Towards Patient Stratification in Systemic Lupus Erythematosus using a Systems Pharmacology Approach

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Objectives: 1) Provide a Systems Pharmacology approach able to identify plausible altered pathways of the immune response that may explain the different and heterogeneous alterations in Systemic lupus erythematosus (SLE) patients, 2) classify patients according to their alterations, and 3) identify possible therapies for each patient subpopulation.

Methods: The immune response after production of autoantigens was modeled by Boolean networks [1,2]. Networks were built focusing on the components of the immune response that have been reported to be altered in SLE patients. Simulations were performed perturbing the network in order to identify which nodes, if perturbed may trigger alterations similar to those observed in SLE patients. Clustering analysis was performed to group the network nodes according to the alterations these nodes may trigger. Simulations and analyses were performed in R.

Results: Different SLE manifestations were linked to different altered pathways of the immune response or initial conditions able to trigger the development of “Lupus like” manifestations. Virtual patients were clustered into different categories according to their manifestations. Group-specific therapies were identified able to reduce the disease alterations for different subpopulations. No single treatment was able to reduce the manifestations in all patient subpopulations.

Conclusions: Heterogeneity of SLE manifestations can be modeled by different underlying altered pathways of the immune system. Patients can be classified into different categories according to their alterations and optimal treatments can be identified for each patient subpopulation.

References: