ANTITHROMBOTIC DRUGS

NEXT-GENERATION THROMBOLYTICS: ENGINEERING STREPTOKINASE FOR ENHANCED ACTIVITY AND REDUCED IMMUNOGENICITY

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Introduction. Streptokinase (SK) is a widely used thrombolytic agent, but its clinical utility is limited due to its high immunogenicity, which results in rapid inactivation by antibodies. This study aimed to engineer a truncated variant of streptokinase to reduce its immunogenicity while maintaining its fibrinolytic activity.

Aim. The primary objective was to reduce the immunogenicity of streptokinase through selective truncation of its C-terminal antigenic segment, and to assess whether this modification could preserve its fibrinolytic activity.

Materials and Methods. A PCR-based truncation strategy was used to remove a C-terminal segment (residues 353–414) of streptokinase. The truncated gene was subcloned into a bacterial expression vector and expressed in Escherichia coli. The protein was purified, and its fibrinolytic activity was evaluated using plasminogen activation and fibrin clot-dissolution assays. Antibody binding was assessed using human sera to measure the reduction in immunogenicity.

Results. The truncated streptokinase variant exhibited a significant reduction in antibody binding, indicating a decrease in immunogenic epitopes associated with the C-terminal region. Despite the truncation, the engineered variant retained robust plasminogen activation activity and effectively dissolved fibrin clots, comparable to the native streptokinase.

Conclusions. C-terminal truncation of streptokinase represents a promising strategy for reducing immunogenicity without compromising therapeutic efficacy. This engineered variant could offer a safer, more effective alternative for thrombolytic therapy, with reduced immunogenic responses and retained fibrinolytic activity, making it a potential candidate for clinical use.