COMBIMS Newsletter

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

Issue no. 4, January 2015

In this issue:

Potential drug combinations to treat MS and their potential side effects have been identified

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

CombiMS update

The CombiMS project is reaching its end having achieved most of its goals. Based on the predictive models developed for the pathogenic mechanism of MS, potential drug combinations to treat MS and their potential side effects, as well as biomarkers of the response to therapy, have been identified. The experimental validation of selected combination therapies, of biomarkers of response to therapy and of predicted side effects are currently undergoing and it is expected to be completed in the following weeks. In parallel, the Consortium is preparing a scientific article that will bring together the results of the projects, as well as the final project report to be submitted to the European Commission.

Identification of potential drug combinations

Potential drug combinations have been identified through literature and database search and by the analysis of the MS network model generated by AX. Iterative simulations of the dynamic logic models generated by EMBL-EBI were also performed, assuming either an additive, synergistic or antagonistic effects of the drugs tested. The different drug combinations were also analysed in the different cell-specific ODE models developed by KI, using search techniques based on swarm optimization in order to extract robust predictions. Reprofiling has been carried out using the phosphoprotein data obtained from healthy and MS patients to assess the synergistic effect of drug combinations of first-line MS treatments and non-MS drugs. The alteration of the MS network models in function of the phosphoprotein data has been evaluated using different patient classifications.

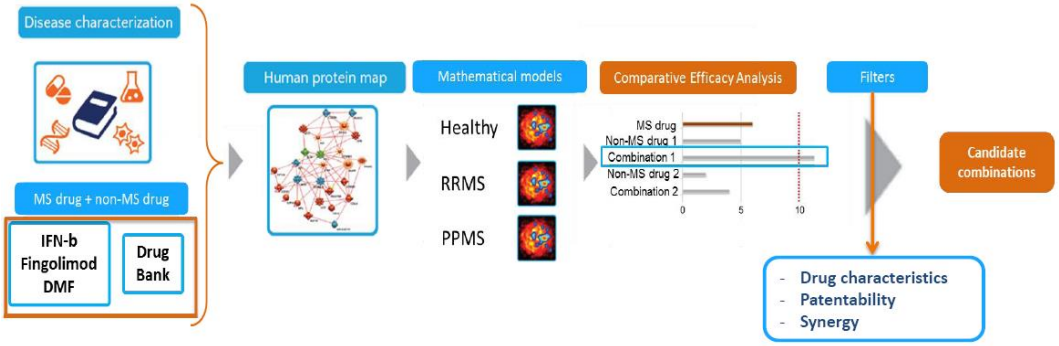

Fig.1. Reprofiling protocol. Figure kindly provided by Anaxomics

The phosphoprotein data allowed the models to be customized in order to make them better reflect the real situation. Four of the drug combinations tested have shown synergism, i.e. an increase in the efficacy of the drugs alone, in all the models tested.

Dissemination activities

A **CombiMS promotional video** has been prepared to promote and explain the project. The CombiMS video is now available publically through You Tube at the following link: https://www.youtube.com/watch?v=KnpCnJsp_d4. Partners have been encouraged to ensure that the video receives the best dissemination possible, recommending it where possible and uploading it to sites that might be of interest.

A **CombiMS promotional pamphlet** has been prepared for the general public and to be circulated among the patients that have participated in the study, as well as other patients that may be interested in participating in other or future studies.

A talk on "**Genetics of adult-onset MS and interaction with environmental risk factors for MS"** was presented by Ingrid Kockum (Karolinska Institute) at the ***2014 Joint ACTRIMS-ECTRIMS Meeting*** in Boston (September 10-13, 2014).

An open seminar and lecture was given by Marti Bernardo-Faura from EMBL-EBI at the ***Advanced proteomics course for molecular biologists and clinicians*** that took place at the CRG in Barcelona (July 7-11, 2014).

Anaxomics has presented the methodology and results of the CombiMS project at several brokerage and partnering events, such as ***Biospain 2014*** in Santiago de Compostela (24-26/09/2014) and **BIO-Europe 2014** in Frankfurt (3-5/11/2014).

Partners

bionure – Biomedicine heading to future
ANAXOMICS
PROT AT ONCE – THE ART IN MULTIPLEXED ASSAYS
IDIBAPS – Institut D'Investigacions Biomèdiques August Pi i Sunyer
University of Zurich[UZH]
Karolinska Institutet
CHARITÉ – UNIVERSITÄTSMEDIZIN BERLIN
EMBL-EBI

Final Consortium meeting

The final meeting of the CombiMS Consortium was hosted by Anaxomics in Barcelona (Spain) on the 17th of December, 2014. During the meeting, the members of the Consortium took stock of the work carried out during the last stage of the project and presented their latest achievements, laying down the conclusions reached by the project. Special attention was paid to the achievements of the objectives and deliverables due at the end of the project and the necessary arrangements to prepare the final report to be submitted to the European Commission. In addition, plans for the exploitation of the final results were also discussed. During the meeting, Fabien Richard, representative of eTRIKS and a member of the Scientific Advisory Board, provided the Consortium with his feedback on the latest results and recommendations on future activities of the consortium.

Forthcoming tasks

- Complete the validation studies *in vitro* and in animal models of the selected drug combinations predicted by the models.
- Prepare the main article with the results of the project and an additional one on the methods of phosphoproteomic analysis.
- Take appropriate measures to adequately protect biomarkers and combination therapy for future development.
- Prepare the final project report to be submitted to the European Commission.

SEVENTH FRAMEWORK PROGRAMME

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