Towards hemocompatible surfaces: Interactive coating directs blood to fight against thrombi

Lena Witzdam[1,2,3], Fabian Obstals[2,3], Manuela Garay-Sarmiento[2,4], Jonas Quandt[2,3], Nina Yu. Kostina[1], Oliver Grottke[5], Cesar Rodriguez-Emmenegger*[1,2,6]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain
[2] DWI – Leibniz Institute for Interactive Materials e.V., Aachen, Germany
[3] Institute of Technical and Macromolecular Chemistry, RWTH Aachen University, Aachen, Germany
[4] Chair of Biotechnology, RWTH Aachen University, Aachen, Germany
[5] Department of Anesthesiology, University Hospital of the RWTH Aachen University, Aachen, Germany
[6] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain
lwitzdam@ibecbarcelona.eu

The contact of blood with the artificial surface of medical devices inevitably causes the activation of coagulation leading to a number of serious complications. In nature, the lining of healthy endothelium is capable of sensing and maintaining a tightly regulated equilibrium, called hemostasis that prevents hemorrhages and excessive coagulation. In this work, we developed a coating system that mimics the fundamental hemostatic regulation exerted by endothelium. In its dormant state the coating is stealth to blood components and prevents activation of coagulation. However, the presence of a clot turn the coating into an active state in which it directs blood to digest the clot. The coating consists of ultra-low fouling poly(N-hydroxypropyl methacrylamide-co-carboxybetaine methacrylamide) brushes on which tissue plasminogen activator (tPA) is immobilized. We exploited the allosteric activation of tPA by fibrin clot as a positive feedback mechanism to reversibly switch the coating into its active state/dormant state, that coupled with an amplification mechanism, transformed sufficient amount of endogenous plasminogen into plasmin to locally digest fibrin clots. Impressively, the amplification mechanism allowed that only few nanograms of immobilized tPA could orchestrate the complete digestion of macroscopic clots while prohibiting the adhesion of blood components, molecules, and cells and displaying no cytotoxicity. We envision that the extremely low density of tPA required in this coating system and the safety of this approach make this strategy a promising route towards the improvement of the hemocompatibility of blood contacting medical devices.

References

[1] F. Obstals, L. Witzdam, M. Garay-Sarmiento, N. yu. Kostina, J. Quandt, S. Singh, O. Grottke, C. Rodriguez-Emmenegger, ACS Appl. Mater. Interfaces, 13 (2021) 11696-11707.

Figures

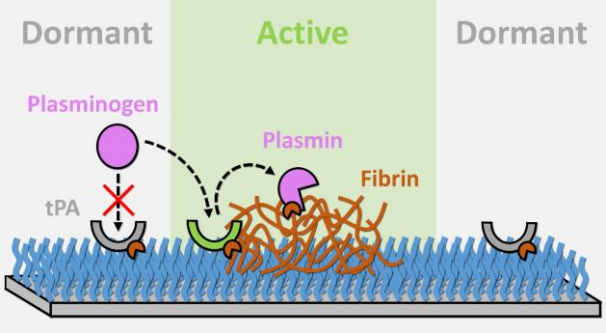

Figure 1. Fibrinolytic coating system developed in the present study. Polymer brushes are decorated with tPA. The coating can detect the presence of a fibrin clot by its binding to tPA. This lead to the activation of tPA and the fibrinolytic system. Afterwards tPA returns to its dormant state [1].