

## Aptamers to Glycoprotein VI

### Duke File (IDF) Number

IDF #:T-003465

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### Value Proposition

Millions of Americans have received antiplatelet agents to prevent pathological blood clot formation (thrombosis). Platelets are the key prothrombotic element, forming aggregates that lead to blood clots. Antiplatelet therapies can counteract this process. However, current agents pose a significant risk to patients as they increase the risk of bleeding, especially in high-risk surgery, and have no antidote to rapidly reverse function. The platelet glycoprotein VI (GPVI) is a platelet membrane protein that participates in platelet adhesion and aggregation. Blocking of GPVI may be able to prevent blood clot formation without increasing the risk of bleeding, making it an ideal drug target.

### Technology

Ribonucleic acid ligands, or aptamers, are a class of drugs that are ideal for blocking GPVI. Using the SELEX methodology, the inventors generated multiple high affinity aptamers against GPVI from a pool of modified RNA sequences. The aptamers were tested in a platelet functionality assay (PFA-100) which measures time until platelet plug formation *in vitro*. The novel aptamers developed in this invention are able to selectively and specifically bind GPVI and may therefore prevent or treat thrombosis. Furthermore, the inventors engineered inactivating aptamers that control GPVI aptamer activity, making it possible to fine-tune the clinical effect in patients.

### Advantages

Current anti-coagulative therapy results in an increased risk of bleeding and the clinical effect cannot easily be reversed. In contrast, the aptamer technology presented here has a number of advantages:

- Decreased risk of bleeding: targeting of GPVI is an effective anticoagulation approach that may decrease the risk of bleeding that is common in therapeutics currently in use.
- Selective and specific binding of GPVI: Aptamers have a high affinity for their target which improves bio-distribution and makes it feasible to use lower concentrations of drug
- Rapid reversibility: Antidotes to the efficacious aptamers developed against GPVI allow for the fine-tuning of clinical response and can quickly abrogate the clinical effect if medically necessary.

