

Antibody Discovery Using the Galaxy[®] Library Platform



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Introduction

We have engineered and constructed the Galaxy[®] antibody library that underpins our proprietary platform. Our 'glass spleen' approach incorporates the learnings of the *in vivo* selection process and allows us to access a far greater fraction of relevant antibody space. Based on the principle of 'smart randomness', the Galaxy[®] library harnesses the incredible diversity found within human B cells in a focused way, maximising the proportion of correctly folded functional antibodies. This process results in potent antibodies without the need for excessive mutational load. The Galaxy[®] platform is geared for generation of 'clinic ready' antibodies straight out of the library. Furthermore, the design provides the potential to rapidly generate cheap to manufacture bispecifics without the need for any special technology or engineering. At RxBiologics our capabilities extend to screening for desired specificity and cross-reactivity, NGS analysis, *in silico* developability and immunogenicity screening, profiling for functional activity, antibody production, affinity determination, epitope and biophysical characterisation.

GLASS SPLEEN
B cell-like evolution

SMART RANDOMNESS
Low-risk, targeted diversification

CONTROLLED LIGHT CHAIN DIVERSITY
Diverse but predictable

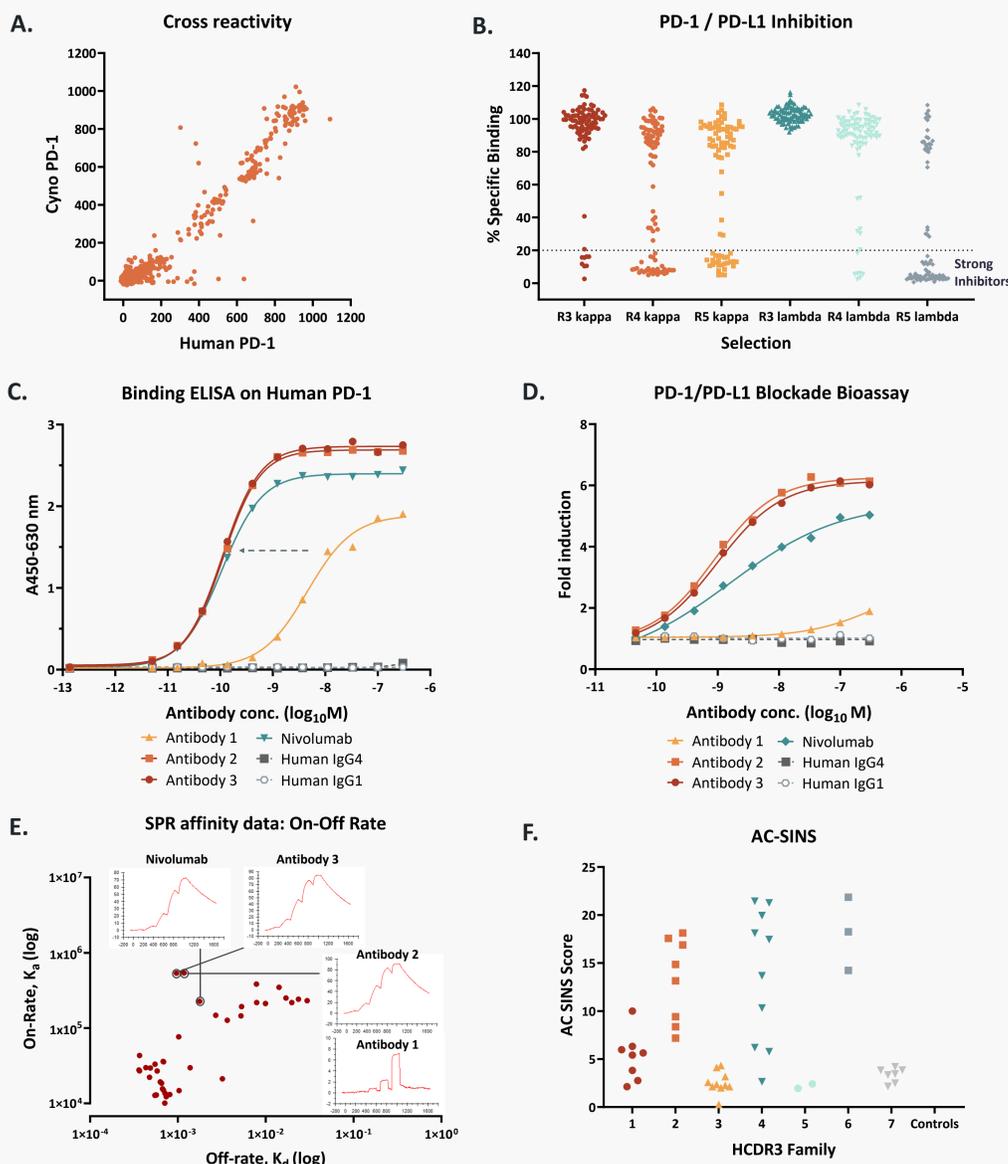


Our Approach



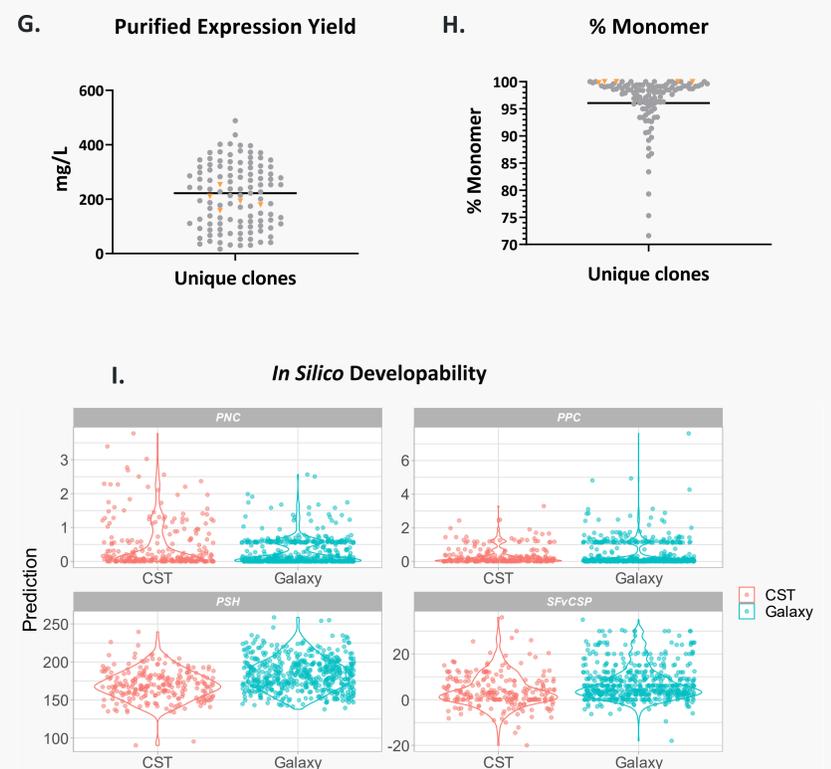
Case Study – Generation of Antibodies to PD-1

After phage selections, clones were expressed as Fab fragments and tested in a TR-FRET direct binding assay (A), showing human/cyno PD-1 cross-reactivity, and a competition assay (B), with many showing a large reduction in % specific binding due to inhibition of the PD-1/PD-L1 receptor ligand complex. A binding ELISA (C) shows the improvements achieved through incorporating our smart randomness and glass spleen approach, as antibodies 2 & 3 were derived from parent clone, antibody 1. (D) Demonstrates that the *in vitro* functional activity of a Galaxy derived antibody is on par with clinical antibody Nivolumab. SPR affinity data (E) shows the on- and off-rates for a panel of IgG's, highlighting the improvement in affinity antibodies 2 & 3 over the parental antibody 1. Affinity-Capture Self-Interaction Nanoparticle Spectroscopy (AC-SINS) data (F) predicts self-association propensity. Our approach gives a choice of clones within each HCDR3 family so the most developable can be selected.



Properties of Antibodies from the Galaxy[®] Platform

Hits to a variety of target classes were produced as IgG1 (grey). The expression yields (G) and percentage monomer fraction (H) were compared to antibodies in the clinic (orange). We also carried out an *in silico* developability analysis (I) using the Therapeutic Antibody Profiler (TAP) software (Raybould M *et al.* 2019). A large proportion of antibodies, straight out of the Galaxy[®] platform, have properties comparable to clinical stage antibody therapeutics (CST).



Summary

Our whole process is built around the principle of 'right first time', efficiently delivering high quality biologics with drug-like properties. ProsaRx extends our service to provide computer aided drug discovery that incorporates AI/ML. With our parent company RxCelerate we are able to support an entire drug programme, small molecule, protein or antibody, from concept to clinic.

