PhysioPD™ Research Utilizes Mechanistic Physiological Models to Enhance Immunology Research and Drug Development

Katherine Kudrycki*, Michael Weis, Meghan Pryor, Rebecca Baillie, Vincent Hurez, Douglas Chung, Mike Reed, Christina Friedrich

Rosa & Co., LLC, San Carlos, CA. *kkudrycki@rosaandco.com

Objectives: To investigate and elucidate the role of different parts of the immune system in the etiology, pathogenesis, and treatment of various diseases. To improve the identification of promising candidate therapies and reduce risks associated with drug development.

Methods: Immunological processes are complex and feature a wide array of cell types and mediators with interacting and overlapping functions. Mechanistic modeling can help clarify immunological disease processes. With participation from industry clients, Rosa has developed PhysioPD Research Platforms containing detailed immunology functionality in a range of indications, including dermatology, oncology, and rheumatology in over two dozen research projects. Platforms are quantitative systems pharmacology (QSP) models that incorporate engineering approaches and scientific analysis to clarify physiology and drug mechanisms of action (MOA). Each Platform was qualified in accordance with Rosa’s Model Qualification Method, including running simulated protocols to ensure Platform results are qualitatively and quantitatively consistent with relevant published and/or proprietary research. Simulated experiments were then run to test hypotheses, elucidate the connections between drug action and immunological outcomes, select the correct drug targets, prioritize drug candidates, and select choice and timing of endpoints and biomarkers in clinical trials.

Results: In atopic dermatitis, research clarified MOA, helped prioritize compounds targeting different immunological pathways, and identified opportunities for competitive differentiation. In acne, research identified inflammation as a top driver for pathophysiology and clarified the contribution of specific cytokines. In immuno-oncology, simulated treatment for leukemia improved understanding of heterogeneous responses to therapy and the factors that influence those responses. Research in rheumatology clarified the relationship between patient response to anti-TNFα and novel immunological therapy.

Conclusions: In the context of immunology R&D, PhysioPD Platforms are effective tools for elucidating the role of different components of the immune system in the pathogenesis and treatment of diseases. Mechanistic QSP modeling enables focused use of resources by informing go/no-go decision points early in the drug development process.