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Gene Section

Mini Review

IL1B (interleukin 1, beta)

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Identity

Other names: Catabolin; IL-1; IL-1B; IL1-BETA; IL1F2; pro-interleukin-1-beta
HGNC (Hugo): IL1B
Location: 2q13
Note: IL-1beta is a pro-inflamatory cytokine and is expressed by many cells including macrophage, NK cells, monocytes, and neutrophils. It belongs to the IL-1 family cluster that includes the IL-1a, and IL1-RN genes. The caspase 1 (CASP1/ICE) gene proteolitically activates IL-1β. This gene is involved in the proliferation, differentiation and apoptosis of cells. Inflammatory hypersensitivity has been found to be the result of IL-1β activation of cyclooxygenase-2 (PTGS2/COX2). IL-1beta has also been associated with septic shock, and wound healing.

DNA/RNA

Note
IL-1beta is located on Chromosome 2 at location 113,303,808-113,310,827. It is located in the middle of IL-1a and IL1-RN between 40 and 110kb from IL-1a. The pro IL-1β gene is composed of seven exons with a primary transcription product length of 7,008 nucleotides.

Description

The gene spans a region of 7.5 kb and the coding part is divided into seven exons.

Transcription

Transcript length: 1,498 bps; Translation length: 269 residues.

Protein

Description

269 amino acids.

Function

IL-1 proteins are considered endogenous pyrogens since they are involved in inflammatory responses and also have been observed to foment prostaglandin and collagenase release from synovial cells. Additionally, IL-1 is responsible for the induction of IL-2 release, B-cell maturation/proliferation, and fibroblast growth factor activity, that stimulates thymocyte proliferation.

Homology

IL-1beta shares sequence homology with IL-1a and IL1-RN. IL-1beta and IL-1a have an amino acid homology between them of approximately 25%.

Implicated in

Gastric cancer

Note
Interleukin-1 beta overexpression is associated with the increased risk of both hypochlorhydria induced by H. pylori and gastric cancer (El-Omar et al., 2000). Enhancement of IL-1beta production was determined to be caused by polymorphisms in the interleukin-1 gene cluster. The pro-inflammatory properties of the IL-1 beta cytokine could explain the association with gastric cancer, also considering it is an important inhibitor of acid secretion.

Growth of estrogen-dependent tumors

Oncogenesis

In the pathogenesis of estrogen-dependent cancers, particularly, breast and ovary, the role of IL-1β is implicated in protumorigenic insults, cell proliferation, angiogenesis and cell adhesion. It appears that it is the concentration of the peptide interleukin-1 beta which determines its stimulatory or inhibitory paracrine and/or autocrine signals that regulate the growth of estrogen-dependent tumors. The IL-1β over expressing stable MCF7 cell secreting high level of IL-1β peptides shows inhibition of cell growth compared to nontransfected cells, and elevated level of p53 protein is detected in these cells (Roy et al., 2006). Stably IL-1beta transfected cells secreting moderate level of IL-1β peptides stimulate the clonal expansion of MCF7 cells. Different cellular signaling may operate in response to varying levels of IL-1β leading to genotoxic damage, cell apoptosis or cell growth .

Tumorigenesis

Oncogenesis

Il-1 beta has also been found to stimulate the local production of chemotactic factors for polymorphonuclear leukocytes (PMN's) in tumors; PMN's may play an important role in the inhibition of tumor growth.

On the other hand, other studies have found IL-1 beta to promote tumor growth. According to Vidal-Vanaclocha et al. (2000), IL-1 beta along with tumor necrosis factor-alpha (TNF-alpha), up-regulate the expression of vascular cell adhesion molecule-1 (VCAM-1) on hepatic sinusoidal endothelium (HSE) in vivo which promotes cancer cell adhesion and liver metastases.

Cardiovascular risk, cardiovascular diseases

Note

Increased Cardiovascular Risk, Cardiovascular Diseases

Prognosis

SNPs in the interleukin-1beta gene has been reported to be associated with lower expression of basal CRP, a heritable acute-phase plasma protein, in healthy individuals. Elevated basal CRP has been associated with increased cardiovascular risk.

Additionally, an inflammatory cascade involving TNF, IL-1 beta and IL-6 has been suggested to play an important role in the pathogenesis of common postoperative problems associated with cardiac surgery involving a cardiopulmonary bypass. Increased levels of IL-6 release were associated with higher serum levels of TNF-a and IL-1β after surgery, in patients undergoing coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB).

Liver surgery

Note

Changes in tumor necrosis factor-a and interleukin-1 beta production following liver surgery.

Oncogenesis

For cirrhotic patients undergoing liver surgery, changes of IL-1B and tumor necrosis factor-a levels are observed, suggesting that these two genes play an important role in the pathogenesis of postoperative liver failures. Important tissue injury and/or endotoxin, organ failures could develop and progress after stimulation of cytokine production in monocytes by factors such as insufficient blood supply (ischemia).

Inflammation

Prognosis

IL-1 beta gene might be an important neuroregulator of responses to inflammatory stressors in the central nervous system considering that overexpression of the IL-1 beta gene has been found in the CNS during systemic inflammation. IL-1a and IL-1b induction in the hypothalamus may regulate neuroendocrine functions during infection and inflammation. Wong et al (1997) propose that actions of brain IL-1 beta during systemic inflammation are an indicator of limited gene expression of cytokines in the brain to counteract IL-1 bioactivity.

Rheumatoid arthritis, osteoarthritis

Prognosis

IL-1 Beta activity has been linked to a TNF-alpha/cAMP pathway involved in rheumatoid arthritis. Synergistic up-regulation in IL-1 beta synthesis by TNF-alpha/cAMP has been proposed to play a role in the permanent IL-1 beta levels continuously present in chronically inflamed joints. IL-1 beta production is regulated by the TNF-alpha/cAMP pathway at the transcription level requiring a cAMP response element located between -2762 and -2755 bp in the upstream regulatory sequence of IL-1 beta.

Periodontal disease

Prognosis

The severity of periodontal disease could be evaluated through IL-1 beta activity. Liu et al. (1996) identified IL-1beta as playing a pivotal role in the pathogenic mechanism of periodontal tissue destruction. According to the authors, clinical parameters such as gingival index (GI), probing depth (PD) and GCF flow were significantly correlated with gingival crevicular fluid (GCF) and tissue IL-1beta activity. Moreover, the degree of inflammation within periodontal disease tissue could be measured IL-1beta activity in GCF or diseased tissues based on the classification of clinical parameters.

An additional study corroborated above mentioned finding of IL-1 beta levels as a biomarker of

periodontal disease. Elevated salivary levels of MMP-8 or IL-1beta or both combined, were found to significantly increase the risk of periodontal disease. Salivary levels of MMP-8 and IL-1beta could serve as biomarkers of periodontitis.

Erosive hand osteoarthritis (OA)

Note

There is a significant association between the genomic region containing the IL1B 5810 SNP and erosive hand OA in a group of US Caucasoid population (Stern et al., 2003). The IL1B 5810 AA genotype was significantly associated with the erosive hand OA subgroup (relative risk 3.8, p=0.007). The same genotype association was found significant between erosive and non-erosive hand OA subjects (relative risk 4.01, p=0.008). The IL1B 5810A allele occurs most frequently on haplotypes with the SNP alleles IL1B 1423C, IL1B 1903T, IL1B 5887C, and IL1A (-)889C.

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