Dose

Customary

- Amount of drug administered, infusion rate, dosing schedule

Immunotherapy

- Immunomodulator dosing time or concentration time course at the site of action for immune response

(Pharmaco)Kinetics

Customary

- Drug concentration or summary PK (Cmax, AUC)

Immunotherapy

- Profile and characteristics of immune response mediators (immune cells or antibodies) elicited by the immunomodulator

(Pharmaco)Dynamics

Customary

- Suitably accessible biomarker proximal or distal to patient response

Immunotherapy

- Suitably accessible biomarker proximal or distal to patient response

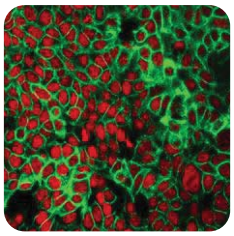

Figure S1 Legend

A view of the traditional dose-exposure-response paradigm is compared with modifications required to accommodate the unique features of immunomodulation. We propose that the correlate of drug exposure (pharmacokinetics) should be the raised immune system component, either polyclonal antibody concentration or immune cell populations. The drug dose equivalent is provided by the schedule and time course of the antigenic challenge. Pharmacodynamic response does not change: it should still be assessed by the changes elicited in a proximal or distal biomarker relevant to the disease being studied, not by the raised immune response. Some of these biomarkers are exemplified in Table 1.
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