



Donnelly Centre
for Cellular + Biomolecular Research
UNIVERSITY OF TORONTO



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“Systems Approach to Engineering of Antibodies for Therapeutic Use”



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Donnelly Centre James Friesen |
Cecil Yip Red Seminar Room

Abstract:

While therapeutic antibodies have attracted a lot of attention from bio-pharmaceutical industry, their development continues to be challenging. Most of the failures occur in Phase II, where the biological hypothesis is typically being tested for the first time. If this testing is successful, the pathology of the disease becomes linked to the blockade of the specific antigen creating “validated” targets that are often interrogated by follow-on antibodies. These molecules can be engineered to have improved target affinity, enhanced crosslinking or degradation, better engagement of immune system, optimized circulation half-life, decreased immunogenicity, improved tolerability, higher concentration formulation for self-administration and other useful qualities that are suggested by clinical practice. The successful design of follow-on antibodies requires comprehensive analysis of the limitations of innovator molecules, engineering of modes of action that address these deficiencies, prioritization the design objectives, and delineation of the success criteria. These principles will be illustrated with the case study of the development of MM-141, a clinical stage tetravalent antibody inhibitor of IGF-1R and ErbB3, which expands the utility of monospecific antibodies by inducing rapid degradation of oncogenic receptor tyrosine kinase receptor complexes.

Host: Dr. Sachdev Sidhu