

CytokineDB: a database collecting biological information

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Abstract:

Cytokines are subdivided in 12 sub-families and are described as multi-functional molecules that play an important biological activity in host defense system against pathogens, in homeostasis, tissue repair, cell growth and development. CytokineDB is an annotated database that collects biological information regarding the cytokines family in human and will be periodically updated by including new biological information. This database is freely available online and can be accessed at the URL: <http://www.cro-m.eu/CytokineDB/>

Keywords: cytokines, chemokines, database

Background:

Cytokines are a family of low molecular weight soluble proteins, peptides, or glycoproteins which are released by many different types of cells as neutrophils, lymphocytes, monocytes, macrophages, Natural Killer, endothelial and epithelial cells and function as intercellular signaling molecules to control cellular proliferation, differentiation and function [1]. They are important in innate and adaptive immune response and they mediate processes as inflammation, hematopoiesis, phagocytosis and apoptosis [2]. These proteins are produced *ex novo* in response to an immune stimulus, and generally operate on short-haul for short periods and at very low concentration. Cytokines act by binding specific membrane receptors and subsequent transduction of the signal through second messengers, generally a tyrosine kinase that trigger a cascade process that leads to the activation of a specific set of genes [1]. In relation to their structure and predominant biological activity, in humans they are produced in the different types of cells involved in the immune system and are subdivided in sub-families [3]. To understand the biology of the cytokines it is necessary to refer to a complex molecular network, in which the positive and negative action of cytokines is balanced by reciprocal interactions, regulated by implicated cells as well as other inducing and inhibiting

molecules. Cytokines are described as multi-functional molecules, which play important biological activity in host defense system against pathogens, in homeostasis, tissue repair, cell growth and development [4]. Because cytokines and related receptors function in a complex regulatory network where one cytokine influences production of many other cytokines and vice versa, there is a need for profiling an array of cytokines in a given pathological condition. In fact, some profound changes in the cytokine profile, that were observed during the course of various diseases, have highlighted that these molecules play a pivotal role also in promoting tumorigenesis and metastatic networks [5]. Cytokines are defined as chemokines, interleukins, and lymphokines depending upon their targets and function. Initially, the interleukins were used to define cytokines that targeted leukocytes, but the term is now used to describe newer cytokines with no bearing on the presumed function or target. The chemokine term is used to describe cytokines that are important in chemoattraction between cells. Hence, with essential and comprehensive information on all known cytokines we projected an annotated database that includes hundreds of entries with detailed descriptions of cytokine genes, proteins, cell sources and biological activities.

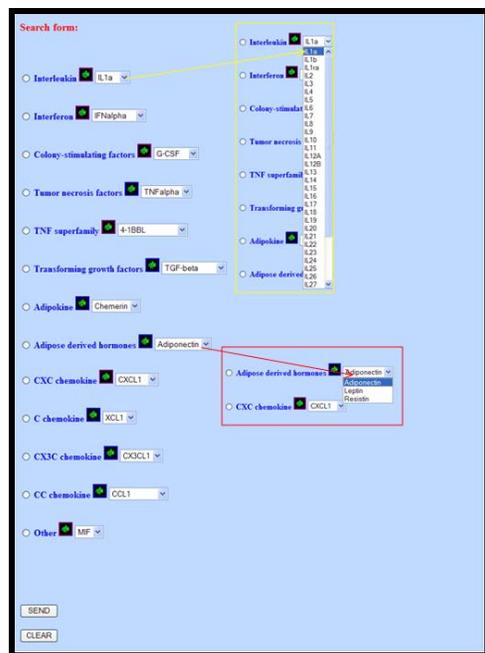


Figure 1: Example of input page in CytokineDB

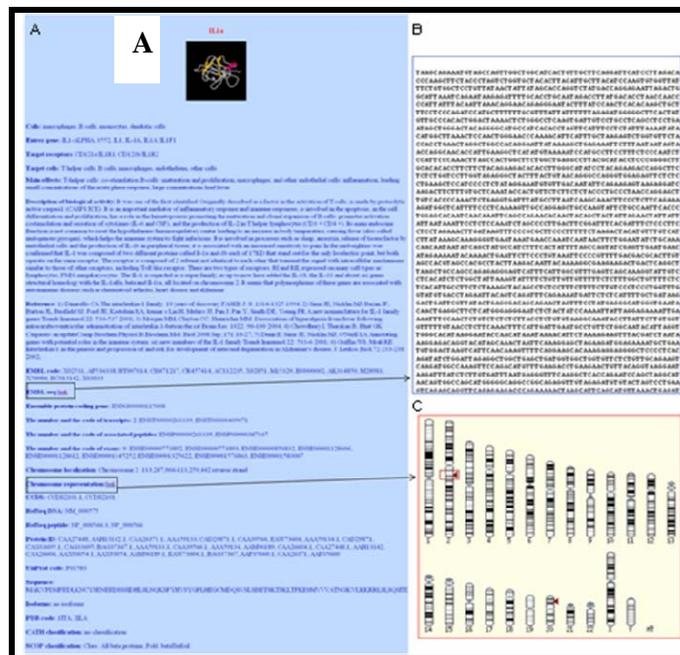


Figure 2: Example of output page in Cytokine DB

Methodology:

Data collection

Some databases were used to collect gene and protein data regarding the human cytokine family: Pubmed and OMIM for biological activity, ENSEMBL for gene records, SRS retrieval system for searching DNA and protein sequences, PDB for three-dimensional structures [6], DSSP for secondary structure assignment [7] and CATH and SCOP for structural classification [8-9]. Search form is based on a CGI script written in PERL language.

Features of Cytokine Database

The human cytokine family was subdivided in 12 sub-families: Interleukin, Interferon, Colony-Stimulating Factors, Tumor Necrosis Factors, TNF superfamily, Transforming Growth Factors, Adipokine, Adipose derived hormones, CXC chemokine, C chemokine, CX3 chemokine, CC chemokine. The user can click on the image near to the name of each cytokine family and have a short description of the structures of these families. Moreover, in these pages there are the links related to the comparisons between the structures belonging to each family obtained by MultiProt (Multiple Protein Structure Alignment) and MASS (Multiple Protein Structure Alignment by Secondary Structures) servers [10-11].

In each subgroup, all the known cytokines were inserted. The user can select a sub-family and choose the protein of which want have information (Figure 1). The output page for each cytokine reports the cell type, where the protein is located, Entrez Gene, the target receptors and cells, the main effects, the description of biological activity, the references, EMBL code, Ensembl protein_coding gene, the number of transcripts, associated peptides and exons, the number and the code of transcript, the number and the code of associated peptides, the number and the code of exons, the chromosome location, CCDS, RefSeq DNA, RefSeq peptide, Protein ID, UniProt code, Sequence isoforms, amino acid sequence, PDB code, CATH and SCOP classifications, and structural features (Figure 2A). Moreover, in the output page there are the links for the nucleotide sequence (Figure 2B) and the scheme of gene localization on the related chromosome (Figure 2C).

Utility:

The database can find utility in the scientific community for a quick review of the cytokines and their involvement in disease and use in clinical treatment. References are also provided for each protein and updated with recent published paper.

Conclusions and future development:

The main objective of CytokineDB is to provide an easy access to cytokines and chemokines for researchers working in immunological laboratories and for other users of scientific discipline. Database categorization reveals an user-friendly access to data. The database shall be updated periodically by including information regarding human cytokine receptors and cytokines as well as from other organisms.

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