

High affinity mouse-human chimeric Fab against hepatitis B surface antigen.

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Abstract

AIM: Passive immunotherapy using antibody against hepatitis B surface antigen (HBsAg) has been advocated in certain cases of Hepatitis B infection. We had earlier reported on the cloning and expression of a high affinity scFv derived from a mouse monoclonal (5S) against HBsAg. However this mouse antibody cannot be used for therapeutic purposes as it may elicit anti-mouse immune responses. Chimerization by replacing mouse constant domains with human ones can reduce the immunogenicity of this antibody. METHODS: We cloned the V(H) and V(L) genes of this mouse antibody, and fused them with CH1 domain of human IgG1 and C(L) domain of human kappa chain respectively. These chimeric genes were cloned into a phagemid vector. After initial screening using the phage display system, the chimeric Fab was expressed in soluble form in E. coli. RESULTS: The chimeric Fab was purified from the bacterial periplasmic extract. We characterized the chimeric Fab using several in vitro techniques and it was observed that the chimeric molecule retained the high affinity and specificity of the original mouse monoclonal. This chimeric antibody fragment was further expressed in different strains of E. coli to increase the yield. CONCLUSION: We have generated a mouse-human chimeric Fab against HBsAg without any significant loss in binding and epitope specificity. This chimeric Fab fragment can be further modified to generate a full-length chimeric antibody for therapeutic uses.