

In vitro assessment of Fc functional activity: A broad range of solutions for diverse assay needs

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Introduction

The success of many cancer therapeutics lies in their ability to induce ADCC, ADCP and CDC against specific targets, thus, appropriate assessment is crucial before progressing a drug into the clinic. Demonstrating lack of unwanted effector functions is also important for safety purposes.

Here, we consider key aspects for developing successful Fc effector functional assays and weigh up the benefits and challenges of a panel of assay formats for different purposes. We present options for choosing the most suitable target cell lines, effector cells and appropriate controls.

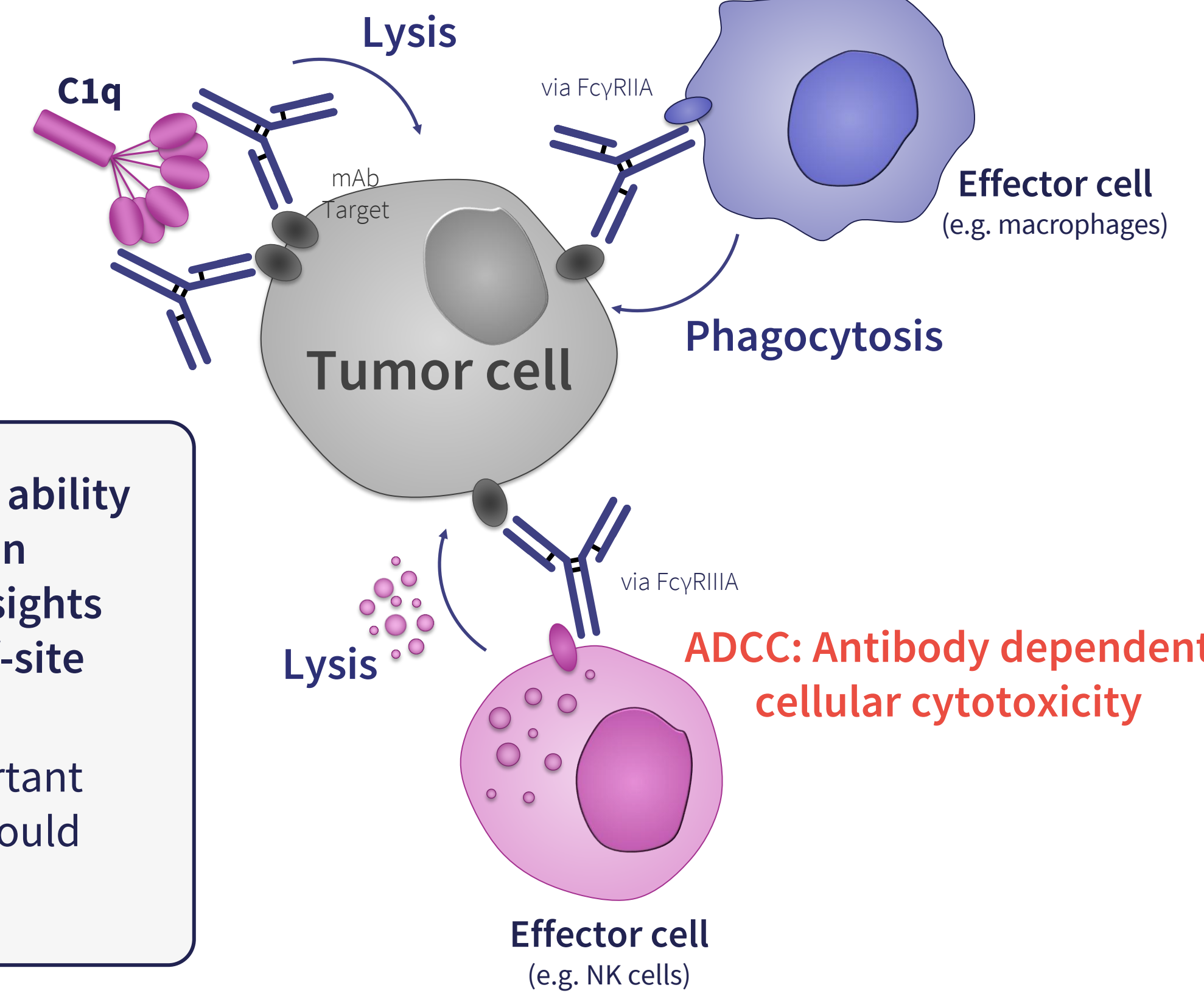
Assessment of FcγR and FcRn function

Along with the choice of isotype, the ability to assess the capacity of antibodies to bind to FcγRs provides fundamental insights into mechanisms of action, half-life and off-site toxicity.

Effector function is primarily triggered through interactions with C1q or FcγRs, consisting of:

- Activating receptors (hFcγRI, hFcγRIIa, hFcγRIIc, and hFcγRIIIa)
- Inhibitory receptor (hFcγRIIb)
- Receptor with unknown function (hFcγRIIIb)
- Receptor involved in recycling and transport of IgG among other functions (hFcRn)

CDC: Complement dependent cytotoxicity

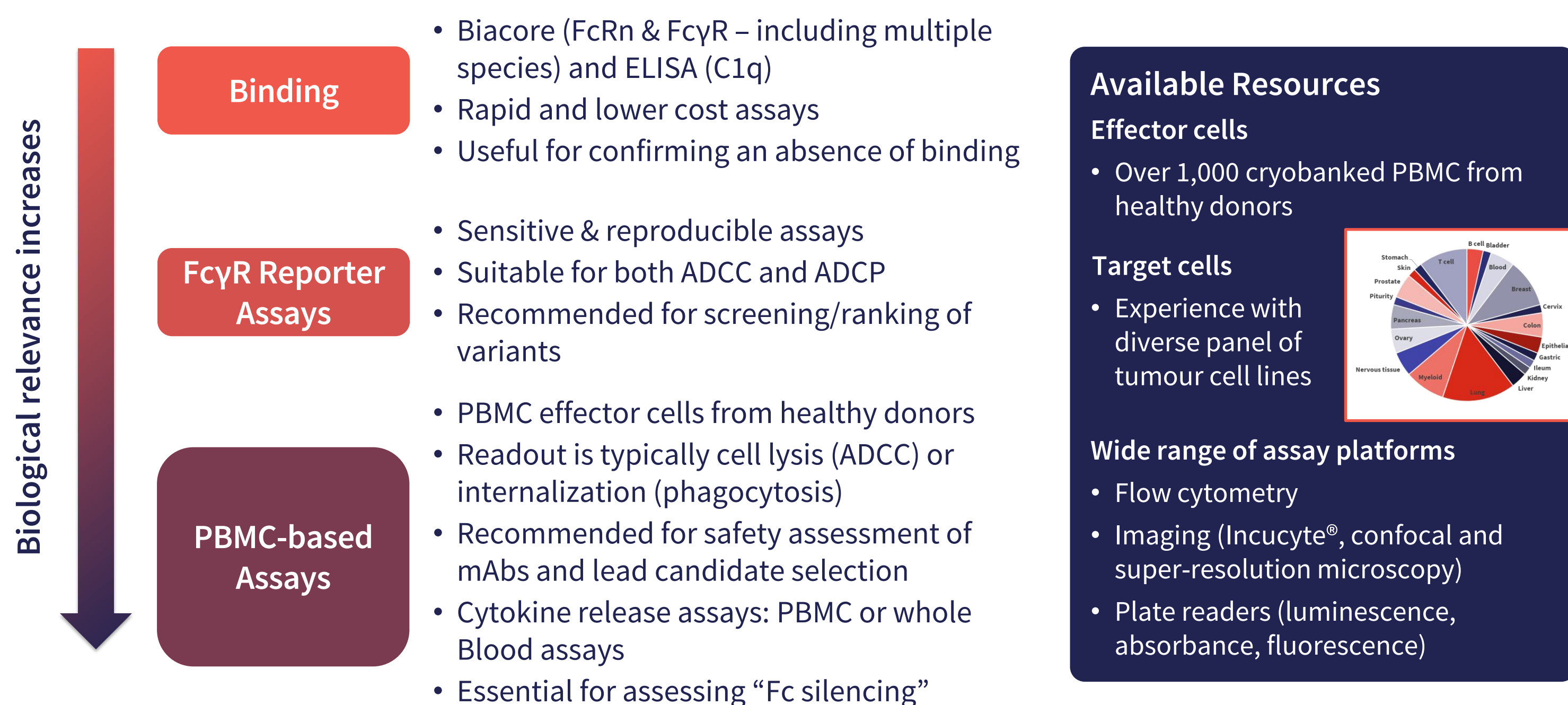


Assessing a therapeutic's ability to induce effector function provides fundamental insights into MoA, half-life and off-site toxicity.

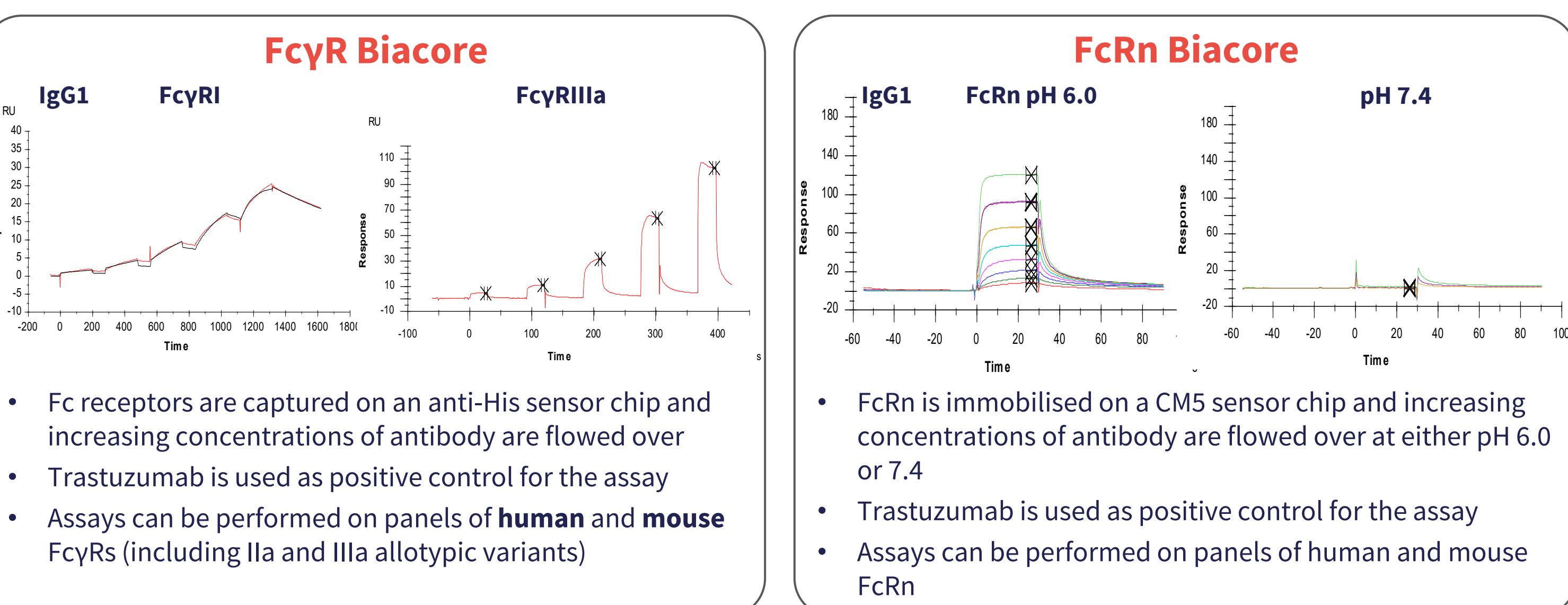
- This is especially important where engaging FcRs could pose safety risks

Approaches to assessing effector function

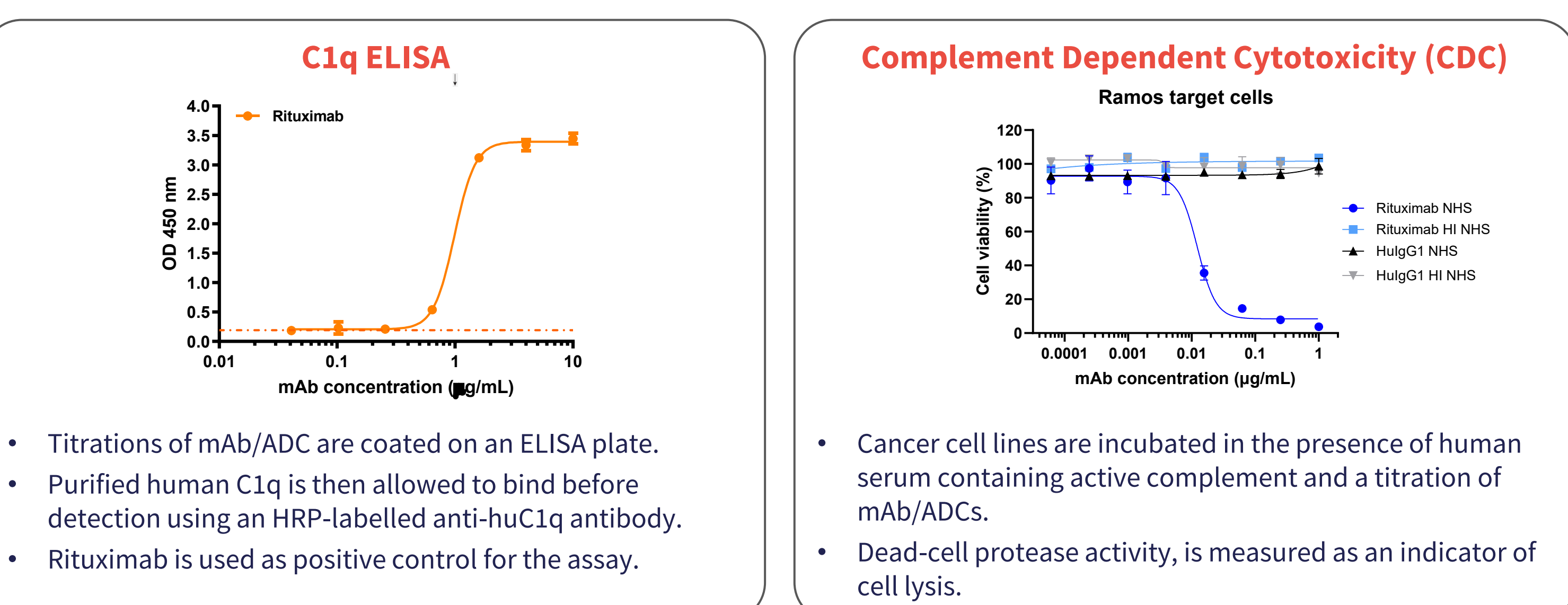
A hierarchy of assays based on specific requirements



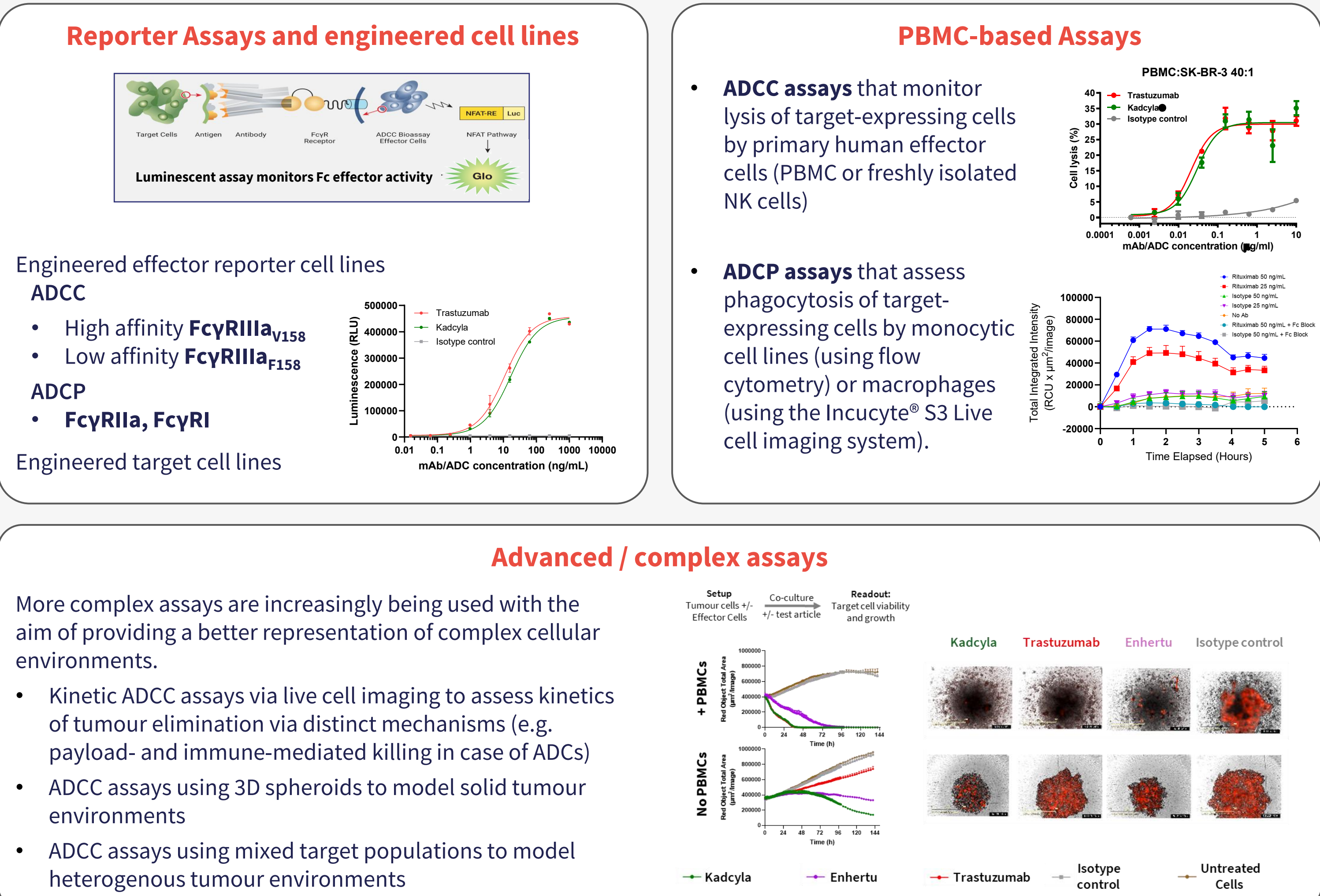
Fc receptor binding by SPR (Biacore) assessment



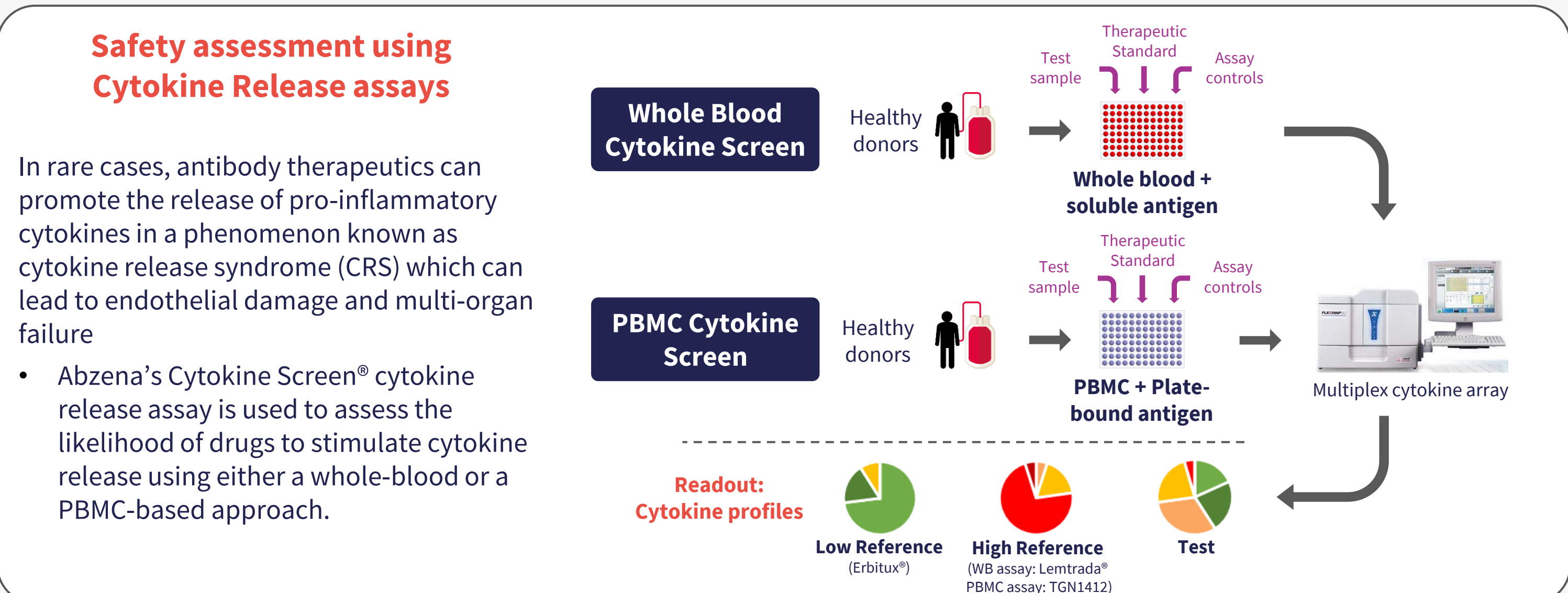
Complement and CDC assays



ADCC and ADCP assays



Cytokine Release assays



Summary

Understanding the mode of action of a drug candidate is essential for every drug development program, however selecting the right assay can be complex and depends upon what question you are trying to answer and what stage of development you are at.

Abzena has developed a comprehensive suite of assays to support the characterization of the Fc-mediated activity of antibodies, Fc fusions or ADC products.

Each assay can be tailored to the specific requirements of your project and our team of experts will work with you to provide solutions to suit your specific needs, considering aspects such as mode of action, assay sensitivity, complexity and regulatory requirements.