Weibel-Palade body formation and exocytosis in von Willebrand disease

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Curriculum Vitae

Jiong-Wei Wang was born on 20th October 1982 in Shangcai, China. After graduation from high school at Shangcai First Senior Middle School in Shangcai in 2000, he started his biological training at Henan Normal University (2000-2004), Xinxiang, China. He was awarded the National Scholarship&Stipend in 2003 and obtained the bachelor degree in Life Sciences with honors in 2004. In the same year, he moved to Beijing Normal University for a master study at the Key Laboratory for Cell Proliferation and Regulation Biology of Ministry of Education, supervised by Prof. dr. Zong-Jie Cui. 2005-2007 he did an internship and worked on the integrity of rat liver lysosomes under the supervision of Prof. Guo-Jiang Zhang, at the Institute of Biophysics, Chinese Academy of Sciences, Beijing. 2005-2006 he received the Chongde-Kexing Stipend and obtained his master degree in Cell Biology with honors in 2007. Late 2007 he joined a PhD program in medicine at Leiden University Medical Center, Leiden, the Netherlands. After a short internship he started his PhD research on the role of Weibel-Palade body in von Willebrand disease since February 2008 at the Department of Thrombosis and Haemostasis, Einthoven Laboratory for Experimental Vascular Medicine, under the supervision of Prof. dr. H.C.J Eikenboom and Prof. dr. P.H. Reitsma. The research was conducted in close collaboration with the Department of Molecular Cell Biology, Section Electron Microscopy, and the Department of Nephrology, of the Leiden University Medical Center, and the Department of Plasma proteins, Sanquin-AMC Landsteiner Laboratory, Amsterdam. The work described in this thesis has been presented (orally or by posters) in several (inter)national congresses or symposia and he was awarded twice the *Young Investigator Award* by the International Society on Thrombosis and Haemostasis (ISTH 2009 Boston and 2011 Kyoto) and the *NVTH Science Prize (Basic research)* by the Dutch Society on Thrombosis and Haemostasis (2011, Koudekerke). During the PhD training, he followed the PhD courses held by the Dutch Heart Foundation. Apart from the scientific work, he has been serving as the Chairman of the Chinese Association of Life-Sciences in the Netherlands (CALN) since February 2011.
Since March 2012, he has been working with Prof. dr. D.P. de Kleijn at the Department of Experimental Cardiology, University Medical Center Utrecht.

Publications

Wang JW, Valentijn JA, Valentijn KM, Dragt BS, Voorberg J, Reitsma PH, Eikenboom J. Formation of platelet-binding von Willebrand factor strings on non-endothelial cells. *J Thromb Haemost*. 2012;10(10):2168-2178.

Wang JW, Groeneveld DJ, Cosemans G, Dirven RJ, Valentijn KM, Voorberg J, Reitsma PH and Eikenboom J. Biogenesis of Weibel-Palade bodies in von Willebrand disease variants with impaired von Willebrand factor intrachain or interchain disulfide bond formation. *Haematologica*. 2012; 97(6):859-866.

Wang JW, Valentijn KM, de Boer HC, Dirven RJ, van Zonneveld AJ, Koster AJ, Voorberg J, Reitsma PH and Eikenboom J. Intracellular storage and regulated secretion of von Willebrand factor in quantitative von Willebrand disease. *J Biol Chem.* 2011; 286(27):24180-24188.

Wang JW and Eikenboom J. Von Willebrand disease and Weibel-Palade bodies. *Hamostaseologie* 2010; 30(3):150-155.

de Hoog VC, Timmers L, Schoneveld AH, **Wang JW**, van de Weg SW, Sze SK, van Keulen JK, Hoes AW, den Ruijter HM, de Kleijn DPV, Mosterd A. Serum extracellular vesicle protein levels are associated with acute coronary syndrome. *Eur Heart J. Acute Cardiovascular Care*, Accepted.

Hu JS, Li YB, **Wang JW**, Sun L, Zhang GJ. Mechanism of lysophosphatidylcholine-induced lysosome destabilization. *J Membr Biol.* 2007; 215(1):27-35.

Wang JW, Sun L, Hu JS, Li YB, Zhang GJ. Effects of phospholipase A2 on the lysosomal ion permeability and osmotic sensitivity. *Chem Phys Lipids.* 2006; 144(2):117-126.