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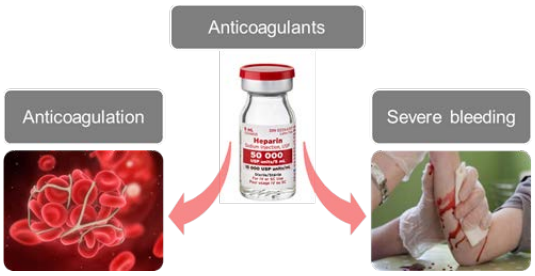
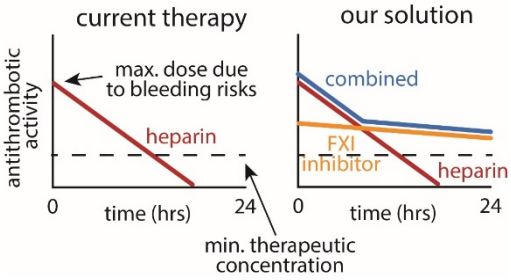
Licensing Opportunity

TTO – Technology Transfer Office

Potent peptide-based coagulation factor XI inhibitors for improved thrombosis prevention





Cyclic peptide-based coagulation factor XI (FXI) inhibitors offer a more efficacious anticoagulation strategy. Classic anticoagulants (e.g. heparin and vitamin K antagonists) carry a high risk of severe bleeding, a life-threatening condition. This translates into an extremely narrow therapeutic window, which leads to events of suboptimal treatment. FXI has been recently identified as an ideal target for thrombosis prevention without bleeding side effects. Our potent FXI-targeting peptides present an optimal PK profile, which would allow for combination with established anticoagulants such as heparin. This can lead to a strong increase in efficacy without compromising the safety profile.

Ref. Nr

6.2051

Keywords

Thrombotic diseases, anticoagulation, venous thromboembolism, cyclic peptides, safer drugs.

Intellectual Property

Patent application n. EP 20 15 3848.5

Publications

EPFL Thesis n. 7223

Date

07/09/2020

Description

Thrombotic diseases are the leading cause of death worldwide. Anticoagulants are widely used for reducing the risk of thrombosis. The limitation of all existing anticoagulant drugs is that they have a narrow therapeutic window due to bleeding side effects and that the highest applied doses do not fully suppress thrombosis. For example, after knee replacement surgery, up to 35% of patients experience venous thrombosis despite the use of anticoagulant drugs.

Research in the last 10 years has featured coagulation factor XI (FXI) as a novel antithrombotic target. In contrast to other anticoagulation targets found downstream in the cascade (thrombin, FX), inhibition of FXI does not increase the risk of bleeding, and this property has raised a great deal of interest in the pharmaceutical industry.

At EPFL, we have developed potent and selective peptide-based FXI inhibitors and demonstrated anticoagulation activity *in vivo*. The absence of bleeding side effects and the tailored pharmacokinetic properties allow the inhibitors to be combined with established anticoagulants, such as heparin. This would ensure anticoagulation activity in case heparin falls below therapeutic concentrations.

Advantages

Our peptides are characterized by:

- High potency (K_i = 4 nM) and selectivity
- Strong anticoagulation *ex vivo* in plasma (aPTT EC_{2x} = 1.5 μM) and in whole blood, and *in vivo* in rabbits
- Optimal PK properties (once daily administration, ideal for combination with heparin)
- Low risk of toxicity derived from metabolic products
- Low risk of immunogenic responses
- Cost-effective manufacturing

Applications

Further development as:

- In combination with heparin: therapy with superior efficacy for thrombosis prevention after major surgeries
- Safer anticoagulant in the context of hemodialysis

Offering

We are looking for a partner with experience in the field (licensing) for the further development of the molecules into a more efficacious and safer anticoagulation therapy.