Core-to-Core Program

THE UNIVERSITY OF TOKYO

東京大学ナノバイオ国際研究教育拠点セミナー #01

C2CNB Seminar Series

International Core Research Center for NanoBio , The University of Tokyo

The role of platelets in activation of the complement and contact systems in thromboinflammation

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Date: Friday, February 14, 2014
Time: 14:00 - 15:00
Venue: #205 Seminar Room, Faculty of Engineering Bldg. 4, The University of Tokyo

Thromboinflammatory mechanisms are involved in a number of pathological conditions and therapeutic modalities e.g. ischemia reperfusion, cardiovascular disease, transplantation of whole organs and cells, extracorporeal treatments etc. Thromboinflammation can be induced both by direct activation of the coagulation system but also indirectly through activation of the complement system or by cells exposed to stress; mainly by expression of tissue factor. The complement system links thromboinflammation to the innate immune system.

It has become increasingly evident that the cascade systems of the blood such as the complement and coagulation systems interact at various levels in thromboinflammation, which has identified new targets for therapeutic intervention. Blood cells have been shown to mediate many of these interactions. For instance, platelets promote coagulation and do also activate the complement system by different mechanisms. Our work has in recent years been targeted on mechanisms and therapeutic regulation of thromboinflammation. Particularly the interaction between platelets and the contact system and the lectin pathway of complement has been the focus of these investigations, which involves studies in patients with trauma and cardiovascular disease.

In therapeutic medicine, biosurfaces (i.e., biomaterial and cell surfaces) inevitably come in contact with human blood and tissues and induce thromboinflammation. Examples of high clinical importance are biomaterial implants (e.g., heart valves, stents), extracorporeal circuits (e.g., in hemodialysis or cardiopulmonary bypass surgery), bioengineered devices (e.g. pumps or drug delivery vehicles), soft and hard tissue implants, whole organ transplants, and cell therapies. Such interactions frequently trigger activation of innate defense systems such as the complement, contact and coagulation cascades, which mediate thrombinflammation that negatively affect the clinical outcome.

Optimal tissue integration and modulation of foreign body reactions is therefore essential for preserving anticipated functions and avoiding adverse effects. We have studied and developed various modifications of biosurfaces and pharmaceutical interventions as viable strategies to avoid adverse reactions mediated by thromboinflammation. Among the strategies that we have used to protect material and cell surfaces are conjugation of biomolecules e.g. heparin and CD39, and peptides that have affinity for soluble regulators of the complement system e.g. factor H and C4BP. Combinations of these surface treatments provide an efficient protection of the biosurfaces against many aspects of thromboinflammation.

Organizer: International Core Research Center for NanoBio, The University of Tokyo

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