Novel Ligands of Prothrombin as Inhibitors of Blood and Extravascular Coagulation

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Technology description

Pathological activation of the coagulation cascade leads to the generation of blood clots which can travel in the circulation and restrict blood flow causing heart attacks and strokes. Numerous pharmaceutical approaches to inhibiting the clotting cascade are associated with an increased risk of bleeding and/or rebound hypercoagulation when therapy is stopped. We have taken two approaches to develop safer anticoagulants by targeting the local sites of pathogenic thrombin generation resulting from vascular or tissue injury.
In the first approach, new divalent VH-domain proteins were designed to target membrane-bound prothrombin as locally active inhibitors of thrombin generation.
In the second approach, a new generation of bivalent direct thrombin inhibitors (DTIs) was endowed with functionalities to home to the physicochemical characteristics of atherosclerotic vasculatures and inflamed tissues. These site-specific inhibitors of thrombin would avoid excessive bleeding side effects of systemic anticoagulants and provide a safer alternative to current therapies

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