Isolation and characterization of novel phage displayed scFvantibody for human tumor necrosis factor alpha and molecular docking analysis of their interactions

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Abstract:

Introduction:

Tumor necrosis factor alpha (TNF-α) expression amplifies to excess amounts in several disorders such as rheumatoid arthritis and psoriasis. Although, Anti-TNF biologics have revolutionized the treatment of these autoimmune diseases, formation of anti-drug antibodies (ADA) has dramatically affected their use. The next generation antibodies (e.g. Fab, scFv) have not only reduced resulted immunogenicity, but also proved several benefits including better tumor penetration and more rapid blood clearance.This study highlights the use of phage display for identification of human single chain fragment antibody against disulfide-bonded TNF-α using phage display technology.

Methods and Results:

Using affinity selection procedures in this study, a scFv antibody clone was isolated from naïve Tomlinson I phage display library that specifically recognizes and binds to TNF-α. The TNF-α recombinant protein was expressed in genetically engineered Escherichia coli SHuffle® T7 Express, for the first time, which is able to express disulfide-bonded recombinant proteins into their correctly folded states.

Conclusions:

ELISA-based affinity characterization results indicated that the isolated novel 29.2 kDa scFv binds TNF-α with suitable affinity. *In silico* homology modeling study using 'ModWeb' as well as molecular docking study using Hex program confirmed the scFv and TNF-α interactions with a scFv-TNF- α binding energy of around -593 kj/mol which is well in agreement with our ELSIA results. The cloned scFv antibody may potentially be useful for research and therapeutic applications in the future.

Key words:

Homology modeling, Molecular docking, Phage display, SHuffle® T7 Express, Single chain variable fragment (scFv), Tumor necrosis factor alpha.

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