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

CCL14

ensembl_gene_id: ENSG00000277236

description: C-C motif chemokine ligand 14 [Source:HGNC Symbol;Acc:HGNC:10612]

chromosome_name: HSCHR17_7_CTG4

start_position: 217855

end_position: 221568

strand: -1

band:

external_gene_name: CCL14

transcript_count: 4

percentage_gene_gc_content: 50.89

gene_biotype: protein_coding

external_synonym: CKB1

phenotype_description:

name_1006: [intracellular calcium ion homeostasis, positive regulation of cell population proliferation, antimicrobial humoral immune response mediated by antimicrobial peptide, cell chemotaxis, chemokine-mediated signaling pathway]

namespace_1003: biological_process

go_id: [GO:0006874, GO:0008284, GO:0061844, GO:0060326, GO:0070098]

go_linkage_type: [TAS, IBA]

ncbi: Gene: CCL14 (Homo sapiens)

--- Summary ---

This gene, chemokine (C-C motif) ligand 14, is one of several CC cytokine genes clustered on 17q11.2. The CC cytokines are secreted proteins characterized by two adjacent cysteines. The cytokine encoded by this gene induces changes in intracellular calcium concentration and enzyme release in monocytes. Multiple transcript variants encoding different isoforms have been found for this gene. Read-through transcripts are also expressed that include exons from the upstream cytokine gene, chemokine (C-C motif) ligand 15, and are represented as GeneID: 348249. [provided by RefSeq, Dec 2009]

--- Representative Expression ---

Summary: Broad expression in spleen (RPKM 229.5), fat (RPKM 134.4) and 15 other tissues

Category: Broad expression

Tissues: spleen, fat, liver, gall bladder, urinary bladder, endometrium, lung, lymph node, skin, adrenal, prostate, esophagus, heart, small intestine, colon, thyroid, duodenum

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

CCL14

ensembl_gene_id: ENSG00000276409

description: C-C motif chemokine ligand 14 [Source:HGNC Symbol;Acc:HGNC:10612]

chromosome_name: 17

start_position: 35983288

end_position: 35987004

strand: -1

band: q12

external_gene_name: CCL14

transcript_count: 4

percentage_gene_gc_content: 50.85

gene_biotype: protein_coding

external_synonym: CKB1

phenotype_description:

name_1006: [intracellular calcium ion homeostasis, positive regulation of cell population proliferation, antimicrobial humoral immune response mediated by antimicrobial peptide, cell chemotaxis, chemokine-mediated signaling pathway]

namespace_1003: biological_process

go_id: [GO:0006874, GO:0008284, GO:0061844, GO:0060326, GO:0070098]

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This gene, chemokine (C-C motif) ligand 14, is one of several CC cytokine genes clustered on 17q11.2. The CC cytokines are secreted proteins characterized by two adjacent cysteines. The cytokine encoded by this gene induces changes in intracellular calcium concentration and enzyme release in monocytes. Multiple transcript variants encoding different isoforms have been found for this gene. Read-through transcripts are also expressed that include exons from the upstream cytokine gene, chemokine (C-C motif) ligand 15, and are represented as GeneID: 348249. [provided by RefSeq, Dec 2009]

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Summary: Broad expression in spleen (RPKM 229.5), fat (RPKM 134.4) and 15 other tissues

Category: Broad expression

Tissues: spleen, fat, liver, gall bladder, urinary bladder, endometrium, lung, lymph node, skin, adrenal, prostate, esophagus, heart, small intestine, colon, thyroid, duodenum

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 your genes, their popularities, and key insights, with a focus on oncology:

The popularities (frequency of citation) for your genes, obtained after mutation enrichment analysis in Homo sapiens, are: * IL1B: 0.310 * TLR4: 0.234 * TLR2: 0.150 * CCL14: 0.004

Gene-Specific Insights:

• IL1B (Interleukin 1 Beta) Popularity: High (0.310) Key Insights: A crucial pro-inflammatory cytokine, processed by caspase 1. It plays a central role in the inflammatory response, influencing cell proliferation, differentiation, and apoptosis. It's explicitly linked to gastric cancer and contributes to inflammatory pain and osteoarthritis. Elevated IL1B levels are also observed in severe COVID-19, contributing to lung damage.

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• TLR4 (Toll-Like Receptor 4) Popularity: High (0.234) Key Insights: A fundamental pattern recognition receptor of the innate immune system. TLR4 recognizes pathogen-associated molecular patterns (PAMPs) like lipopolysaccharide (LPS) from Gram-negative bacteria and has been shown to bind the SARS-CoV-2 spike protein. Its activation leads to cytokine production and inflammatory responses. It's associated with Behcet disease and COVID-19.

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• TLR2 (Toll-Like Receptor 2) Popularity: Moderate (0.150) Key Insights: Another key Toll-like receptor involved in innate immunity. TLR2 forms heterodimers to recognize various PAMPs (e.g., bacterial lipoproteins, lipoteichoic acid), modulating the host's inflammatory response. It also promotes apoptosis in response to bacterial lipoproteins and is explicitly linked to colorectal cancer and autoimmune diseases.

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• CCL14 (C-C Motif Chemokine Ligand 14) Popularity: Low (0.004) Key Insights: A secreted chemokine that induces changes in intracellular calcium and enzyme release in monocytes. It's involved in cell chemotaxis (guiding cell movement) and chemokine-mediated signaling. Notably, it plays a role in the positive regulation of cell population proliferation. (Note: Two identical entries for CCL14 were provided, both pointing to the same gene information).

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Commonalities and Oncology Context:

The most striking commonality among these genes, particularly relevant to your interest in oncology, is their central and interconnected role in inflammation and innate immune responses.

• Inflammation as a Driver of Cancer: All four genes are integral to the inflammatory cascade, a well-established hallmark of cancer. Chronic inflammation can promote tumor initiation, progression, metastasis, and resistance to therapy. IL1B: As a potent pro-inflammatory cytokine, its direct link to gastric cancer underscores how inflammation can fuel tumor growth and survival by influencing cell proliferation and apoptosis. TLR4 & TLR2: These innate immune receptors detect "danger signals" (PAMPs) and initiate inflammatory signaling pathways (e.g., MyD88-dependent pathway). This inflammatory response, while protective against pathogens, can be co-opted by tumors to create a pro-tumorigenic microenvironment. The explicit link of TLR2 to colorectal cancer highlights this direct involvement. CCL14: As a chemokine, it orchestrates the recruitment of immune cells (like monocytes) to sites of inflammation, including the tumor microenvironment. This immune cell infiltration can either suppress or promote tumor growth, depending on the specific cell types and context.

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• Regulation of Cell Proliferation and Apoptosis: These are fundamental processes dysregulated in cancer. IL1B is involved in both cell proliferation and apoptosis. CCL14 is noted for its "positive regulation of cell population proliferation," directly contributing to uncontrolled cell growth, a hallmark of cancer. TLR2 promotes apoptosis, which could be an anti-tumor mechanism, but its overall role in cancer is complex and context-dependent.

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• Immune Microenvironment and Cancer: The interplay of these genes shapes the tumor microenvironment. TLRs activate immune cells, leading to the release of cytokines (like IL1B) and chemokines (like CCL14). This intricate network dictates the immune response against the tumor, influencing immune evasion, angiogenesis, and metastatic potential.

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• Broader Biomedical Significance: The high popularities of IL1B, TLR4, and TLR2 reflect their fundamental and well-studied roles in immunity and inflammation, extending beyond cancer to other significant diseases like severe COVID-19. This underscores their potent biological impact, which can be both protective and detrimental, depending on the context of disease.

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In summary, your genes represent key players in the intricate dance between the innate immune system, inflammation, and cellular processes critical for cancer development and progression. Understanding their roles, especially in the context of inflammation, offers valuable insights for oncology research and potential therapeutic targets.