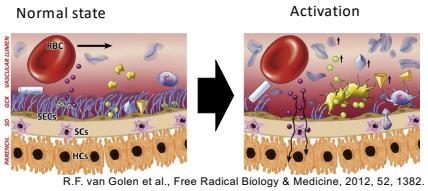
Cell surface modification with heparin-conjugated lipids for improving blood compatibility

Yuji Teramura[1] and Kazuhiko Ishihara[2]

[1]National Institute of Advanced Industrial Science and Technology (AIST), AIST Tsukuba Central 5, 1-1-1 Higashi, Tsukuba 305-8565, Japan,
[2]Department of Materials Engineering, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

Introduction

Ischemia-reperfusion (I/R) injury is one of the most serious problems in organ transplantation. Since innate immune responses are involved in I/R injury, systemic administration of selected inhibitors has been attempted. However, the systemic regulators are not effective in inhibiting I/R injury.

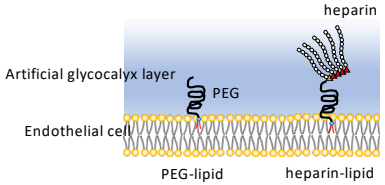


R.F. van Golen et al., Free Radical Biology & Medicine, 2012, 52, 1382.

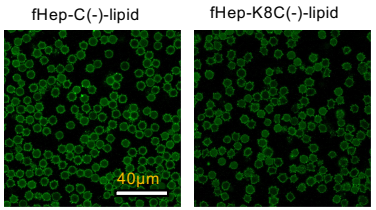
Here, we propose the new regulator for the I/R injury using local immune inhibition via cell-surface modification technique[1]. Here we synthesized heparin-conjugated lipid (heparin-lipid) to mimic glycocalyx, which is damage or lost during I/R injury, and tried to compensate for the damaged glycocalyx with our materials[2].

Methods

Heparin is polysaccharides belonging to the glycosaminoglycan (GAG) family as well as heparan sulfate (HS).

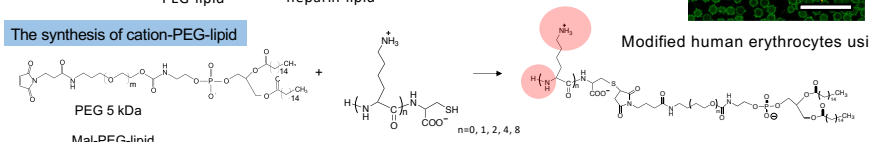


Heparinization by single step coating for blood vessel in organ

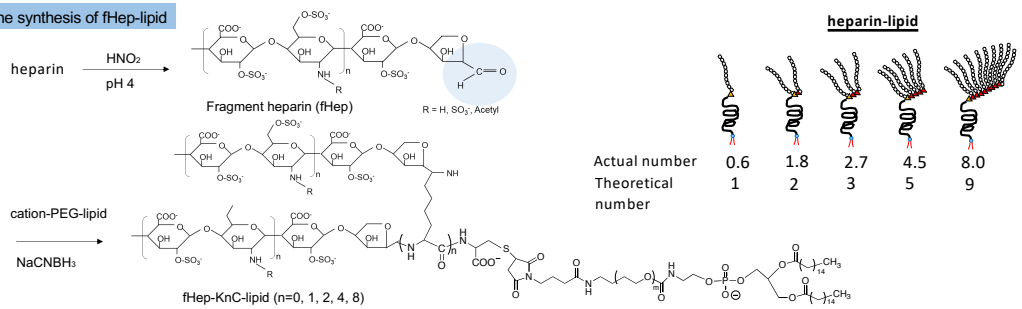


Modified human erythrocytes using Alexa488 antithrombin

The synthesis of cation-PEG-lipid

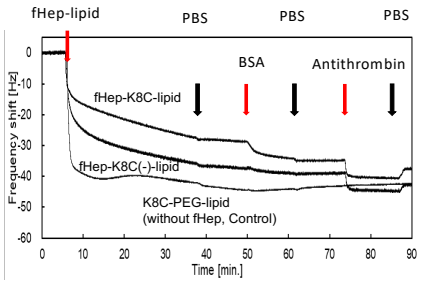


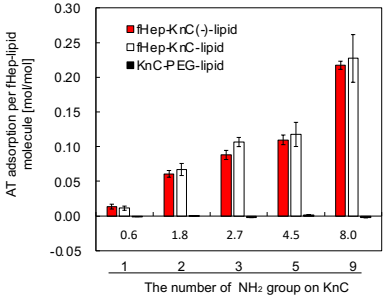
The synthesis of fHep-lipid

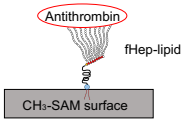


Results

AT-binding activity of fHep-lipid on QCM-D sensor chip

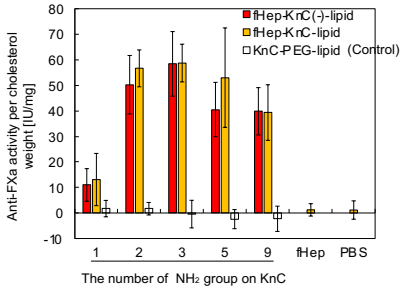






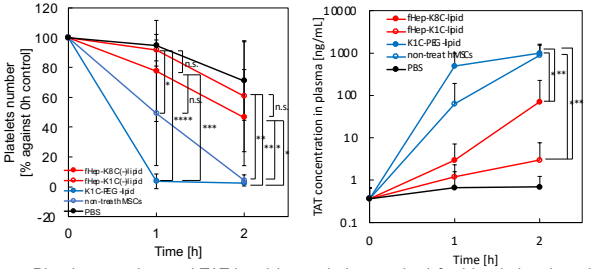
AT-binding activity depends on the number of conjugated fHep of fHep-lipid

Anti FXa activity of liposome modified with fHep-lipid



fHep-lipids inserted on the liposome surface show anti-FXa activity

Platelet count and coagulation maker in whole blood



Platelets number and TAT level (coagulation marker) for bloods incubated with hMSCs (10^5 [cells/mL]) (N=6)

There was significant difference between fHep-K1C/K8C(-)-lipid and K1C-PEG-lipid/non-treated hMSCs

Summary

Cellular membrane could be uniformly modified with fHep-lipid and showed strong antithrombogenicity in human whole blood.

References:

1) Teramura, et al., *Langmuir*, **36**, 12088–12106 (2020).
2) Asawa, et al., *Advanced Functional Materials*, **31**, 2008167 (2021).