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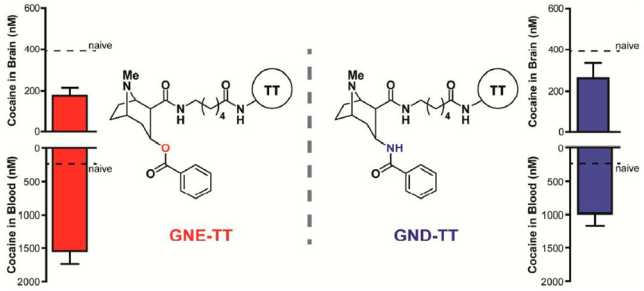
EFFICIENT SYNTHESES OF COCAINE VACCINES AND THEIR IN VIVO EVALUATION

Cocaine addiction and abuse remain major health and societal issues in the United States. Despite this, no therapeutic treatment for cocaine addiction is available and current interventions only address withdrawal symptoms interventions.

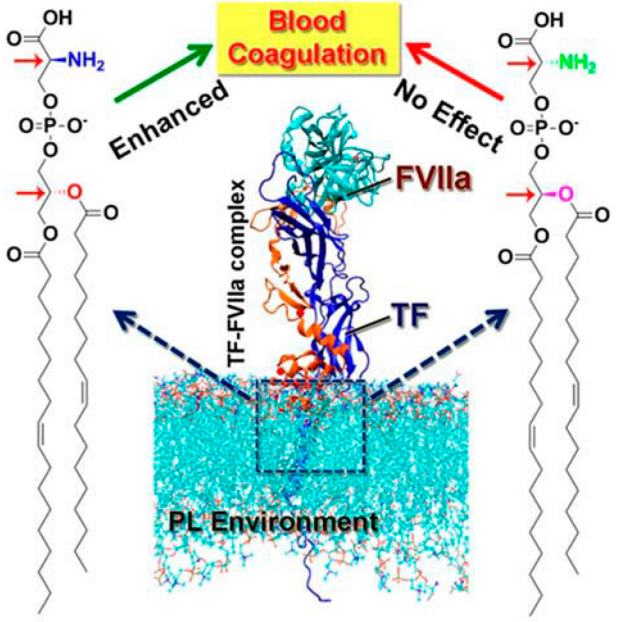
In this issue, Janda and colleagues (DOI: 10.1021/acsmedchemlett.8b00051) present the development and *in vivo* evaluation of two cocaine vaccines. Each vaccine consists of one of two hydrolytically stable haptens developed previously by the researchers, GND or GNE, conjugated to tetanus toxoid (TT) and formulated with alum and cytosine-guanine oligonucleotide (CpG ODN 1826) adjuvants. Both vaccines, termed GND-TT and GNE-TT, triggered the production of antibodies with high affinity for cocaine in mice, and these newly generated antibodies successfully blocked the stimulatory activity of cocaine. Biodistribution studies revealed the ability of GND-TT and GNE-TT to sequester free cocaine in the blood and to reduce the drug's concentration in the brain. These results suggest that GND- and GNE-TT conjugates are suitable for further preclinical development.



SYNTHESIS OF PHOSPHATIDYLSERINE AND ITS STEREOISOMERS: THEIR ROLE IN ACTIVATION OF BLOOD COAGULATION

Blood coagulation is initiated by the formation of a complex between a transmembrane protein called tissue factor (TF) and circulatory factor VIIa (FVIIa). Phosphatidylserine facilitates this process; however, the mechanism by which this occurs remains enigmatic. Herein, Mallik et al. (DOI: 10.1021/acsmedchemlett.8b00008) report the synthesis of all stereoisomers of phosphatidylserine (PS) using a novel synthetic method and subsequent studies of each phosphatidylserine isomer with circulatory factor VIIa and tissue factor TF. An assay involving recombinant FVIIa and full length TF present in a reconstituted membrane model revealed that the configuration of both the headgroup and the glycerol backbone of PS play a role in enhanced TF-FVIIa complex activity. The authors also performed molecular dynamics simulations and suggest that changes in chiral centers affect the interactions between the PS headgroups and glycerol backbone with TF and FVIIa.

This study thus provides new insights into structure−activity relationship and protein−lipid interactions in the blood coagulation.



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