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Quantitative proteomics reveal new insights into platelet signaling and function

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As circulating sentinels of vascular integrity, platelets act as crucial hemostatic cells as well as important inflammatory and immune cells, whereas under pathological conditions platelets drive thrombotic but also non-thrombotic diseases related to chronic inflammation. In addition, platelets serve as an important cellular model to study the biology and pharmacology of signal transduction pathways. Platelet inhibition and activation responses are mediated by multiple signaling networks, which are tightly regulated by balanced catalysis of protein phosphorylation and dephosphorylation through protein kinases and protein phosphatases, respectively. However, we are only at the beginning of understanding the complexity of interacting signaling pathways and their impact on platelet function. The lecture gives and overview about functional and proteomic approaches that lead to novel concepts of understanding the proteome, kinome and phosphatome in relation to the function of human platelets.

Curriculum Vitae

Dr Kerstin Jurk

Research topics: Regulation of platelet signaling and function; platelet interaction with leukocytes and vascular cells; platelet function disorders

Academic training:

1988 - 1994	Diploma in Biology, Westfälische Wilhelms University, Muenster
1995 - 1999	Doctoral Fellowship University Hospital Muenster

Academic degrees:

1999	Doctoral thesis (Ph.D. (Dr. rer. nat., summa cum laude) at the Westfälische Wilhelms University, Muenster, Dept. of Biology (W. Stöcker) and Dept. of Internal Medicine A (B. Kehrel)
2012	Habilitation (Priv.-Doz.) at the University-Hospital Muenster, Westfälische Wilhelms University, Muenster, Venia Legendi: Experimental Vascular Medicine

Scientific career:

since 2015	Independent Group Leader CTH Mainz
since 2012	Head of platelet platform and platform coordinator, CTH Mainz
2006 - 2011	Research Associate, Dept. of Anaesthesiology and Intensive Care, Exp. And Clin. Haemostasis, University-Hospital Münster
2004 - 2006	Lise-Meitner Habilitation Fellow of North Rhine-Westphalia
1999 - 2004	Postdoctoral Research Fellow, Dept. of Anaesthesiology and Intensive Care, Exp. and Clin. Haemostasis, University-Hospital Münster

Awards, honors & scientific activities:

since 2016	Member of the ISTH/SSC committee “Platelet Physiology”
since 2015	Coordinator of the GTH/GPOH THROMKID-Study Group Module “Diagnostics of inherited platelet function disorders – Quality management and competence centers”
since 2014	DZHK-Scientist

2009	Eberhard Mammen 'Excellence in Thrombosis and Hemostasis' Award for most popular articles in “Seminars in Thrombosis and Hemostasis 2007/2008”
2006	"Clinical Scholar Research Award 2007", International Anesthesia Research Society (IARS)
2005	"Best of Meeting Award" 79th Clinical and Scientific Congress, International Anesthesia Research Society (IARS)
2004	Lise-Meitner Habilitation Fellowship of North Rhine-Westphalia
2004	Professor Landbeck Award, German society of thrombosis and haemostasis research (GTH)
2000	Dissertation Award, Faculty of Mathematics and Natural Sciences, University of Muenster

Selected publications:

1. Makhoul S, Walter E, Pagel O, Walter U, Sickmann A, Gambaryan S, Smolenski A, Zahedi RP, **Jurk K**. Effects of the no/soluble guanylate cyclase/cgmp system on the functions of human platelets. ***Nitric Oxide***. 2018;76:71-80.

2. Loroch S, Trabold K, Gambaryan S, Reiss C, Schwierczek K, Fleming I, Sickmann A, Behnisch W, Zieger B, Zahedi RP, Walter U, **Jurk K**. Alterations of the platelet proteome in type i glanzmann thrombasthenia caused by different homozygous delg frameshift mutations in itga2b. ***Thromb Haemost***. 2017;117:556-569.

3. Kossmann S, Lagrange J, Jackel S, **Jurk K**, Ehlken M, Schonfelder T, Weihert Y, Knorr M, Brandt M, Xia N, Li H, Daiber A, Oelze M, Reinhardt C, Lackner K, Gruber A, Monia B, Karbach SH, Walter U, Ruggeri ZM, Renne T, Ruf W, Munzel T, Wenzel P. Platelet-localized fxi promotes a vascular coagulation-inflammatory circuit in arterial hypertension. ***Sci Transl Med***. 2017;9.

4. Beck F, Geiger J, Gambaryan S, Solari FA, Dell'Aica M, Loroch S, Mattheij NJ, Mindukshev I, Potz O, **Jurk K**, Burkhart JM, Fufezan C, Heemskerk JW, Walter U, Zahedi RP, Sickmann A. Temporal quantitative phosphoproteomics of adp stimulation reveals novel central nodes in platelet activation and inhibition. ***Blood***. 2017;129:e1-e12.

5. de Witt SM, Swieringa F, Cavill R, Lamers MM, van Kruchten R, Mastenbroek T, Baaten C, Coort S, Pugh N, Schulz A, Scharrer I, **Jurk K**, Zieger B, Clemetson KJ, Farndale RW,Heemskerk JW, Cosemans JM. Identification of platelet function defects by multi-parameter assessment of thrombus formation. ***Nat Commun***. 2014;5:4257.

6. **Jurk K**, Lahav J, Van Aken H, Brodde MF, Nofer JR, Kehrel BE. Extracellular protein disulfide isomerase regulates feedback activation of platelet thrombin generation via modulation of coagulation factor binding. ***J Thromb Haemost***. 2011;9:2278-2290.

7. Gunay-Aygun M, Falik-Zaccai TC, Vilboux T, Zivony-Elboum Y, Gumruk F, Cetin M, Khayat M, Boerkoel CF, Kfir N, Huang Y, Maynard D, Dorward H, Berger K, Kleta R, Anikster Y, Arat M, Freiberg AS, Kehrel BE, **Jurk K**, Cruz P, Mullikin JC, White JG, Huizing M, Gahl WA. Nbeal2 is mutated in gray platelet syndrome and is required for biogenesis of platelet alpha-granules. ***Nat Genet***. 2011;43:732-734.

8. **Jurk K**, Ritter MA, Schriek C, Van Aken H, Droste DW, Ringelstein EB, Kehrel BE. Activated monocytes capture platelets for heterotypic association in patients with severe carotid artery stenosis. ***Thromb Haemost***. 2010;103:1193-1202.

9. **Jurk K**, Jahn UR, Van Aken H, Schriek C, Droste DW, Ritter MA, Bernd Ringelstein E, Kehrel BE. Platelets in patients with acute ischemic stroke are exhausted and refractory to thrombin, due to cleavage of the seven-transmembrane thrombin receptor (par-1). ***Thromb Haemost***. 2004;91:334-344.

10. **Jurk K**, Clemetson KJ, de Groot PG, Brodde MF, Steiner M, Savion N, Varon D, Sixma JJ, Van Aken H, Kehrel BE. Thrombospondin-1 mediates platelet adhesion at high shear via glycoprotein ib (gpib): An alternative/backup mechanism to von willebrand factor. ***FASEB J***. 2003;17:1490-1492.