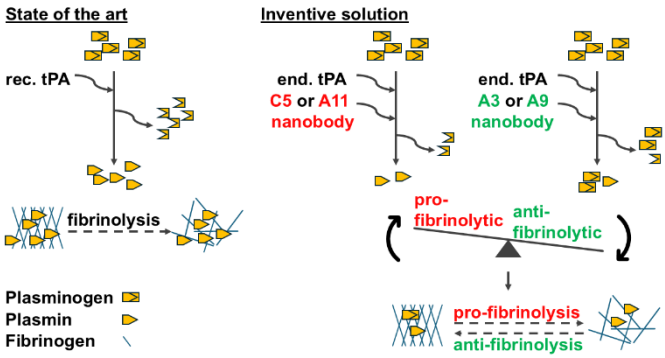
# Bidirectional Nanobody System For Fibrinolysis

## The precise and reversible control of thrombolytic activity

### Invention

Effective and timely recanalization of thrombosed vessels is critical for patient survival and for minimizing long-term impairments following myocardial infarctions, ischemic strokes, or pulmonary embolisms. Systemic fibrinolytic therapy using plasminogen activators (e.g., recombinant tPA or uPA) is the pharmacological state of the art, aiming to enzymatically degrade fibrin, the structural backbone of thrombi. However, current therapies require supraphysiological dosages to be effective, leading to major bleeding complications and exhibit neurotoxic and immunogenic side effects. Thus, there is a medical need for fibrinolytic treatments that offer improved clot dissolution efficacy with a lower risk of bleeding and enhanced control over treatment duration and intensity. Ideal therapeutic agents would permit dynamic modulation of fibrinolytic activity in emergency settings to maximize benefit and minimize harm.




Schematic overview of the bidirectional nanobody system for controlled fibrinolysis

The invention introduces a novel system of dual-functioning nanobodies, designed to enable precise and reversible control of thrombolytic activity. Derived from immunized alpacas, two potent pro-fibrinolytic nanobodies (A11 and C5) were developed. These bind allosterically to plasminogen/plasmin and enhance the activation of plasminogen by tPA/uPA in a dose-dependent manner, significantly accelerating clot lysis in both plasma and whole blood in vitro models – closely simulating in vivo thrombolysis.
Crucially, two anti-fibrinolytic nanobodies (A3 and A9) were also isolated. These effectively inhibit plasminogen activation by allosteric binding and therefore act as anti-fibrinolytics, also in terms of being functional antidotes to the pro-fibrinolytic nanobodies. This feature introduces a unique safety mechanism, allowing immediate and controlled cessation of fibrinolysis in the event of bleeding complications.

### Commercial Opportunities

On behalf of the Rheinische Friedrich-Wilhelms-Universität Bonn, PROvendis offers an access to rights for product development and commercial use of the invention including the C5, A11, A3 and A9 nanobodies.

### Current Status

- binding characteristics towards plasminogen / plasmin and related enzymes such as t-PA, epitope characterization
- influence on the catalytic function of plasmin with small substrates including Michaelis-Menten kinetics
- fibrinolysis studies in plasma and whole blood
- influence on plasmin-mediated cytotoxicity
- influence on in-vitro clot lysis
- generation and functional evaluation of homo- and heterodimeric nanobody variants

### Relevant Publications

Patent applications are pending:
US 2025/0179215, CA 3250857 and EP 4519325 (C5 and A11)
Unpublished application (A3 and A9)

An invention from the University of Bonn.

### Advantages

- Allosteric modulation of plasmin activity
- Targeted, dose-controllable thrombolysis
- Lower bleeding risk
- Reversible therapeutic effect

### Technology Readiness Level

1 2 3 4 **5** 6 7 8 9

Technology validated in relevant environment

### Sector(s)

- pharmaceutical industry

### Ref.-No.

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