COMBIMS Newsletter

A novel drug discovery method based on systems biology: combination therapy and biomarkers for Multiple Sclerosis

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The collection of phosphoproteomic and cytokine data from healthy controls and MS patients is complete

More information:
http://www.combims.eu

CombiMS update

The CombiMS project has reached its final stage and it is close to an end. So far the project has generated several outcomes. The consortium has already completed the collection of phosphoproteomic, cytokine and genotyping data from Multiple Sclerosis (MS) patients and healthy controls. The logic model has been adjusted to the experimental data and different signatures have been identified that may possibly serve as potential drug targets. This will be further complemented with the genotyping data in order to determine genetic differences. In parallel, the model is being used to determine the pathogenic mechanism of MS and potential treatments, both of which will still await validation.

Phosphoproteomic and cytokine data collection

ProtATonce has successfully obtained the phosphoproteomic and cytokine data from healthy controls and MS patients through xMAP assays. This has been filtered and curated to generate a robust dataset from 169 patients and healthy donors.

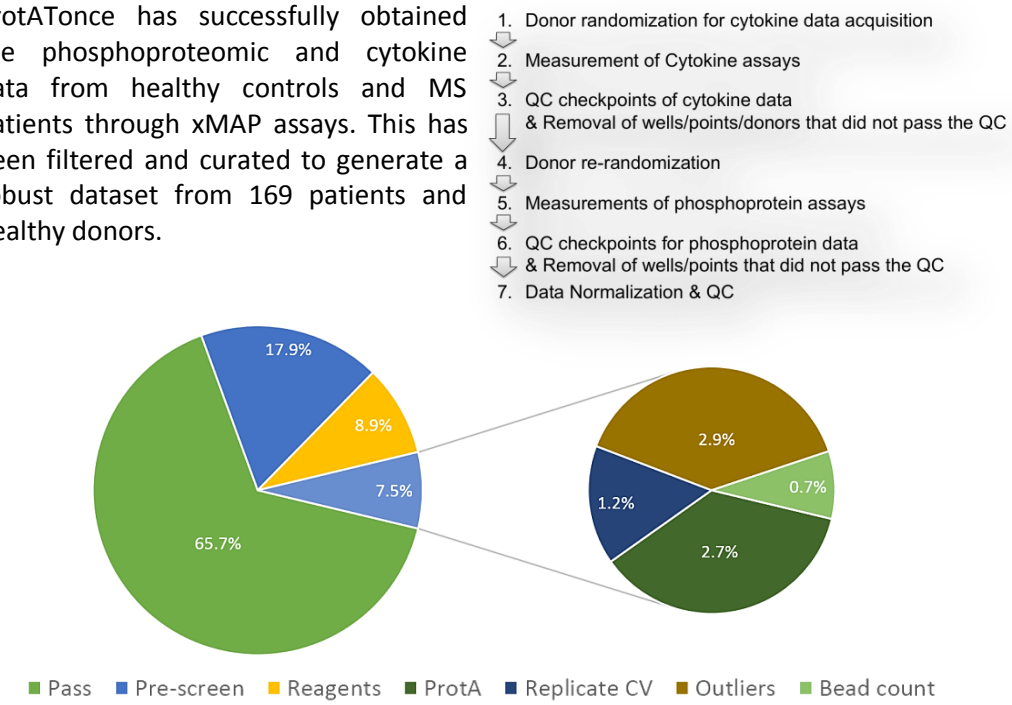

Fig1. Data filtering processes and their effect upon the whole dataset. Figure kindly provided by Leonidas Alexopoulos and Dimitris Messinis from ProtAtonce.

This data was further normalised by the Systems Biomedicine group at EMBL-EBI (Julio Saez-Rodriguez) in order to be able to compare the different stimulation conditions and the phosphorylation levels of the different proteins, as well as opening the data to Boolean logic modelling.

Fitting of logic models to data from MS patients and healthy controls

The normalised data obtained from healthy controls and MS patients has been used to generate a robust signalling network for each patient. Characteristic protein-protein interactions for each group of patients have been determined by the Systems Biomedicine group at EMBL-EBI (Julio Saez-Rodriguez) according to disease subtype and drug treatment. To identify a MS signalling signature associated with the disease and the response to current therapies, the patient-specific models were compared. The analysis revealed interactions that might explain the differences between the groups and the signatures of interest as therapeutic targets. These results are now entering the final phase of validation.

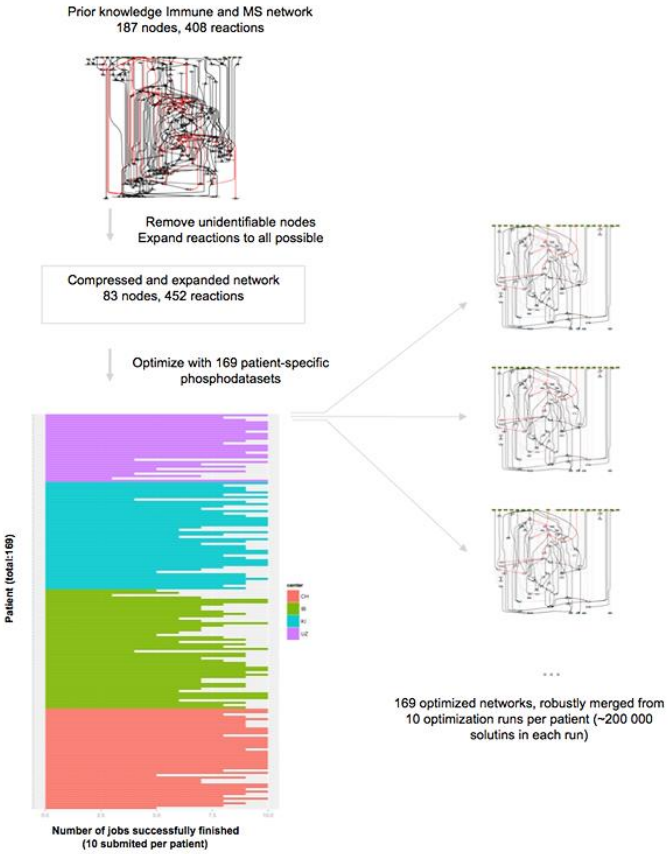

Figure 2: Workflow for the calculation of a patient-specific network.
Figure kindly provided by Julio Saez-Rodriguez and Marti Bernardo-Faura.

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Final Consortium meeting

The Final Meeting of the CombiMS Consortium will be hosted by Anaxomics in Barcelona on the 17th of December, 2014. The members of the Consortium will take stock of the work carried out during the last stage of the project and the latest achievements, and arrange for the publication of the final results of the project. Special attention will be paid to assess the achievements of the objectives and all deliverables due at the end of the project and the necessary arrangements to prepare the final report to be submitted to the European Commission.

Forthcoming tasks

- Incorporation of the genotyping data to the computational models to define the differences due to genotype and to derive personalized models of drug response.
- Based on the predictive models, identify potential drug combinations to treat MS, their potential side effects and biomarkers of response to therapy.
- Validate in vitro and in animal models the mechanism of MS pathogenesis and drug combinations proposed from the models.

SEVENTH FRAMEWORK PROGRAMME

The CombiMS project has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 305397.