

Drug-Disease systems analytics for optimization of preclinical drug combination study design in immuno-oncology



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à l'invitation de la professeure Fahima Nekka

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In the preclinical development of anti-tumor immuno-modulatory compounds, knowledge around the mechanism(s) of action is typically derived from syngeneic mice inoculated with various histo-compatible tumor cell lines. In the present work, we used a quantitative systems analytics approach, to address recurring questions on dose, dose scheduling and sequencing for combinations, while also searching for therapeutic combinations which may overcome intrinsic or acquired resistance to existing treatments. As result, we developed a generalized systems model describing tumor size and biomarker dynamics data derived from syngeneic murine tumors. Furthermore, upon model qualification, predictive simulations were performed, addressing questions around mechanisms of action and optimal combination strategy.