Controlling coagulation with aptamer combinations and aptamer-drug combinations and their antidotes

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Value Proposition

Millions of Americans have received anticoagulative agents to prevent pathological blood clot formation (thrombosis). For decades, warfarin and heparin have been the centerpiece of anticoagulative treatment. In the past decade, new anticoagulative agents have entered the market, which target a variety of factors involved in the coagulation process. However, both the mainstay and new agents continue to pose a significant risk to patients since they increase the risk of bleeding and have no antidote to rapidly reverse function. In the context of surgery, anticoagulative therapy can thus lead to high-risk perioperative haemorrhage. Thus, there is a need for novel anticoagulative agents that are efficacious and rapidly reversible.

Technology

Aptamers, or single-stranded oligonucleotides, are nucleic acid ligands that bind specifically to their therapeutic targets with high affinity. In this invention, multiple aptamers targeting different proteins involved in blood clot formation are shown to effectively control blood clot formation in combination or alone. Specifically, the inventors developed aptamers against the clotting factors FVIIa, FIXa, FXa, and prothrombin and tested their anticoagulative effect in an *in-vitro* clinical clotting assay. Furthermore, the inventors developed antidotes for these aptamers that enable rapid inactivation of the therapeutic agents, making it possible to fine-tune the clotting effect . Thus, the use of combinatorial coagulative protein inhibitors described in this invention could provide patients with necessary efficacious agents to control thrombosis while also providing for a unique way to reverse the clinical effects using antidotes.

Advantages

Clinical treatment of inappropriate thrombin generation, or thrombosis, must be adapted to fit the precise clinical indication and there is thus debate regarding the optimal therapeutic target. Furthermore, current anticoagulative therapy cannot easily be reversed. In contrast, the aptamer technology presented here can reversibly target multiple therapeutic targets and has a number of advantages:

1. Rapid onset anticoagulation: Combinatorial targeting of proteins in the coagulation pathway using multiple or singular aptamers is an effective, rapid, and novel

anticoagulation approach.
2. Selective and specific binding to therapeutic targets: Aptamers have a high affinity for their target which improves bio-distribution and makes it feasible to use lower concentrations of drug
3. Rapid reversibility: Antidotes to an efficacious aptamer allow for the fine-tuning of clinical response and can quickly abrogate the clinical effect if medically necessary.

Publications

- Website

Patents

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