# IL1B

ensembl_gene_id: ENSG00000125538

description: interleukin 1 beta [Source:HGNC Symbol;Acc:HGNC:5992]

chromosome_name: 2

start_position: 112829751

end_position: 112836816

strand: -1

band: q14.1

external_gene_name: IL1B

transcript_count: 8

percentage_gene_gc_content: 45.51

gene_biotype: protein_coding

external_synonym: IL-1B

phenotype_description: GASTRIC CANCER GASTRIC CANCER INTESTINAL INCLUDED

name_1006: [cellular response to mechanical stimulus, cellular response to xenobiotic stimulus, cytokine-mediated signaling pathway, defense response to Gram-positive bacterium, hyaluronan biosynthetic process]

namespace_1003: biological_process

go_id: [GO:0071260, GO:0071466, GO:0019221, GO:0050830, GO:0030213]

go_linkage_type: [IEP, IDA]

ncbi: Gene: IL1B (Homo sapiens)

--- Summary ---

The protein encoded by this gene is a member of the interleukin 1 cytokine family. This cytokine is produced by activated macrophages as a proprotein, which is proteolytically processed to its active form by caspase 1 (CASP1/ICE). This cytokine is an important mediator of the inflammatory response, and is involved in a variety of cellular activities, including cell proliferation, differentiation, and apoptosis. The induction of cyclooxygenase-2 (PTGS2/COX2) by this cytokine in the central nervous system (CNS) is found to contribute to inflammatory pain hypersensitivity. Similarly, IL-1B has been implicated in human osteoarthritis pathogenesis. Patients with severe Coronavirus Disease 2019 (COVID-19) present elevated levels of pro-inflammatory cytokines such as IL-1B in bronchial alveolar lavage fluid samples. The lung damage induced by the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is to a large extent, a result of the inflammatory response promoted by cytokines such as IL-1B. This gene and eight other interleukin 1 family genes form a cytokine gene cluster on chromosome 2. [provided by RefSeq, Jul 2020]

--- Representative Expression ---

Summary: Biased expression in bone marrow (RPKM 72.5), appendix (RPKM 32.9) and 12 other tissues

Category: Biased expression

Tissues: bone marrow, appendix, urinary bladder, gall bladder, brain, endometrium, spleen, stomach, lung, lymph node, placenta, colon, adrenal, liver

# TLR4

ensembl_gene_id: ENSG00000136869

description: toll like receptor 4 [Source:HGNC Symbol;Acc:HGNC:11850]

chromosome_name: 9

start_position: 117704175

end_position: 117724735

strand: 1

band: q33.1

external_gene_name: TLR4

transcript_count: 4

percentage_gene_gc_content: 38.47

gene_biotype: protein_coding

external_synonym: ARMD10

phenotype_description: Behcet disease

name_1006: [I-kappaB phosphorylation, MyD88-dependent toll-like receptor signaling pathway, cellular response to amyloid-beta, cellular response to lipopolysaccharide, cellular response to mechanical stimulus]

namespace_1003: biological_process

go_id: [GO:0007252, GO:0002755, GO:1904646, GO:0071222, GO:0071260]

go_linkage_type: [IDA, IEP]

ncbi: Gene: TLR4 (Homo sapiens)

--- Summary ---

The protein encoded by this gene is a member of the Toll-like receptor (TLR) family which plays a fundamental role in pathogen recognition and activation of innate immunity. TLRs are highly conserved from Drosophila to humans and share structural and functional similarities. They recognize pathogen-associated molecular patterns that are expressed on infectious agents, and mediate the production of cytokines necessary for the development of effective immunity. The various TLRs exhibit different patterns of expression. In silico studies have found a particularly strong binding of surface TLR4 with the spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of Coronavirus disease-2019 (COVID-19). This receptor has also been implicated in signal transduction events induced by lipopolysaccharide (LPS) found in most gram-negative bacteria. Mutations in this gene have been associated with differences in LPS responsiveness, and with susceptibility to age-related macular degeneration. Multiple transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Aug 2020]

--- Representative Expression ---

Summary: Broad expression in spleen (RPKM 17.1), appendix (RPKM 15.6) and 22 other tissues

Category: Broad expression

Tissues: spleen, appendix, fat, placenta, lung, bone marrow, urinary bladder, adrenal, lymph node, gall bladder, brain, colon, liver, kidney, thyroid, ovary, heart, small intestine, endometrium, esophagus, prostate, stomach, duodenum, testis

# TLR2

ensembl_gene_id: ENSG00000137462

description: toll like receptor 2 [Source:HGNC Symbol;Acc:HGNC:11848]

chromosome_name: 4

start_position: 153684050

end_position: 153706260

strand: 1

band: q31.3

external_gene_name: TLR2

transcript_count: 14

percentage_gene_gc_content: 38.85

gene_biotype: protein_coding

external_synonym: CD282

phenotype_description: Colorectal Cancer

name_1006: [I-kappaB phosphorylation, cellular response to diacyl bacterial lipopeptide, cellular response to lipoteichoic acid, cellular response to triacyl bacterial lipopeptide, cellular response to type II interferon]

namespace_1003: biological_process

go_id: [GO:0007252, GO:0071726, GO:0071223, GO:0071727, GO:0071346]

go_linkage_type: IDA

ncbi: Gene: TLR2 (Homo sapiens)

--- Summary ---

The protein encoded by this gene is a member of the Toll-like receptor (TLR) family which plays a fundamental role in pathogen recognition and activation of innate immunity. TLRs are highly conserved from Drosophila to humans and share structural and functional similarities. This protein is a cell-surface protein that can form heterodimers with other TLR family members to recognize conserved molecules derived from microorganisms known as pathogen-associated molecular patterns (PAMPs). Activation of TLRs by PAMPs leads to an up-regulation of signaling pathways to modulate the host's inflammatory response. This gene is also thought to promote apoptosis in response to bacterial lipoproteins. This gene has been implicated in the pathogenesis of several autoimmune diseases. Alternative splicing

results in multiple transcript variants. [provided by RefSeq, Jan 2016]

--- Representative Expression ---

Summary: Broad expression in appendix (RPKM 15.9), bone marrow (RPKM 12.6) and 18 other tissues

Category: Broad expression

Tissues: appendix, bone marrow, lung, spleen, gall bladder, adrenal, urinary bladder, placenta, lymph node, esophagus, salivary gland, stomach, colon, thyroid, small intestine, fat, brain, kidney, duodenum, endometrium

Here's a summary of the provided genes, their popularities, and key insights, with a focus on oncology and commonalities.

## Gene Popularities (Frequency of Citation)

• CCLX: NA

• TLR4: 0.234

• TLR2: 0.150

• IL1B: 0.310

## Gene Summaries

• IL1B (Interleukin 1 Beta) Popularity: 0.310 (Highest among the provided genes) Key Insights: A crucial pro-inflammatory cytokine produced by activated macrophages. It mediates inflammatory responses, influencing cell proliferation, differentiation, and apoptosis. It's implicated in inflammatory pain, osteoarthritis, and severe inflammatory responses in COVID-19. Notably, it is explicitly linked to gastric cancer in the provided information. It forms part of a cytokine gene cluster on chromosome 2.

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• TLR4 (Toll-like Receptor 4) Popularity: 0.234 Key Insights: A fundamental component of innate immunity, recognizing pathogen-associated molecular patterns (PAMPs), particularly lipopolysaccharide (LPS) from Gram-negative bacteria. It activates cytokine production and is involved in signal transduction. Mutations are associated with LPS responsiveness and age-related macular degeneration. It has also been implicated in the inflammatory response to SARS-CoV-2 spike protein in COVID-19.

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• TLR2 (Toll-like Receptor 2) Popularity: 0.150 Key Insights: Another key Toll-like receptor involved in innate immunity and pathogen recognition. It forms heterodimers with other TLRs to recognize various PAMPs (e.g., bacterial lipopeptides, lipoteichoic acid), leading to the upregulation of inflammatory responses. It is also thought to promote apoptosis in response to bacterial lipoproteins and has been implicated in autoimmune diseases and colorectal cancer.

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CCLX

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## Commonalities and Oncology Context

The genes IL1B, TLR4, and TLR2 exhibit striking commonalities, particularly in their roles in innate immunity, inflammation, and cellular signaling, which are highly relevant to oncology. The fact that these genes were identified after mutation enrichment in Homo sapiens suggests that alterations in their function could be significant.

Key Commonalities and Biological Context:

• Innate Immunity and Inflammation: All three genes are central players in the innate immune system and the inflammatory response. TLR4 and TLR2 are pattern recognition receptors that detect microbial components (PAMPs), initiating immune signaling. IL1B is a potent downstream inflammatory cytokine produced in response to such activation.

• NF-kappaB Signaling Pathway: The gene set enrichment analysis (GSEA) strongly highlights "positive regulation of NIK/NF-kappaB signaling" as a top enriched term for IL1B, TLR4, and TLR2. This is a critical commonality. The NF-kappaB pathway is a master regulator of immune and inflammatory responses, controlling the expression of numerous genes involved in cell survival, proliferation, and cytokine production.

• Cytokine Production: The GSEA also shows enrichment for "positive regulation of chemokine production," "interleukin-8 production," and "interleukin-6 production" for IL1B, TLR4, and TLR2. This indicates a shared role in orchestrating the cytokine milieu, which is crucial for immune cell recruitment and activation.

• Response to Bacterial Origin Molecules: "Cellular response to molecule of bacterial origin" is another enriched term, directly linking TLR4 (LPS) and TLR2 (lipopeptides, lipoteichoic acid) to their primary function of detecting bacterial components, which then triggers IL1B production.

Relevance to Oncology:

The strong involvement of these genes in inflammation and NF-kappaB signaling is highly significant in the context of oncology:

• Inflammation and Cancer: Chronic inflammation is a well-established hallmark of cancer. It can promote tumor initiation, progression, metastasis, and resistance to therapy. The genes identified here are key drivers of inflammatory processes.

• NF-kappaB Pathway in Cancer: Constitutive activation of the NF-kappaB pathway is frequently observed in various cancers. It promotes cell survival, proliferation, angiogenesis, and immune evasion, making it a critical target in cancer therapy. The enrichment of NF-kappaB related terms for IL1B, TLR4, and TLR2 suggests that mutations in these genes could lead to dysregulated NF-kappaB activity, contributing to oncogenesis.

• Pro-inflammatory Cytokines (IL-1B, IL-6, IL-8) in Cancer: IL1B: Directly implicated in gastric cancer in your data. Elevated IL-1B levels are often associated with poor prognosis in many cancers, promoting tumor growth, angiogenesis, and immunosuppression. IL-6 and IL-8: These cytokines, whose

production is positively regulated by IL1B, TLR4, and TLR2, are also potent pro-tumorigenic factors, driving proliferation, survival, and metastasis in various cancers.

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• TLRs in Cancer: TLRs, including TLR2 (linked to colorectal cancer in your data) and TLR4, have complex and often dual roles in cancer. While they can activate anti-tumor immunity, chronic activation by the tumor microenvironment or microbial dysbiosis can promote pro-tumorigenic inflammation, immune suppression, and resistance to therapy. The "mutation enrichment" finding suggests that specific mutations in TLR2 and TLR4 might shift their function towards promoting cancer.

Overall Conclusion:

The genes IL1B, TLR4, and TLR2 are tightly interconnected components of the innate immune and inflammatory response, primarily through the NF-kappaB signaling pathway and the production of key pro-inflammatory cytokines. Given your interest in oncology, the strong enrichment of these pathways is highly relevant. Mutations in these genes, as suggested by your initial analysis, could significantly impact the inflammatory microenvironment, potentially driving cancer development, progression, or influencing therapeutic responses. The explicit links of IL1B to gastric cancer and TLR2 to colorectal cancer further underscore their direct relevance to cancer biology.