

## **“Development of contact pathway inhibitors for the treatment of thrombotic diseases”**

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Mission Statement: Our goal is to develop the final preliminary data in order to generate a competitive Program Project grant to the NHLBI focused on the translation of factor XII/factor XI contact pathway inhibitors for the treatment and prevention of thrombotic diseases.

### **Abstract:**

Thrombotic diseases remain the leading cause of morbidity and mortality in the US. While conventional anticoagulants are effective at both preventing and treating thrombosis, the potential for bleeding side effects limits their use or requires sub-optimal therapeutic dosing when bleeding risks are high. Consequently, a critical unmet medical need remains for a safe antithrombotic drug. Our goal is to develop contact pathway inhibitors that specifically target pathological thrombus formation while preserving hemostatic mechanisms. Our team has demonstrated that pathological activation of the FXII/FXI axis contributes to occlusive thrombus formation, inflammation, and circulatory changes in rodent and primate models of thrombosis, stroke and sepsis. We hypothesize that the FXII/FXI axis represents a promising antithrombotic drug target. We have generated a set of unique neutralizing monoclonal antibodies against the FXII/FXI axis. Our promising preliminary data provide a rationale for the development of a novel class of safe anticoagulants targeting contact activation. Our program is designed to develop these inhibitors for the prevention of thrombus formation in medical devices and prevention of pathological thrombus formation in the macro- and micro-circulation.