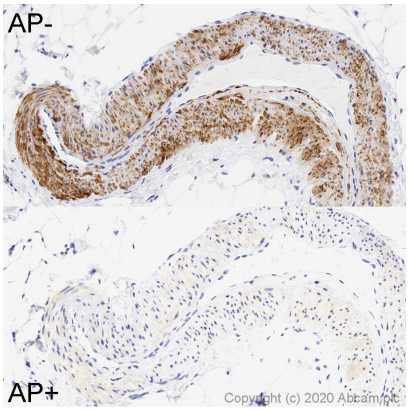
Although the pathogenesis of IBD is still unknown, several disease-associated genes, including *NOD2* and *ATG16L1* and *IL23R,* have been identified[1-2, 6].

NOD2 (CARD15)

Nucleotide oligomerization domain (NOD2), also known as CARD-15 or IBD1, is an intracellular pattern-recognition receptor involved in gastrointestinal immunity and expressed in monocytes and macrophages. Mutations in the *NOD2* gene are associated with Crohn's disease[7].

Browse all NOD2 antibodies | NOD2 AAAI

ATG16L1



Autophagy related 16 like 1 (ATG16L1) is an intracellular protein that plays a critical role in the autophagy pathway. Several single-nucleotide polymorphisms (SNPs) in the *ATG16L1* gene have been linked to an increased risk of Crohn's disease[8].

Browse all ATG16L1 antibodies | ATG16L1 cell lines and lysates | ATG16L1 proteins and peptides

Figure 1. IHC images of vessel staining of ab195242, ATG16L1 (phospho S278), in sections of formalin-fixed paraffin-embedded normal human skeletal muscle tissue

IL23R

Interleukin-23 receptor (IL23R) is strongly expressed on the cell membrane of memory T cells and other immune cells, including monocytes, dendritic cells and natural killer cells. IL23R interacts with the cytokine IL23, which regulates immune cell activity and is essential in the inflammatory response. Several *IL23R* variants are associated with Crohn's disease[9].

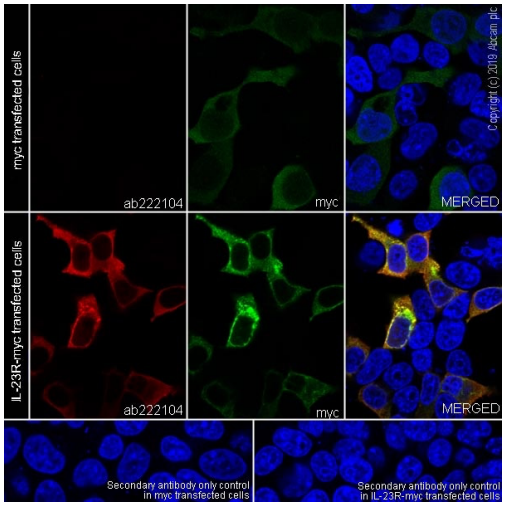


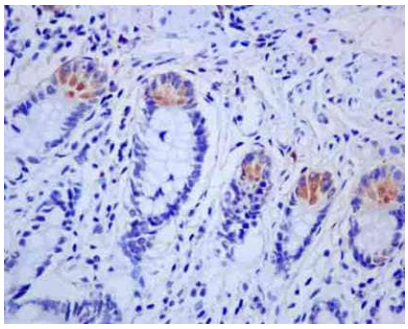
Figure 2. Immunofluorescent analysis of 4% PFA-fixed, 0.1% TritonX-100 permeabilized HEK-293T cells labeling IL-23R with ab222104 at 1/100 dilution, followed by ab150077 AlexaFluor®488 Goat anti-Rabbit secondary antibody at 1/1000 dilution (Green).

Browse all IL23R antibodies | IL23R ELISA and matched antibody pairs | IL23R proteins and peptides | IL23R cell lines and lysates

Antimicrobial molecules and bacterial recognition

Mucosal epithelium of IBD patients has decreased secretion of antimicrobial molecules, impaired bacterial recognition and defective IgA production leading to changes in microbiota composition and bacteria translocation[1-5].

Defensins



Defensins are small antimicrobial peptides produced by epithelial cells and innate immune system cells. Altered defensin production has been implicated in IBD pathogenesis[10].

Browse all Defensin antibodies | Defensin proteins and peptides | Defensin ELISA kits and antibody pairs

Figure 3. Immunohistochemical analysis of paraffin-embedded human small intestine tissue labeling alpha Defensin 5 with ab180515 at 1/4000 dilution. Anti-rabbit HRP secondary antibody was used and counter staining with hematoxylin performed.

REG3

Regenerating islet-derived protein 3 (REG3) is a member of the REG family – a group of small secretory proteins involved in intestinal homeostasis. REG3 is abundantly expressed in the small intestine and modulates the host defense mechanism in the gut via bactericidal activity[11]. However, the precise roles of REG proteins in IBD have not yet been defined[12].

Browse all REG3 antibodies | REG3 proteins and peptides | REG3 ELISA kits

Cathelicidins

Cathelicidins are small antimicrobial peptides that play a crucial role in the innate and adaptive immune systems by acting as "natural antibiotics". Human cathelicidin, LL-37, has been suggested to play an essential role in the development and progression of IBD. Thus, cathelicidin expression is increased in the intestinal mucosa of patients with ulcerative colitis[13].

Browse all Cathelicidin antibodies | Cathelicidin proteins and peptides

Toll-like receptors

Toll-like receptors (TLRs) are a family of pattern recognition receptors that constitute the first line of the antimicrobial defense system and are critical for maintaining intestinal homeostasis. TLRs act as key immune sensors of gut microbiota, recognizing abnormal microbes and inducing an immune response. Overactivation of TLRs can ultimately disrupt immune homeostasis, increasing the risk for inflammatory diseases and autoimmune disorders[14]. Both TLRs and TLR-activated signaling pathways have been implicated in the pathogenesis of IBD[15].

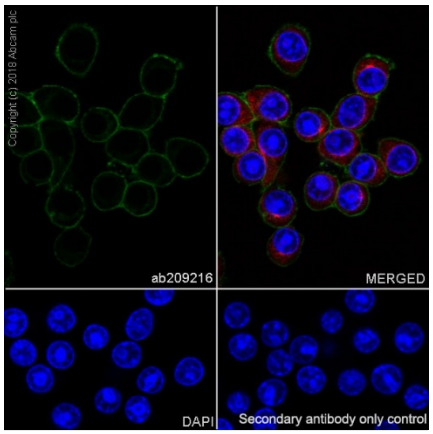


Figure 4. Immunofluorescent analysis of 100% methanol-fixed RAW 264.7 (mouse macrophage cell line transformed with Abelson murine leukemia virus) cells labeling TLR2 with ab209216 at 1/100 dilution, followed by Goat Anti-Rabbit IgG H&L (Alexa Fluor® 488) (ab150077) secondary antibody at 1/1000 dilution (green).

Browse all products for TLR1, TLR2, TLR4, TLR9

Pro-inflammatory cytokines

In response to microbial products, CD4+ T cells (Th1, Th2, Th17) are infiltrated to the lamina propria and secrete pro-inflammatory cytokines including TNF, IFN, IL-5, IL-6, IL-13, IL-17 or IL-22 [5,16,17] through activation of certain STATs[1-5].

In addition to T cells, innate lymphoid cells (ILC), NK cells and macrophages also secrete pro-inflammatory cytokines promoting epithelial damage, ulcers, and, in some cases, the development of colitis-associated cancer[3]. Several of these cytokines are being investigated as potential targets for IBD treatment[5, 16].

TNF

Tumor necrosis factor (TNF) is a major factor produced by various immune and stromal cell types during the onset of IBD and is therefore widely used in the clinics[5, 16].

Browse all products for TNF | TNF alpha | TNF receptors

Other pro-inflammatory cytokines

Browse all products for IFN | IL-5 | IL-6 | IL-13 | IL-17 | IL-22

Anti-inflammatory cytokines

In healthy individuals, regulatory T cells (Tregs) maintain immune tolerance and suppress effector T cell responses through anti-inflammatory cytokines such as IL-10 and TGFβ. In contrast, Tregs are decreased in the gut of IBD patients [1,2]

IL-10

Interleukin 10 (IL-10) is an anti-inflammatory cytokine that plays an essential role in maintaining mucosal homeostasis and preventing pro-inflammatory responses. Loss-of-function mutations in genes encoding IL-10 cytokine and IL-10 receptor have been linked to the very early-onset IBD[16].

Browse IL-10 ELISA kits | IL-10 multiplex assays | IL-10 antibodies | IL-10 proteins and peptides

TGF-β

Transforming growth factor-β (TGF-β) is an immune-suppressive cytokine produced by many cell types, including immune cells. TGF-β signaling pathway regulates mucosal immune system reactions and is shown to be impaired in the intestines of patients with IBD[18].

Browse all TGF-β ELISA kits | TGF-β multiplex assays | Browse all TGF-β products

Chemokines

Other inflammatory molecules, including chemokines, inflammasomes, or microRNAs, also contribute to the intestinal inflammatory process and are being investigated for potential relevance in IBD treatment.

Chemokines play a key role in the pathogenesis of Crohn's disease and ulcerative colitis, triggering multiple inflammatory response actions, including leukocyte activation and chemoattraction. Several chemokines have been investigated in the

IBD setting, with the receptors CCR9 and CXCR3 and their respective ligands CCL25 and CXCL10 being the principal targets for anti-chemokine therapy in IBD[19,20].

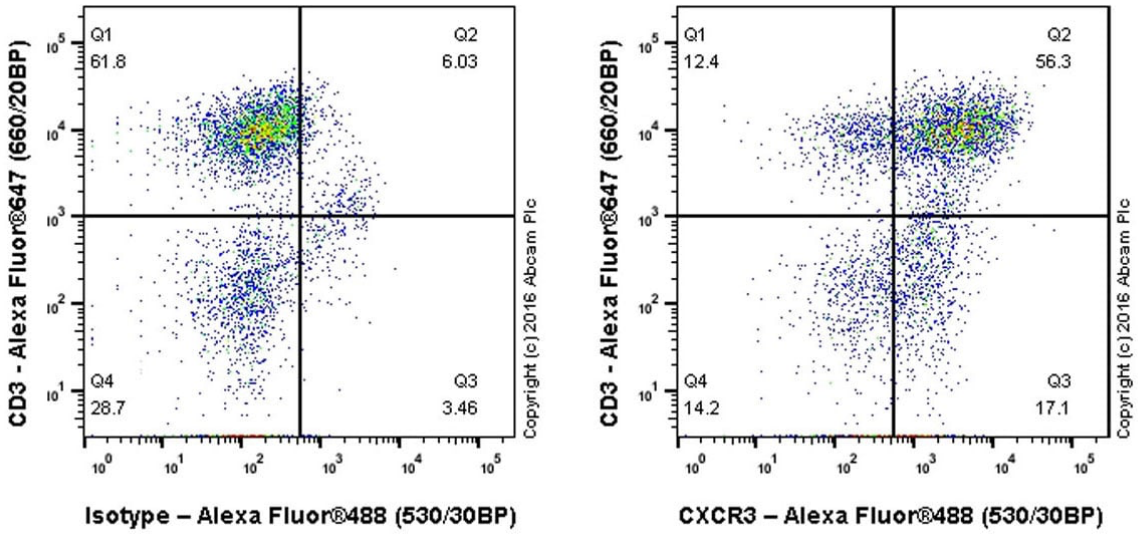


Figure 5. Flow cytometric analysis of human PBMC (treated with 200U/ml IL-2 and 1µg/ml PHA for 6 days) labelling CXCR3 with ab259865 at 1/500 dilution (0.1µg) (Right)compared with a Rabbit monoclonal IgG (ab172730) isotype control (Left).

Browse all products for CCR9 | CXCR3 | CCL25 | CXCL10

Inflammasomes

Inflammasomes are cytosolic protein complexes of the innate immune system that induce inflammatory responses. Inflammasome activation results in the release of pro-inflammatory cytokines IL-1β and IL-18 and cleavage of Gasdermin D (GSDMD), subsequently inducing pyroptotic cell death.

The NLRP3 inflammasome has been linked to the pathogenesis of several inflammatory disorders, including Alzheimer's disease and diabetes, but its detailed role in IBD is still being investigated[21].

Explore all products for NLRP3, IL-1β, GSDMD, IL-18

Our product range for inflammasome targets includes highly cited knock-out (KO) validated recombinant monoclonal antibodies, such as anti-GSDMD antibody (ab209845) cited in over 100+ references and anti-NLRP3 antibody (ab263899) cited in 40+ references.

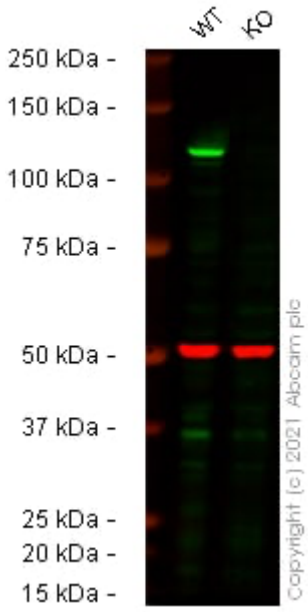


Figure 7. Western blot image with the anti-NLRP3 antibody (ab263899) staining at 1/500 dilution, shown in green. Mouse anti-Alpha Tubulin [DM1A] (ab7291) loading control staining at 1/20000 dilution, shown in red. In Western blot, ab263899 was shown to bind specifically to NLRP3. A band was observed at 118 kDa in wild-type THP-1 cell lysates with no signal observed at this size in NLRP3 knockout cell line ab280063 (knockout cell lysate ab280122).

microRNAs

MicroRNAs (miRNAs) are short (~22 nucleotides) non-coding RNAs that post-transcriptionally regulate gene expression. Epithelial microRNAs have been shown to play critical roles in regulating gut homeostasis. Also, numerous studies demonstrated distinct microRNA expression profiles in blood and tissue samples of patients with IBD, suggesting microRNAs could serve as potential markers for IBD[22].

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Allergy and asthma markers

Up to 30% of the population in industrialized countries suffers from allergy, and its prevalence is increasing overtime[23]. Allergic rhinitis and allergic asthma are the main allergic diseases affecting the upper and lower airways and are often seen co-existing in allergic patients[24].

Immunoglobulin E (IgE), histamine, and leukotriens

Allergy is characterized by the presence and production of immunoglobulin E (IgE), which binds to its main receptor (FcεRI) in basophils and mast cells, and the subsequent release of histamine and leukotrienes[25].

Browse all products for IgE | Histamine | Leukotrienes

Key cytokines released by epithelial cells

Allergic patients frequently suffer from a disrupted epithelial barrier[26] and impairment in lung function, including goblet cell hyperplasia and mucus hypersecretion. Lung epithelial challenge triggers the release of TSLP, IL-25 and IL-33 by epithelial cells, promoting the activation of CD4 T cells and ILC2.

TSLP

Thymic stromal lymphopoietin (TSLP) is a cytokine strongly expressed in lung and skin-derived epithelial cells. TSLP is involved in the initiation of allergic inflammatory responses. Furthermore, recent human and mouse studies have linked TSLP to the development and progression of allergic diseases, including asthma and allergic rhinitis[27].

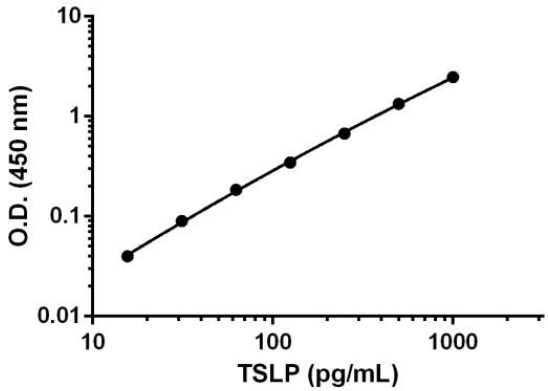

Figure 8. Example of TSLP standard curve prepared in Sample Diluent 50BS.

Browse all TSLP antibodies | TSLP proteins and peptides | TSLP ELISA kits | TSLP multiplex assays

IL25

IL-25 (also known as IL-17E) belongs to the IL-17 cytokine family, which are mostly produced by epithelial cells and innate immune cells and are critical in host defense responses and inflammatory diseases. Multiplex human and animal studies implicate IL-25 in the pathogenesis of some endotypes of asthma[28].

Browse all IL25 antibodies | IL25 proteins and peptides | IL25 ELISA kits | IL25 multiplex assays

IL33

IL-33 is a cytokine involved in type-2 innate immunity via activation of allergic inflammation-related immune cells, including eosinophils, basophils, mast cells, and macrophages.

Browse all IL33 primary antibodies | IL33 proteins and peptides | IL33 ELISA kits | IL33 multiplex assays

Sensitization phase markers: IL-4 and IL-13

IL-4 and IL-13 are related cytokines regulating multiple aspects of allergic inflammation, including responses of lymphocytes, myeloid and non-hematopoietic cells. These two cytokines are produced by Th2 and ILC2 cells in the early stage of the allergic reaction (sensitization) to induce IgE -producing plasma cells and allergen-specific memory B cells.

Browse all IL-4 primary antibodies | IL-4 proteins and peptides | IL-4 ELISA kits | IL-4 multiplex assays | IL-4 KO cell lines

Browse all IL-13 primary antibodies | IL-13 proteins and peptides | IL-13 ELISA kits | IL-13 multiplex assays | IL-13 KO cell lines

Late allergy phase markers: IL-5, IL-9 and IL-13

During the late phase, endothelial-cell adhesion and **eosinophil** recruitment increase, and T cells are activated. Activated Th1 and Th2 in the lungs secrete IL-5, IL-9 and IL-13, leading to the allergic inflammation[29].

IL-5

IL-5 is a pro-inflammatory cytokine responsible for eosinophil maturation, proliferation, activation, survival, and recruitment to airways. IL-5 plays a central role in the pathogenesis of eosinophilic asthma and represents a valuable target for anti-asthma biological therapies[30].

Browse all IL-5 primary antibodies | IL-5 proteins and peptides | IL-5 ELISA kits | IL-5 multiplex assays

IL-9

IL-9 is a cytokine, produced by multiples immune and epithelial cells, which contributes to various immunopathological processes via activation of different cells (eg, Tregs, Th17 cells, NK cells, mast cells, etc). IL-9 is involved in allergic inflammation and promotes activation and recruitment of inflammatory cells[31].

Browse all IL-9 primary antibodies | IL-9 proteins and peptides | IL-9 ELISA kits | IL-9 multiplex assays | IL-9 KO cell lines

Immune cell markers relevant for the mucosal immune system

Here we summarize the key markers for T cells that play important roles in mucosal immune system:

T-regs: CD4, CD25, FOXP3 , CTLA4
Th1: CD4, T-bet (TBX21), CCR6
Th2: CD4, CCR4, GATA3, IRF4

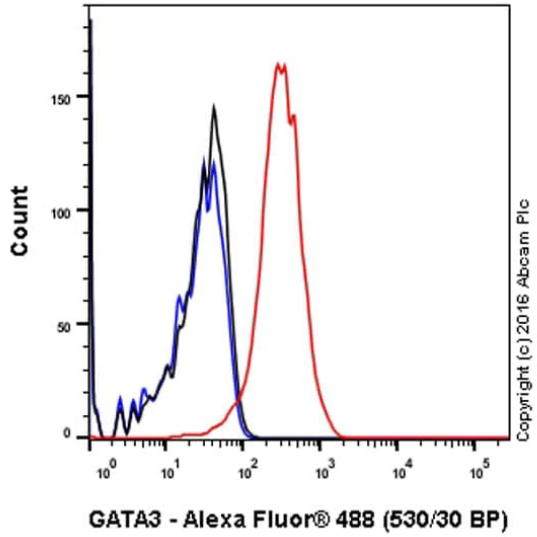

Figure 9. Intracellular flow cytometry analysis of Jurkat cells labelling GATA3 with ab199428 at 1/500 (red).

For more information on immune cell markers, download our Immune cell marker poster.

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