Computational systems biology approach for the study of rheumatoid arthritis: from a molecular map to a dynamical model

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In this talk I will present a systematic effort to summarize and code current biological pathway knowledge concerning Rheumatoid Arthritis (RA), in a way that is both human and machine readable, facilitating the use of a molecular map as an analytical tool, as well as the extraction of an executable logic-based dynamical model.

A detailed molecular map, based on exhaustive literature scanning, strict curation criteria, re-evaluation of previously published attempts and most importantly experts' advice is being constructed using the software CellDesigner. This RA map will be web-published in the form of an interactive google map, using the software MINERVA, allowing for easy access, navigation and search of all molecular pathways implicated in RA.

The user will have access to all literature used, with detailed annotations for every component and reaction, including PubMed IDs, and a list of identifiers such as Uniprot, EntrezGene, Ensembl, HGNC and RefSeq. As the map is constructed using information from various experimental studies, the user will also be able to opt for visualization of data with specific cell origin, highlighting cell-specific sub-networks within the global one. Moreover, the user will have the possibility to spot all known drug targets, and the corresponding drugs up to date for RA. Detailed view of an element will allow the search for drugs, chemicals and miRNAs targeting this particular element. Additionally, user-provided Omic datasets could be displayed as overlay, giving a first estimation of affected pathways and components.

Static representations of molecular networks can provide useful but relatively limited understanding, if one wishes to test more complicated scenarios. A dynamical study can reveal information about the system's behavior under different conditions by in silico simulations, perturbations, complex hypotheses testing and predictions. A detailed molecular map can serve as an excellent basis for a dynamical model, providing a template for the building of a regulatory graph. Leaning on the RA map and using the web platform Cell Collective, a platform that supports annotation and real time simulation and analysis for large scale networks, we are currently working towards the semi- automated inference of a logical (Boolean) model, with a set of preliminary logical rules based on the topology of the network.

One of the main objectives of this collaborative and interdisciplinary work is to facilitate the transition from static representations of biological knowledge to executable dynamical models, addressing among others, issues of interoperability between tools widely used by the systems biology community.