S2: Platelet Adhesion

S2-1 Biologically Validated Model of Platelet Adhesion under Blood Flow Conditions

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Platelet adhesion under blood flow condition is mediated exclusively by its membrane protein of glycoprotein Ibalpha binding with plasma ligand protein of von Willebrand factor (VWF). Recent progress in advance of super computer technology allow us to predicted binding force generated by single GPIbalpha molecule binding with single VWF molecule. We have predicted unit binding force as 67 pN/molecule. This predicted value was validated by measurement of bindig force by atomic force microscopy.

Biological experiments revealed thethering of platelet on immobilized VWF when platelet activation and contribution of activated GPIIb/IIIa binding was blocked by prostagrandine E1 and antibody against GPIIb/IIIa. These tethering interaction is mediated exclusively by glycoprotein Ibalpha binding with VWF. Platelet tethering on VWF become apparent at wall shear rate of 1,500 1/s. The force necessitate to trap plate`1on VWF surface under wall shear rate of 1,500 1/s is predicted around 150 pN.

These molecular dyanamic simulation calculation and biological experiments suggest only a few molecular bond between glycoprotein Ibalpha and VWF is necessary to trap platelet cell under blood flow condition.

S2-2 Glycoprotein Distribution of Surface-Induced Platelet Activation on Medical Materials by Electron Microscopy Technology

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Thrombogenic complications remain one of the main problems for blood-contacting medical devices and can trigger life-threatening device failure. To reduce the risk of thromboembolism, we need to understand of thrombus formation mechanism between platelet and protein on material because platelets play a key role in blood coagulation. Platelets attach to an artificial material surface in the earliest stage of cell-material contact and they change in shape by developing pseudopodia (small leg from the platelet) and release granule contents, finally become flat. The plasma membrane of human platelets is rich in glycoproteins (GP) which play an important role in its interactions with the cell adhesion protein. On material surface, Glycoprotein Ibα and IIb/IIIa binds to von Willebrand factor and fibrinogen respectively, delivers the platelet activation signals to internal. If we understand distribution GP which is signal deliver completely, that lead to new approach of development material.

However, these interactions are complicated, the behavior of glycoprotein have not been fully elucidated or visualized.

In this study, we attempted to observe the glycoprotein distribution on membrane surface, platelet internal structures and adhesion interfaces of human platelets attached to medical material surfaces using immune electron microscopy technology during the platelet activation process. In addition to evaluate platelet reaction under flow condition, fabricating blood flow chamber and changing sheer stress.

S2-3 Hemorheological Effects of Mechanical Stress on Whole Blood of Patients with Prosthetic Heart Valve Failure

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Background: Human blood cells are subjected continuously to mechanical stress in valvular heart diseases and therapeutic intervensions using prosthetic heart valves. However, effects of mechanical stress on circulating blood cells remain unclear. Methods: Venous blood was sampled from patients undergoing heart valve replacement surgery after obtaining written informed consent. Erhythrocyte deformability was investigated by our specified filtration technique using nickel mesh filter with its pore size of 4.55 micrometer, and platelet activation was quantified by serum beta-thromboglobulin (BTG) and platelet factor IV (PF4). Results: Erhthycyte deformability was significantly inpaired and platelet activation was marginal in cases of prosthetic valve failure showing perivalvular leakage. However, these findings were not observed in cases showing normal prostethic valve functions. Microscopic findings of blood smear demonstrated eliptic, segmented or fusiformic deformations of erythrocytes and no remarkable findings in platelet morphology in cases of prosthetic valve failure, but not in cases without perivaluvular leakage. Conclusions: Mechanical stress caused by prosthetic valve failure provides severe damages on circulating blood cells. Erythrocytes deformability was profoundly impaired leading to hemolysis requiring transfusion, and platelet will be activated mechanically leading to adhesion to failed prosthetic valves, unless antiplatelet agents were not administered.

S2-4 Platelet adhesion studies of implantable long-term use Fontan pump biomaterials

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Penn State University is developing a small implantable pump for long-term mechanical support of patients with a failing Fontan circulation. An increasing number of patients who

undergo the Fontan operation are surviving to adulthood and require a device to provide sustained support. Many blood contacting components of this pump are manufactured from polyether ether ketone (PEEK), which has not been thoroughly characterized with regards to its biocompatibility. This study will analyze the surface characteristics of PEEK and compare them to previously characterized pediatric pump polyurethane materials to analyze their thrombosis potential.

PEEK and polyurethane samples were first analyzed using Optical Profilometry to compare surface roughness from their respective manufacturing protocols. A developed rotating disk system (RDS) protocol was then used to test platelet adhesion to the material surfaces at varying shear rates. The material surfaces were immunofluorescently labeled and imaged to quantify the number of adhered platelets. Additionally, x-ray photoelectron spectroscopy (XPS) studies of the PEEK material were performed to determine any surface contamination resulting from the component manufacturing and polishing processes.

PEEK samples were found to be smoother than poly urethane samples with surface roughness's of 20 μm and 70 μm, respectively. From RDS experiments, at a radial location of 6 mm (shear rate of 401.86 s^{-1}), a 71% decrease in platelet adhesion was observed with PEEK compared to polyurethane. However, XPS investigation revealed some contamination of the PEEK with PDMS (approximately 7%) resulting from surface polishing and is being further investigated as to its effect on platelet adhesion.

S2-5 Development of Hemocompatible Materials for Blood Contacting Device by Physical and Chemical Surface Modification

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Medical implants have been growing in importance, and they are widely used in a variety of clinical fields (such as cardiovascular and orthopedic medicine, as well as dentistry) as key applications for the treatment of diseases and the restoration of missing and defective organ functions. Almost all implants come into contact with blood in the human body; however, the insufficient hemocompatibility of implant surfaces still remains a major problem that causes life-threatening device failure. In order to reduce the risk, the hemocompatibility of biomaterials must be improved. On the other hand, adhesive capacity is a fundamental factor in clot formation on artificial surfaces after implantation. Therefore, the prevention of platelet adhesion to material surfaces is directly related to the improvement of surface hemocompatibility. There are two approaches, chemical and physical approaches. In chemical, for example changing surface components control surface characteristics. Physical modification is a unique technique to control the cell adhesion by making the micro order shape to the surface. we previously reported that fluorine incorporated diamond-like carbon

(F-DLC) film with patterned markedly inhibits platelet adhesion and activation compared to polycarbonate.

In this symposium we will introduce our development of newly material through chemical and physical approaches to improve biocompatibility. Appropriate understanding of these technologies will make it possible to develop future medical materials for blood contacting devices.