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CytReD: A database collecting human cytokinome information

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Abstract
The cytokines/related receptors system represents a complex regulatory network that is involved in those chronic inflammatory processes which lead to many diseases as cancers. We developed a Cytokine Receptor Database (CytReD) to collect information on cytokine receptors related to their biological activity, gene data, protein structures and diseases in which these and their ligands are implicated. This large set of information may be used by researchers as well as by physicians or clinicians to identify which cytokines, reported in the literature, are important in a given disease and, therefore, useful for purposes of diagnosis or prognostic.

Availability: http://www.cro-m.eu/CytReD/.

Background:
The cytokines family is composed by many proteins that need to bind to specific receptors on the cell surface to perform their biological function **[1]**. This binding can stimulate both the expression of receptors for cytokines and the production of other cytokines that in turn act on other target cells **[2-3]**. On the whole, the totality of the cytokines and of their interactions in and around biological cells is defined with the "cytokinome" term **[4-5]**. Often these molecules are involved in cancer-related chronic inflammation and play a pivotal role in promoting tumorigenesis and metastatic processes. Therefore, the knowledge of the structures of cytokine-receptor complexes and the biophysical basis of their binding is important to identify putative antagonists able to block the cytokine-receptor interactions that represent the reason of onset disease **[4-6]**. We have developed a Cytokine Receptor Database (CytReD) that collects biological information regarding the human cytokine receptor families and their related ligands and can be used by researchers as well as physicians and clinicians to identify what cytokines are reported in the literature as significant in a given disease.

Materials and Methodology:
Data Collection:
Different databases were used to collect gene and protein data regarding the human cytokine receptors **[6]**. Moreover, ProtParam tool was used to calculate isoelectric point, hydropathicity and number of charged residues whereas FoldIndex for the prediction of disorder propensity of the cytokine receptors **[7]**.

System features:
To build a dynamic website we used Drupal platform being content management system. Drupal modules provide specific functionality by using MySQL acting as a back-end database server. JMOL was implemented to view the three-dimensional structures of the proteins. For the front end web user interface we have used ZERO POINT theme from Drupal Themes and customized in according to our needs and web user interface is developed in PHP (version 5.3.1). In particular, the creation of the database in MySQL version 5.0.75 by using phpMyAdmin version 3.1.21 includes 34 data fields.

Results:
Database content:
The user can search in Cytokine Receptor Database by selecting "Cytokine Receptor Name", "Ligands", "Cytokine Family" or "Disease". If the user chooses "Cytokine Receptor Name" and writes the receptor name, the output page will report all the information related to the selected receptor, subdivided in three different parts: description, sequences and accession codes and other biological information **(Figure 1)**. In the "description" there are information regarding the biological description, the related ligands, the commonly used synonyms, the cell type where the protein is expressed, its role and the diseases in which it is involved. Indeed, the user can click on disease names to visualize information on involved genes, drugs and pathways reported in PharmGKB database (http://www.pharmgkb.org) or on ligand name to obtain specific information collected in CytokineDB database **[6]**.

Figure 1: Output example of CytReD

In the "sequences and accession codes" part there are the nucleotide and protein sequences with the link to EMBL, UniProt and PDB databases and the possibility to view 3D-structures by JMOL visualization tool. In "other biological information" section the user can find Chromosome localization, Ensemble protein coding gene, References, CATH and SCOP classifications, and different quantitative analysis. In particular, the number of charged residues and unfoldability index were inserted because our previous study has demonstrated that N- and C-terminal regions present in chemokine membrane receptors are characterized from a high disorder propensity **[8]**. When the user chooses "Ligands" and writes a ligand name, the output page will retrieve the list of the receptors which bind that protein. Then, clicking on "View" link, it will be possible to visualize the page with all the related information on chosen receptor. If the user chooses "Cytokine Family" and writes one of the 7 sub-families (Interleukins, Interferons, Colony-Stimulating Factors, TNF family, Transforming Growth Factors, Adipokines, and Chemokines), CytReD will show the list of all the receptors belonging to this receptor cytokine family. As in the previous case the user can choose a receptor, click on "View" link and visualize a page that report all the information related to the chosen receptor. Finally, if the user chooses "Disease" and writes a disease name, CytReD will report the list of all the receptors and of the related cytokines involved in the selected disease on the basis of papers recently published. Also, the user can obtain information on a chosen receptor by clicking always on "View" link.

Utility:
CytReD can find utility in the scientific community for a quick review of the cytokine receptors, of their ligands, of their involvement in diseases and of their use in clinical treatments.

Future developments:
CytReD is part of a broader project aimed to develop tools and portals able to be useful supports for a reliable predictive medicine and will be correlated with CDMS (Clinical Data Mining Software) that collects cytokine profiles evaluated on patients affected by different diseases **[5]**.

References:

[1] Schreiber G & WalterMR. *Current Opinion in Chemical Biology.* 2010 **14**: 511 [PMID: 20619718]
[2] Onischi M *et al. Int Rev Immunol.* 1998 **16**: 617 [PMID: 9646179]
[3] Wang X *et al. Annu Rev Immunol.* 2009 **27**: 29 [PMID: 18817510]
[4] Costantini S *et al. Bioinformation.* 2010 **5**: 166 [PMID: 21364780]
[5] Evangelista D *et al. PEDS.* 2010 **123**: 899 [PMID: 20889532]
[6] Costantini S *et al. Bioinformation.* 2009 **4**: 92 [PMID: 20198179]
[7] Prilusky J *et al. Bioinformatics.* 2005 **21**: 3435 [PMID: 15955783]
[8] Miele M *et al. Plos One.* 2011 **6**: e16690 [PMID: 21311758]

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