

Improving Stability and Secretion of Antibodies

Reference No: B73076



CHALLENGE

The constant domain of the antibody light chain (C_L) is essential for both folding of the heavy chain C_H1 domain and consequently also for quality control of correct antibody assembly. Since the C_H1 domain can only adopt its native conformation after association with the C_L domain, alterations in C_L may have an impact on the efficiency of assembly and secretion of antibodies.

INNOVATION

The present invention improves the biophysical properties of antibodies and results in a **strongly increased secretion**. Following the stabilizing structural elements of shark antibodies, the C_L domain is modified by a conservative exchange of amino acids at two positions. This leads to the formation of an internal salt bridge and an extended hydrophobic core. Compared to the wild type C_L , the melting point of the modified C_L domain is almost **10°C higher** and its **stability against urea-induced denaturation** is also **markedly increased** (see Figure below).

Notably, when light chains comprising this optimized C_L domain were co-expressed with Ig heavy chains, a significant increase in the assembly and subsequent secretion of complete IgG antibody molecules from mammalian cells was observed. Although this technology was established using IgG, it is applicable to all classes of antibodies because of the ubiquitous presence of C_L in all immunoglobulin classes. Furthermore, this invention will also be applicable for the optimization of other constant domains besides C_L .

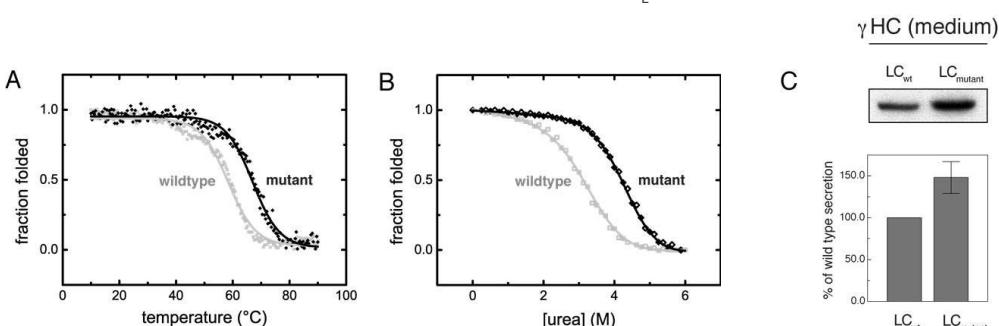


Figure A: Thermal stability of the human wild type κC_L domain (grey) in comparison to the optimized mutant (black). The mutant's melting point is almost 10°C higher; **B:** Chemical stability against urea of the human wild type κC_L domain (grey) in comparison to the optimized mutant (black); **C:** Influence of the optimized C_L domain in the context of a human light chain (LC_{mutant}) on the secretion of human γ heavy chains from COS cells (increase by approx. 50%).

COMMERCIAL OPPORTUNITIES

Antibodies with significantly higher stability and strongly increased secretion.

DEVELOPMENT STATUS

Proof of concept *in vitro*.



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REFERENCE:

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