Building an Inflammatory Bowel Disease Network, a Systems Pharmacology Approach

Ignacio Gonzalez-Garcia1,2*, Itziar Irurzun-Arana1, Leire Ruiz-Cerdá1, Chuanpu Hu3, Honghui Zhou3, An Vermeulen4, Iñaki F. Trocóniz1, José David Gómez-Mantilla1

1Pharmacometrics and Systems Pharmacology. University of Navarra, Pamplona, Spain; 2Pharmacy and Pharmaceutical Technology Department, University of Valencia. Valencia, Spain; 3Janssen Research and Development, LLC, Spring House, USA; 4Janssen Research and Development, a division of Janssen Pharmaceutica NV, Beerse, Belgium

Objectives: Systems pharmacology it is a new tool that allows the study of complex biological systems [1], like immunological response to antigens. Inflammatory Bowel Disease (IBD) is a complex disorder, which evolves through several complicated immunological pathways and is characterized by processes of remission and relapse producing a functional impairment of the gut wall. It includes Crohn Disease (CD) and Ulcerative Colitis (UC) [2]. The objective of the current work was to develop a systems pharmacology model for CD and UC integrating the main known components and reactions as a tool to identify possible therapeutic targets and biomarkers.

Methods: A theoretical disease network was developed using information taken from literature (Figure 1). Boolean functions were designed to link all the components in order to build the network. 5,000 simulations were carried out to validate the network.

Results: The network contains 45 nodes and more than 150 interactions. The network model was able to simulate the gastrointestinal tract state with different underlying alterations. The simulation exercise allowed identification of model elements, whose profiles changed due to the underlying alterations.

Conclusions: A systems pharmacology model was developed integrating the main known pathways in IBD. The model has shown its applicability in identifying altered pathways, which resembled different statuses of the disease, opening up the potential to identify therapeutic targets and biomarkers.

References