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ORIGINAL RESEARCH PAPER

# High-level expression of functional recombinant human coagulation factor VII in insect cells

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**Abstract** Recombinant coagulation factor VII (FVII) is used as a potential therapeutic intervention in hemophilia patients who produce antibodies against the coagulation factors. Mammalian cell lines provide low levels of expression, however, the *Spodoptera frugiperda* Sf9 cell line and baculovirus expression system are powerful systems for high-level expression of recombinant proteins, but due to the lack of endogenous vitamin K-dependent carboxylase,

expression of functional FVII using this system is impossible. In the present study, we report a simple but versatile method to overcome the defect for high-level expression of the functional recombinant coagulation FVII in Sf9 cells. This method involves simultaneous expression of both human  $\gamma$ -carboxylase (hGC) and human FVII genes in the host. It may be possible to express other vitamin K-dependent coagulation factors using this method in the future.

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## Introduction

Bleeding and hemostatic problems in hemophilia A and B diseases can be treated with purified factor VIII and IX preparations obtained from plasma or produced by recombinant DNA technology. However, because of the generation of neutralizing antibodies against these factors which makes the management of bleeding episodes difficult in such patients, it is important to establish new treatment strategies (Shapiro et al. 1998).

Thus far, therapeutic interventions in these situations have included overcoming the inhibitors with large doses of factor VIII; however, this is only feasible when the inhibitor titer is relatively low (Maick 1993; Nillson et al. 1993). Other approaches have included the use of activated and non-activated