Development of a Quantitative Systems Pharmacology (QSP) Model of Psoriasis: Overview and Challenges

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Objectives: Psoriasis is a chronic inflammatory skin disease with a complex pathogenesis involving multiple tissues (skin, systemic circulation and lymph node) and immune response spanning a number of cell types such as Th17 cells, macrophages etc. A QSP model of Psoriasis is being developed to better understand its pathophysiology and to assess the targets/compounds in development within GSK for the treatment of this disease.

Methods: A detailed “PhysioMap” of psoriasis describing its processes and the crosstalk between these processes was developed in collaboration with Rosa & Co. Following this collaboration, ordinary differential equations (ODEs) were added to this map to build a quantitative model of psoriasis. The parameters in this model such as cell turnover rates, production and degradation rates of inflammatory mediators, parameters describing immune regulation by cytokines, or correlations between disease processes and clinical outcomes are being calculated using in-vitro, in-vivo and patient clinical data from literature.

Results: Significant progress has been made in the development of a QSP model of psoriasis with three main compartments (Figure 1): skin, systemic circulation and lymph node. This model describes the processes related to recruitment of immune cells from lymph nodes and blood to skin, production of inflammatory mediators in skin, activation of keratinocytes as well as correlation of these processes to clinical outcomes. In this poster, we will outline the steps for developing the psoriasis model and addressing the challenges that are typical of QSP models of this scale such as in-vitro to in-vivo translation of estimated parameters, estimation of cell and cytokine levels in different tissues, and the need for effective literature mining.

Conclusions: QSP modeling allows integration of data from multiple physiological scales and sources to build a quantitative model of disease progression. This model will be crucial in further understanding the pathogenesis of psoriasis, prioritizing novel targets for its treatment and estimating the efficacy of GSK compounds.

![Figure 5 The main compartments in the psoriasis model and their components. An external insult initiates the activation of keratinocytes in skin. Also, there is transfer of immune cells between the skin and lymph node and systemic circulation.](image-url)