

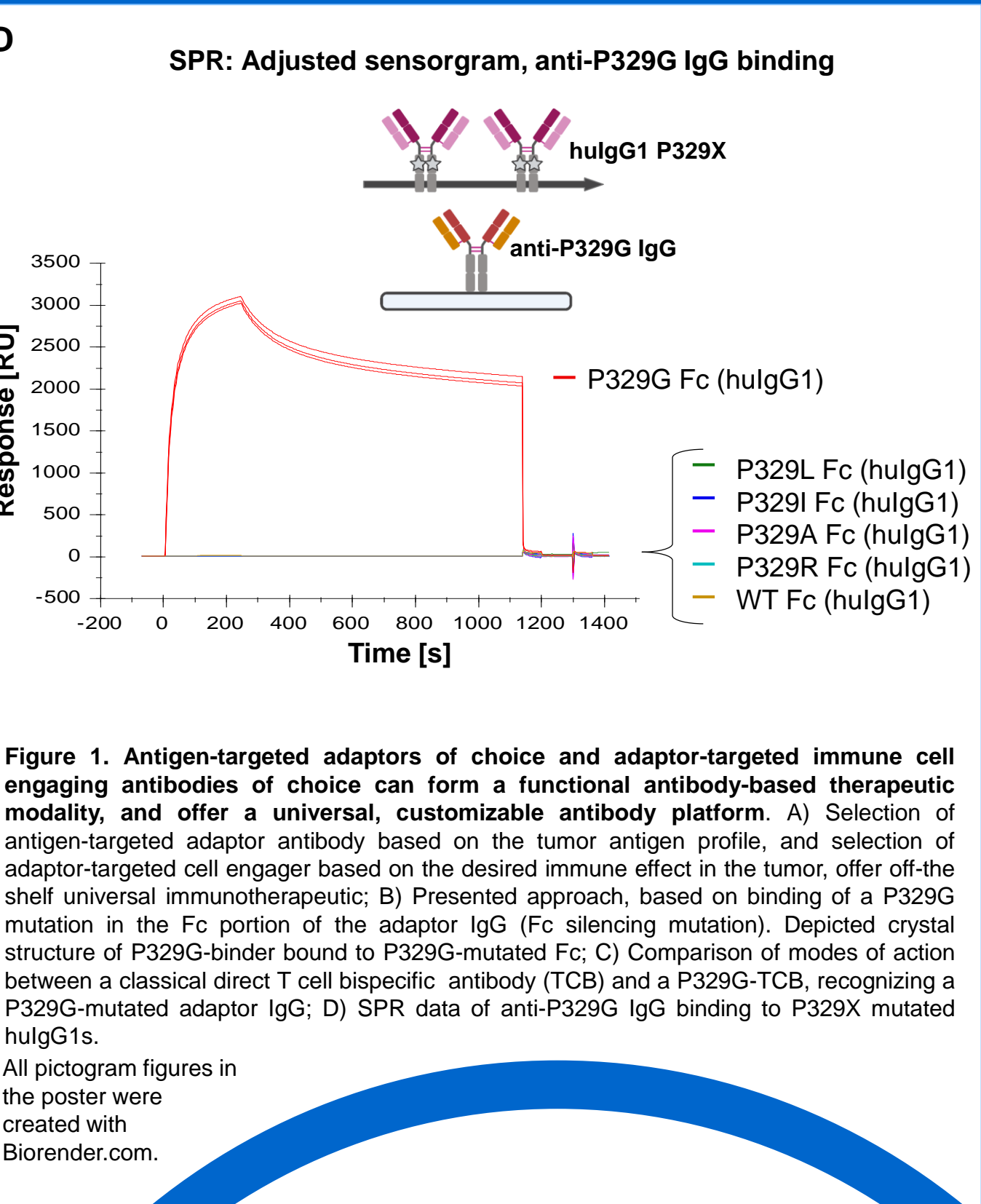
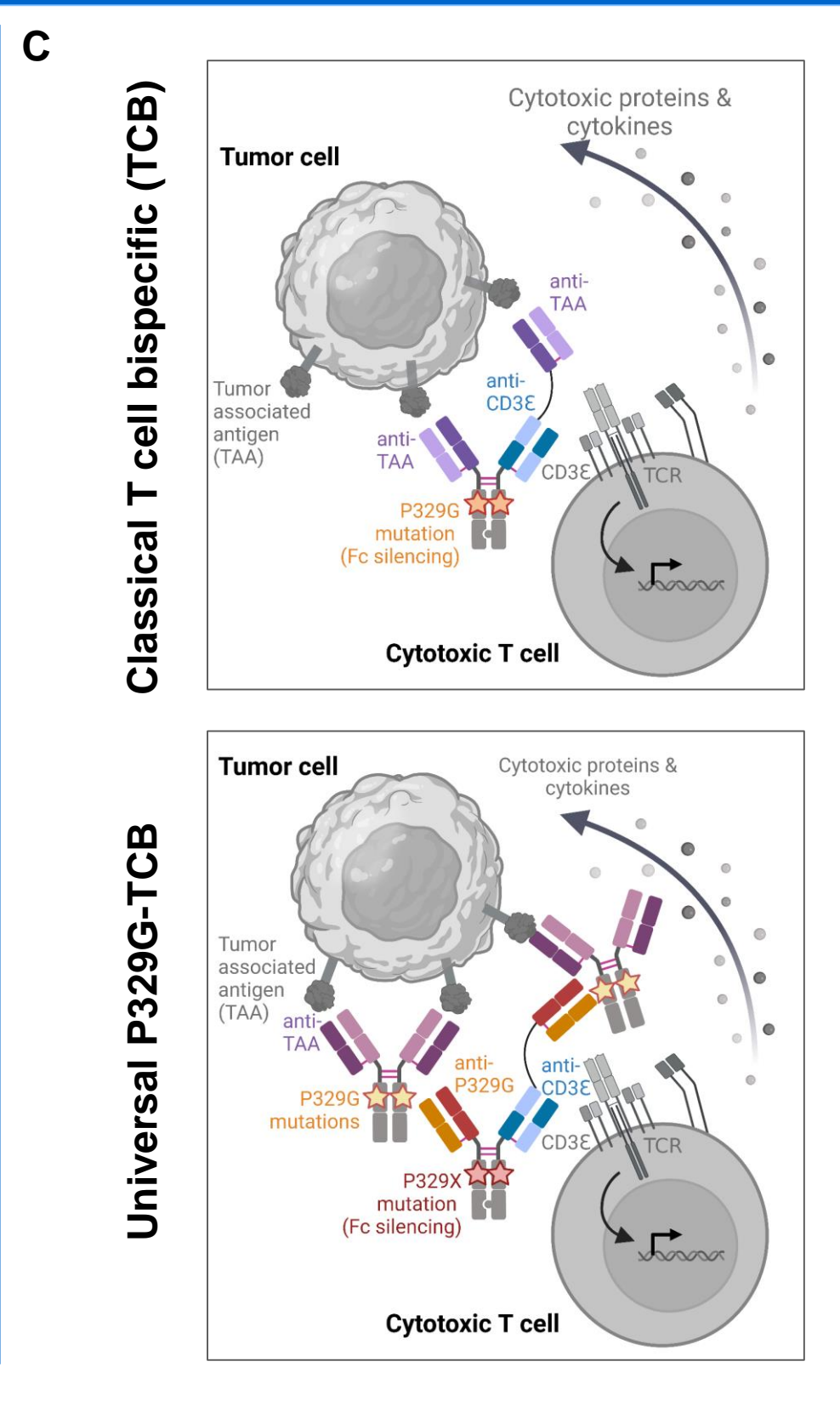
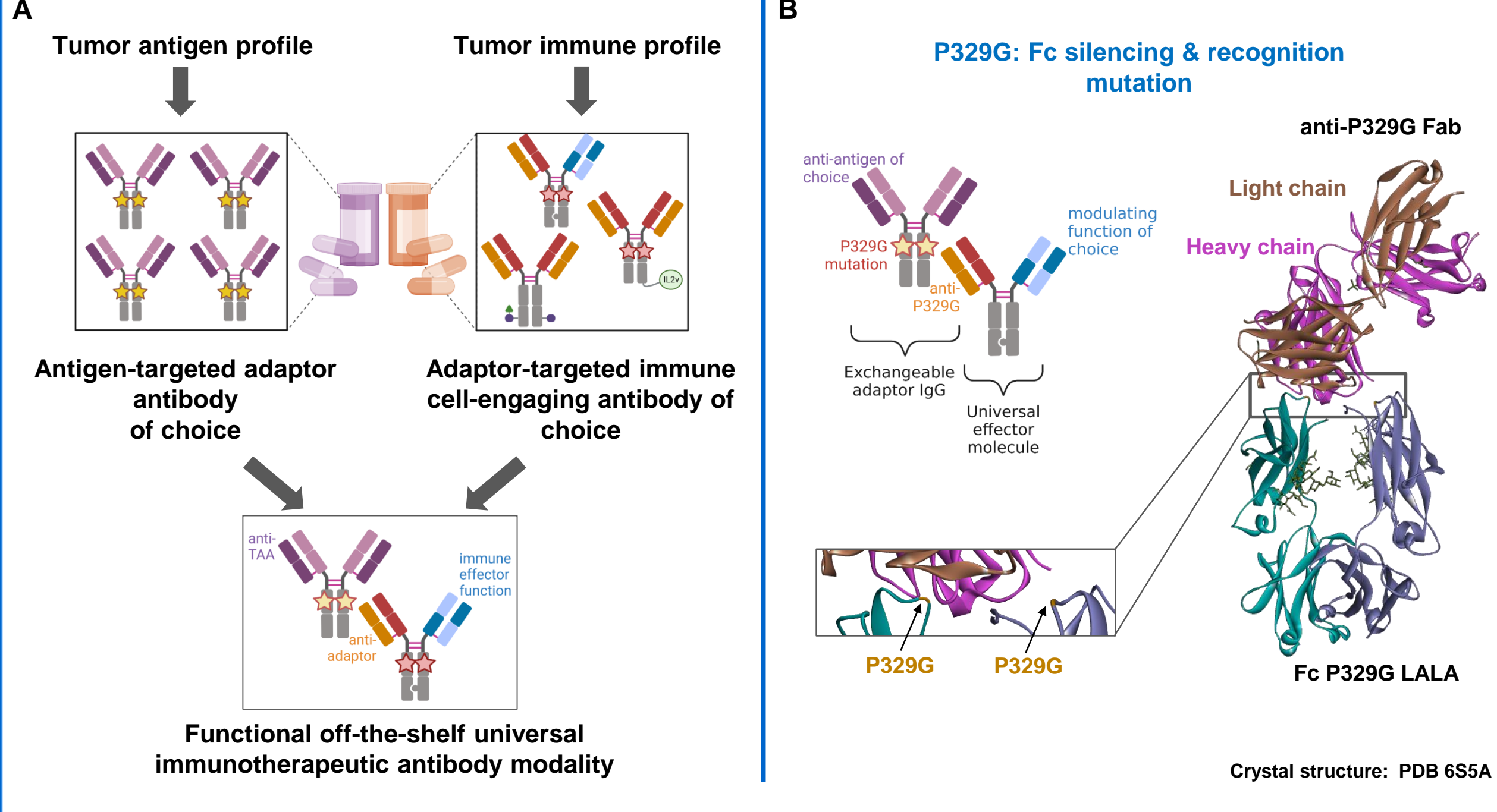
P329G-Engager: A Novel Universal Antibody-based Adaptor Platform For Cancer Immunotherapy

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1 – Universal anti-P329G antibody platform for cancer immunotherapy



2 – P329G immune cell engagers with various MoA show in vitro efficacy

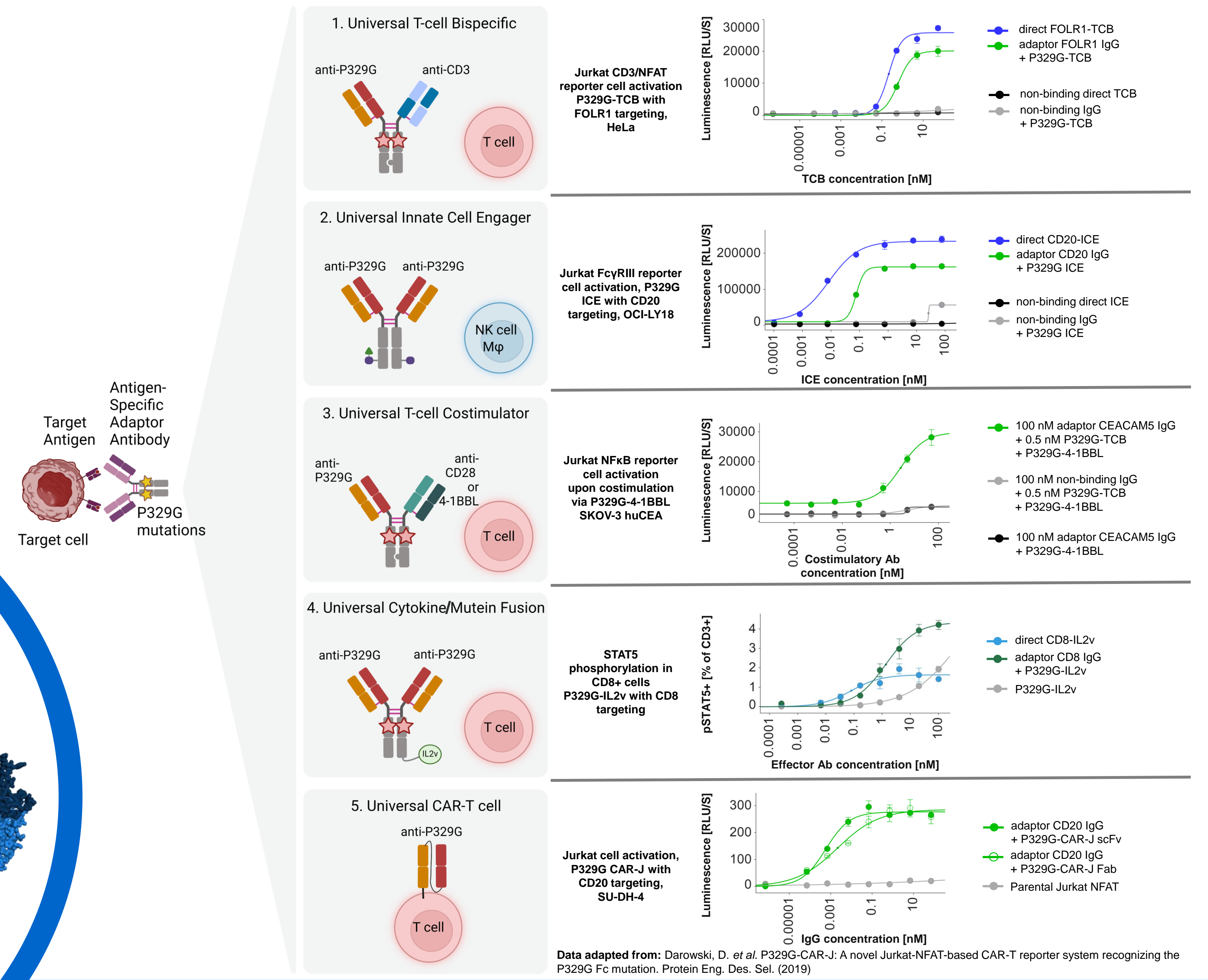
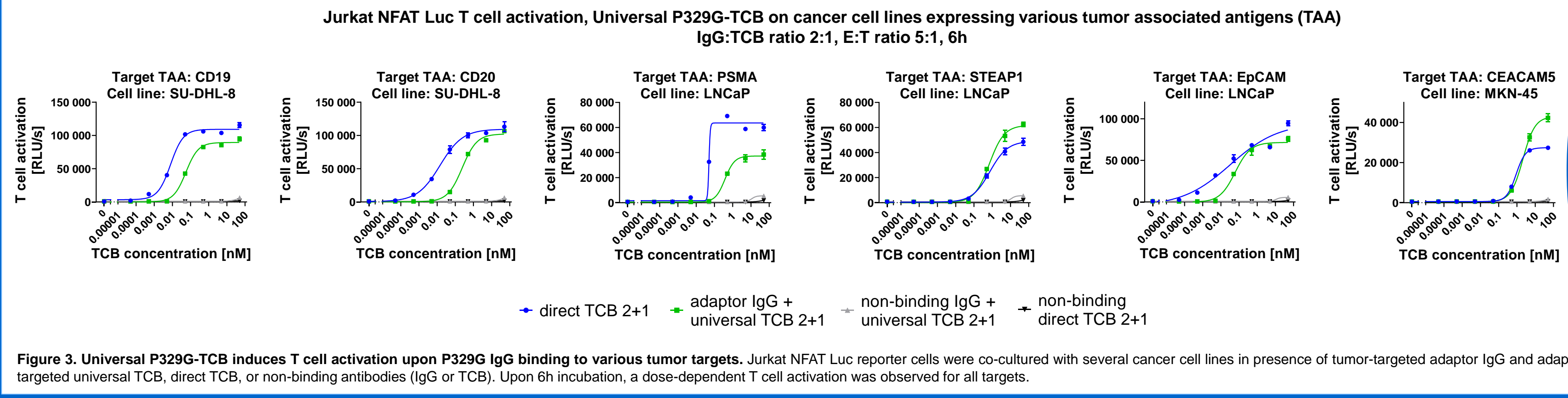
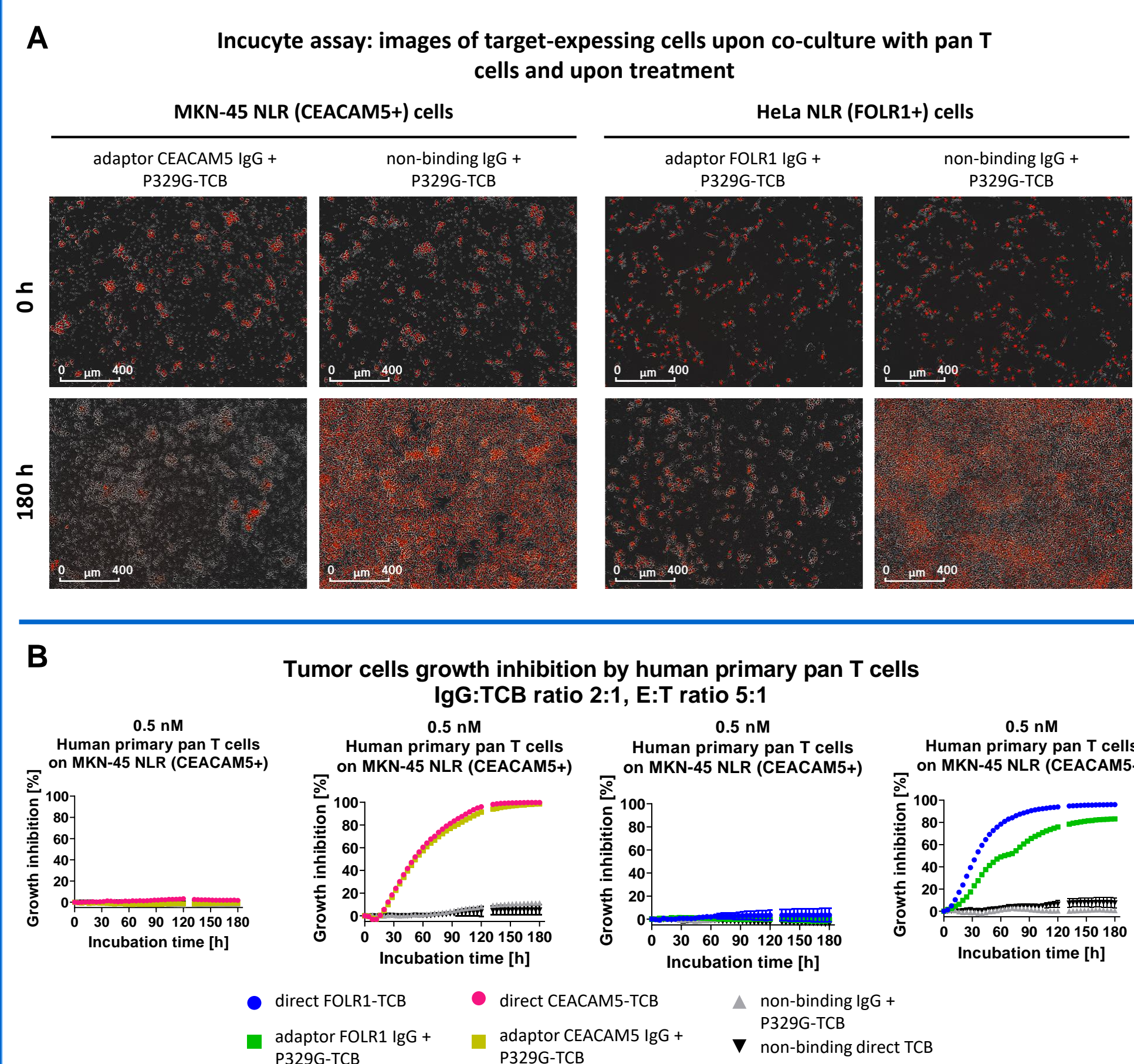


Figure 2. Various tumor/antigen-targeted P329G-mutated adaptor IgGs can be recognized by a range of P329G-Engagers with various modes of action. P329G-T Cell Bispecific (TCB), P329G-Innate Cell Engager (ICE), P329G-Costimulator CD28, P329G-IL2v, Immucytokine and P329G-Chimeric Antigen Receptor Jurkat cells (CAR-J) all show dose-dependent efficacy in assays relevant to their respective mode of action.

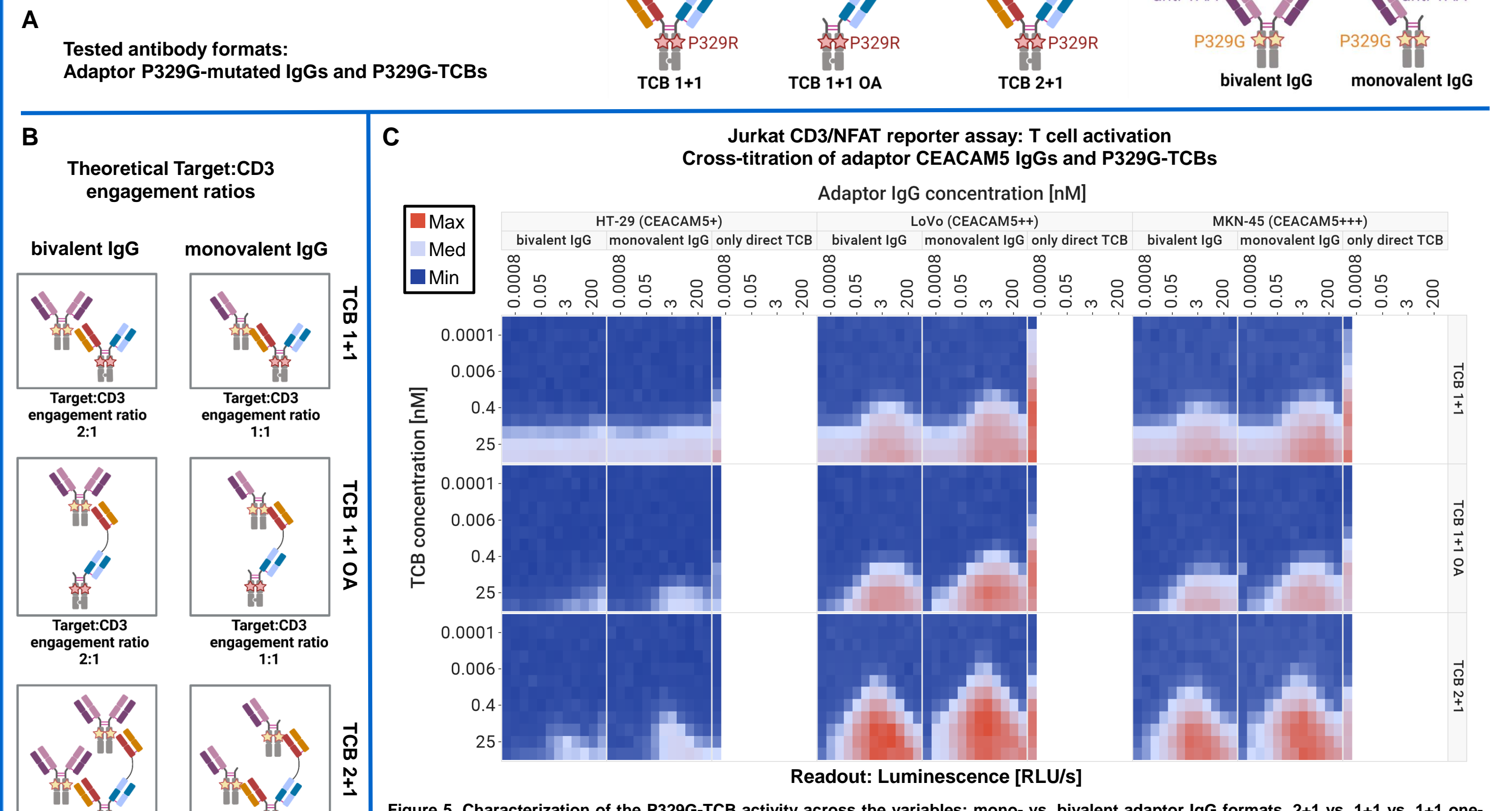
3 – Universal P329G-TCB induces T cell-tumor crosslinking across a set of tumor associated antigens



4 – Universal P329G-TCB induces primary T cell-mediated tumor cell lysis



5 – Universal P329G-TCB shows activity across the following: adaptor antibody format, TCB format, antigen expression level



6 – Universal P329G-TCB has antitumoral activity in vivo in tumor-bearing humanized NSG mice with limited T cell infiltration

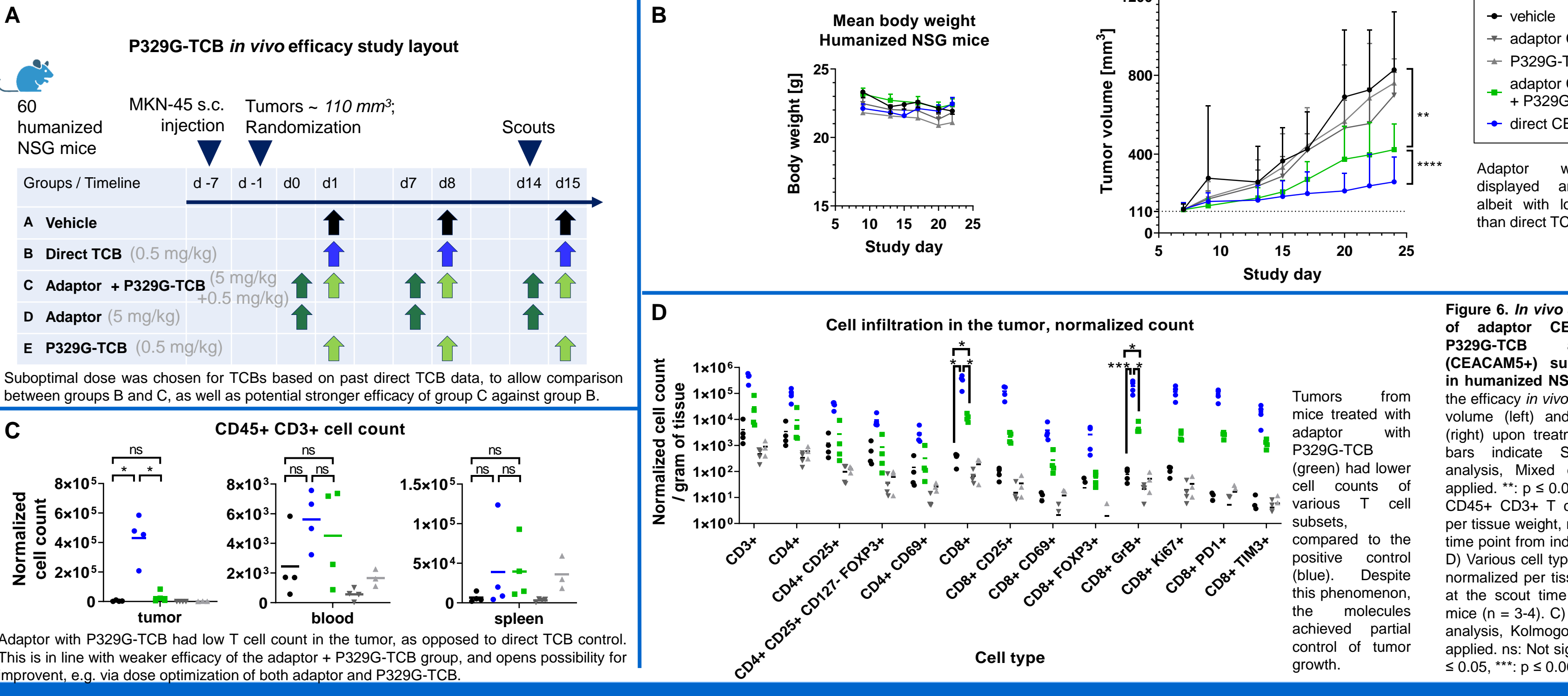


Figure 6. In vivo anti-tumoral efficacy of adaptor CEACAM5 IgG with P329G-TCB against MKN-45 (CEACAM5+) subcutaneous tumors in humanized NSG mice. (A) Details of the efficacy in vivo study. (B) Mean tumor volume (left) and mean body weight (right) upon treatment over time. Error bars indicate SEM. For statistical analysis, Mixed effects analysis was applied. **; p < 0.01, ****; p < 0.0001. (C) CD45+ CD3+ T cell count, normalized per tissue weight, measured at the scout time point from individual mice (n = 3-4). (D) Various cell type counts in the tumor, normalized per tissue weight, measured at the scout time point from individual mice (n = 3-4). For statistical analysis, Kolmogorov-Smirnov test was applied. ns: Not significant, p > 0.05, **; p < 0.05, ****; p < 0.001.

7 – Key takeaways

- ✓ The novel P329G-Engager utilizes recognition of an Fc mutation with P329G-specific binding, with abolished binding to Fc with single amino acid difference: WT Fc or P329L, P329I, P329A, P329R mutations.
- ✓ Universal P329G-Engager platform can be utilized for a wide array of solid and hematological tumor antigens, as well as immune targets, including CD3ε, FcγRIII, 4-1BB, IL2Rβγ.
- ✓ Universal P329G-TCB with the CEACAM5 P329G-mutated adaptor are active in a wide range of relative ratios/concentrations in vitro.
- ✓ Universal P329G-TCB displays antitumoral efficacy in tumor-bearing humanized NSG mice, despite low T cell infiltration.
- ✓ Further optimization adaptor and TCB concentrations for in vivo use is warranted, and may lead to improved T cell infiltration and efficacy.