



COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Pharmaceutical Sciences Seminar Series

Wednesday, April 12, 2023

4:00pm

NCRC Building 10 Research Auditorium or [Zoom](#)

5th Allen J. Sedman Lecture

“Application of mechanistic PK/PD modeling to guide the discovery of antibodies and antibody fragments”

Presented by:



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Abstract: Pharmacokinetic/pharmacodynamic (PK/PD) research is traditionally pursued during drug development (i.e., after drug candidates have been selected) or after drug approval and marketing. This lecture will discuss opportunities for using PK/PD modeling to assist in drug discovery. Examples will be provided for the application of PK/PD to guide each of the major objectives of the discovery process, including: (a) target identification / validation with discussion of use of mechanistic PK/PD modeling to assist in the identification and validation of the Fc receptor of the neonate (FcRn) as a drugable target for treatment of auto- and allo-immune conditions, (b) use of PK/PD to guide hit-to-lead engineering for anti-idiotypic distribution enhancers (AIDEs) that improve antibody distribution within solid tumors, and (c) use of PK/PD concepts to guide lead-optimization for payload-binding selectivity enhancers (PBSEs) that are designed to improve the therapeutic index of antibody-drug conjugates (ADCs). Most of the focus for the lecture will be placed on recent research relating to the use of AIDEs to improve the efficacy of trastuzumab conjugates in the treatment of mouse models of human HER2+ tumors, and relating to the use of PBSE to improve the safety and therapeutic index of MMAE ADCs (e.g., brentuximab vedotin, enfortumab vedotin, trastuzumab vedotin, polatuzumab vedotin) and DM4 ADCs (e.g., mirvetuximab soravtansine, 7E7 [anti-CD123]-DM4).

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