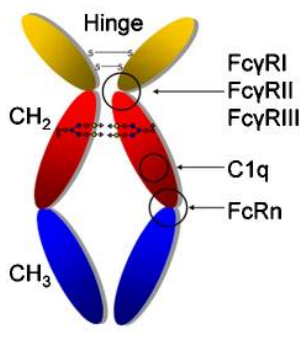


E-CLONALS – FC ENGINEERED AGLYCOSYLATED ANTIBODIES

The most accepted way to increase clinical potential of an antibody is by modulating effector function. Engineering the Fc region is one approach for identifying antibodies with novel effector function. Dr. George Georgiou with laboratories at the University of Texas, Austin, and an investigator for the Clayton Foundation for Research, has turned to *E.coli* to develop a platform that provides the possibility of fine-tuning the Fc region of an IgG antibody.

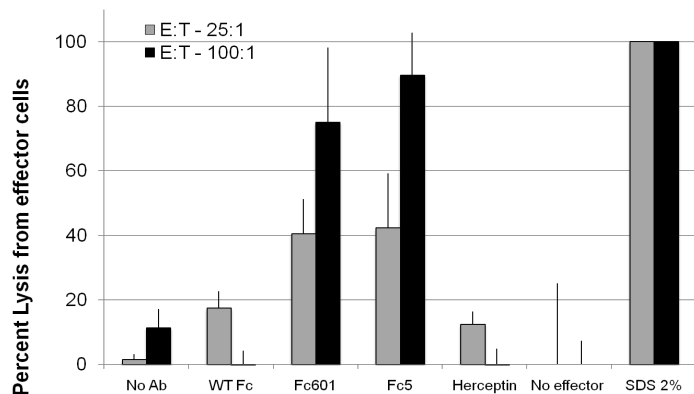
Aglycosylated IgGs represent an attractive new generation of antibodies with four successfully advancing in clinical trials. Aglycosylated antibodies circumvent the problem of glycan heterogeneity that complicates process development. Aglycosylated antibodies cannot bind to Fc receptors and therefore are normally devoid of effector factors and unable to mediate the killing of target cells. Using protein engineering, Georgiou and coworkers have engineered the Fc domain to bind to a specific Fc receptor. Because of the higher flexibility of aglycosylated Fc domains, it is possible to introduce amino acid mutations that stabilize a specific conformer that binds selectively to a particular activating Fc γ receptor and not to the homologous, inhibitory Fc γ RIIb. The result is an antibody with selective enhancement of a therapeutic effector function that is tailored to meet specific clinical needs.



Advantages of the Eclonal Fc Engineering Platform

- Ease of large-scale manipulation at low costs of *E.coli* to engineer the Fc region of IgG antibodies
- Customized Fc engineering to increase or decrease a specific effector function
- No glycan heterogeneity since antibodies are aglycosylated
- Ideal for the generation of biobetters and life cycle management

- Novel mutations induce conformation in aglycosylated antibodies that lead to enhanced effector function for selective binding to one or more activating Fc receptor.
- Technology deploys iterative screening rounds of libraries >10e9 Fc domain variants using *E. coli* display and FACS and therefore can be used to engineer Fc region for increased or decreased binding to any given Fc receptor.
- Engineered, aglycosylated Trastuzumab (Herceptin) binds to Fc γ RI with high affinity and selectivity.
- Engineered aglycosylated variants that display 18 fold higher affinity for the activating Fc γ RIIa receptor over the inhibitory receptor Fc γ RIIb
- Engineered aglycosylated Herceptin (variants Fc601 and Fc5, see below) but not clinical grade Herceptin



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Biotechnol Bioeng. 2010 Sep 1;107(1):21-30.

US patent applications numbers: 12/112971 and 12/827386 and international applications.

Available for licensing or partnering

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