MCB, vol.16, supplemental 1, pp.5-6, 2019

Some Aspects in Mechano-Biology of Platelet and Leukocyte in Blood Flows

Ying Fang[1] and Jianhua Wu[1, *]

Abstract: For hemostasis and thrombosis, some proteins, such as Von Willebrand Factor (VWF, a multimeric plasma glycoprotein synthesized in endothelial cells and megakaryocytes and secreted to circulation or attached to endothelial cells), the metalloprotease ADAMTS13 (a disintegrin and metalloprotease with a thrombospondin type 1 motif, member 13), P-selectin (one of three selectin family members with a N-terminal C-type lectin domain, an epidermal growth factor (EGF)-like module, a series of consensus repeat (CR) units, a transmembrane segment and a short cyto-plasmic domain) and β2 integrin. In adhesion and aggregation of circulating platelets towards to the sites of vascular injury, VWF on vascular wall captures and activates the circulating platelets through interaction with platelet receptor glycoprotein Ibα (GPIbα). The activated platelets will secrete P-selectin, mediating flowing leukocytes to be captured first to and then rolled on the platelets. Activation of β2 integrin on leukocytes makes the rolling cells slow down and adhere firmly to platelet. Pathological hemodynamic environment may cause platelet-induced inflammation overreaction of leukocytes, leading to mechanical instability of thrombotic plaque. Above mentioned events all are referred to their respective un-well known mechano-chemistry processes. For better understanding on the mechano-chemistry mechanism of interaction of leukocyte with platelet under flows, we have investigated the force-dependent Structure-function of VWF-A domain, force-regulated cleavage of A2 domain of von Willebrand factor (vWF) by ADAMTS13, P-selectin secretion from activated platelet, and P-selectin-mediated Activation of β2 integrin on leukocytes under shear stresses, and so on through AFM and flow chamber experiments and molecular dynamics simulation. Our data showed that, these events mentioned above were biphasic force-dependent. Increasing force stabilizes the globular VWF-A conformation first and then makes it become a spread one with higher affinity with platelet receptor glycoprotein Ibα (GPIbα), the force-regulated cleavage of VWF-A2 domain by ADAMTS13 maybe closely related to the induced-fit of ADMATS13 and VWF-A2, Force triggers and quickens P-selectin-induced Activation of β2 integrin on leukocytes.

Keywords: VWF, β2 integrin activation, platelet, leukocyte, shear stress.

Acknowledgments: This work was supported by National Natural Science Foundation of China (NSFC) Grants 11432006 (J.W.) and 11672109 (Y.F.)

[1] Institute of Biomechanics/School of Bioscience and Bioengineering, South China University of Technology, Guangzhou, 510006, China.

[*] Corresponding Author: Jianhua Wu. Email: wujianhua@scut,edu.cn.

Jianhua Wu, Ph.D.
Institute of Biomechanics,
School of Biosciences and Bioengineering,
South China University of Technology,
Guangzhou, China

Email: Wujianhua@scut.edu.cn

Dr. Wu earned his Ph.D. degree in Wuhan University of Technology (Wuhan, China) in 1988 and began his research career in hydrodynamics as a lecturer in Wuhan University of Technology in1988. He went to Peking University as a post-doctoral scientist in 1989, and gained his associate professor position in 1991. Later on, he entered into Sun Yat-sen University (SYSU), and became a full professor of fluid mechanics in 1996. Since 2000, Dr Wu was interested in bioengineering, and was a professor of biochemistry in SYSU School of Life Science. In 2007, he came to South China University of Technology and was a professor of Biomedical Engineering. Dr Wu was a research associate in Hong Kong University in 1993-1995, and he spent two years (2001-2003) in Georgia Tech as a visit professor.

In Dr. Wu's Lab, the current researches include experimental, computational and theoretical studies in bioengineering at the cellular and molecular levels, and focus on the effects of mechanical microenvironment on the receptor-ligand interaction-induced intracellular signaling, cell adhesion and aggregation of cells in the immune system and the vascular system. The goal of Dr. Wu' research is to gain a fundamental understanding of biological processes relative to human health and diseases (such as cardiovascular disease and cancer) at gene, protein, cell and tissue levels. The experiments utilize state-of-the-art technologies, including flow chamber, atomic force microscopy, real-time laser scanning confocal microscopy and etc. The force-induced change of both structure and function of protein is measured experimentally using ultrasensitive techniques at pN and nm levels and analyzed theoretically by molecular dynamics simulations.