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About

Yotis is a British Heart Foundation Senior Research Fellow in the School of Clinical and Experimental Medicine and a senior member of the Birmingham Platelet Group. He was appointed Chair in Cellular Haemostasis in 2013. His main research interests are platelet protein-tyrosine phosphatases and how they regulate platelet activation, thrombosis and haemostasis.

Yotis received his undergraduate and graduate degrees from Queen's University, Canada. He did his postdoctoral training with Professor Stephen Watson at the University of Oxford on platelet signalling and thrombosis. He has been an integral member of the Birmingham Platelet Group since it's inception in 2003. He uses classical cell biology, biochemical and protoemics-based approaches to study novel platelet surface glycoproteins and signalling pathways. His research is mainly funded by the British Heart Foundation.

Yotis has numerous peer-reviewed publications in leading scientific and biomedical research journals. He has written book chapters and edited the first book on platelet proteomics. He is a frequent speaker at national and international conferences on platelets, thrombosis and haemostasis, and does interviews for radio, newspapers and popular science magazines.

Qualifications

- PhD Pathology, Queen's University, Canada
- MSc Pathology, Queen's University, Canada
- BSc(Hons), Life Sciences, Queen's University, Canada

Biography

Yotis earned his BSc(Hons), MSc and PhD degrees at Queen's University, Canada. His MSc degree on the synthesis and secretion of VWF during disseminated intravascular coagulation was done under the supervision of Professor Alan Giles in the Department of Pathology at Queen's University. Following completion of his MSc degree, he worked for a year in the lab of Drs. Gérard Marguerie and Diana Tronik-Le Roux in the Department of Molecular and Structural Biology, Commissariat à l'Energie Atomique, Grenoble, France, developing a megakaryocyte-based cell delivery system for gene therapy of factor VIII-deficiency. He returned to Queen's University in 1997 to do a PhD degree on the involvement of Fps protein-tyrosine kinase in cytokine and ITAM receptor signalling in haematopoietic cells, under the supervision of Professor Peter Greer. He moved to England in 2002 to do postdoctoral work in the lab of Professor Stephen Watson in the Department of Pharmacology at the University of Oxford. His main project was the investigation of signalling events regulating thrombus formation on collagen under flow. In 2003, he move to the University of Birmingham with the Watson group, where he took up a position as Research Fellow, linked to Professor Watson's British Heat Foundation Chair. At this time, Yotis started using proteomics-based approaches to identify novel platelet surface glycoproteins and signalling proteins. Several spin-off project came out of this project, including the investigation of the platelet receptor-like protein tyrosine phosphatase (PTP) CD148 and the novel platelet ITIM receptor G6b-B. Dovetailing from these projects were studies on the non-transmembrane tyrosine phosphatases PTP-1B, Shp1 and Shp2.

Teaching

- Supervising/teaching BMedSci students
- Student Selected Activities for 1st and 2nd year Medical Students

Postgraduate supervision

- Supervising/teaching PhD students in the Platelet Biology Consortium

Research

Platelets are small fragments of megakaryocytes that play a central role in haemostasis and thrombosis. They adhere to sites of vascular damage forming a haemostatic plug that prevents excessive blood lose. Platelets also promote an inflammatory response and wound repair. Platelets can also have a detrimental effect on health by plugging blood vessels in the heart and brain, leading to heart attacks and stroke, two of the leading causes of death in the western world. Understanding how platelet function is regulated has important clinical implications in the treatment and prevention of thrombosis.

Yotis' main research interest is the investigation of platelet protein tyrosine phosphatases (PTPs). PTPs are a family of enzymes that dephosphorylate tyrosine residues in proteins. PTPs work in conjunction with protein tyrosine kinases (PTKs) to regulate phosphorylation of specific sites in proteins. In this way, PTPs and PTKs regulate protein function and compartmentalization and relay signals across the plasma membrane. These signals ultimately control platelet function.

PTPs have been under-investigated in platelets. Work lead by Yotis demonstrates that the receptor-like PTP CD148 is a key regulator of platelet responsiveness to vascular injury. It does so by maintaining a pool of activate Src family kinases (SFKs) in platelets that are important for initiating and propagating signals from a variety of surface receptors, including the collagen activation receptor GPVI and the integrin aIIbb3 that mediates platelet adhesion and aggregation. Absence of CD148 results in attenuated platelet responses to vascular injury. CD148 appears to be the main activator of SFKs in platelets.

Other PTPs of interest are the SH2 domain-containing non-transmembrane PTPs Shp1 and Shp2. Shp1 and Shp2 have been implicated as negative regulators of platelet function, through their interactions with ITIM receptors, such as PECAM-1 and CEACAM1. The functional roles of Shp1 and Shp2 in platelets and megakaryocytes are presently being investigated. The novel platelet ITIM receptor G6b-B is being investigated in parallel.

Other activities

- Member of the Biochemical Society
- Member of the British Society for Haemostasis and Thrombosis
- Member of the American Society for Biochemistry and Molecular Biology
- Member of the International Society on Thrombosis and Haemostasis
- Associate Member of the Faculty of 1000 – Post-Publication Peer Review

Publications

S. Séverin, A. Y. Pollitt, L. Nunez-Navarro, C. A. Nash, D. Mourão-Sá, J. Eble, Y. A. Senis and S. P. Watson. The role of Src kinases in CLEC-2 signalling is ligand dependent. **J Biol Chem** 2010 Nov 22 [Epub ahead of print]

C. A. Nash, S. Séverin, B. B. Dawood, M. Makris, A. Mumford, J. Wilde, Y. A. Senis and S. P. Watson. Src kinases are essential for primary aggregation by G(i)-coupled receptors. *J* **Thromb Haemost** 2010; 8:2273-2282

S. Ellison, J. Mori, A. J. Barr and Y. A. Senis. CD148 enhances platelet responsiveness to collagen by maintaining a pool of active Src family kinases. **J Thromb Haemost** 2010; 8:1575-1583 2010; 8:1575-1583

Y. A. Senis, R. Antrobus, S. Severin, A. F. Parguina, I. Rosa, N. Zitzmann, S. P. Watson and Á. García. Proteomic analysis of integrin □IIb□3 outside-in signalling reveals Src kianse-independent phosphorylation of Dok-1 and Dok-3 leading to SHIP-1 interactions. **J Thromb Haemost** 2009; 7:1718-26

Y. A. Senis, M. G. Tomlinson, S. Ellison, A. Mazharian, J. Lim, Y. Zhao, K. N. Kornerup, J. M. Auger, S. G. Thomas, T. Dhanjal, N. Kalia, J. W. Zhu, A. Weiss and S. P. Watson. The tyrosine phosphatase CD148 is an essential positive regulator of platelet activation and thrombosis. **Blood** 2009; 113:4942-4954

J. Mori, A. C. Pearce, J. C. Spalton, B. Grygielska, J. A. Eble, M. G. Tomlinson, Y. A. Senis and S. P. Watson. G6b-B inhibits constitutive and agonist-induced signalling by G6b-B and CLEC-2. **J Biol Chem** 2008; 283:35419-27

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T. S. Dhanjal, E. A. Ross, J. M. Auger, O. J. T. McCarty, C. E. Hughes, Y. A. Senis, C. Buckley and S. P. Watson. Minimal regulation of platelet activity by PECAM-1. **Platelets** 2007; 18:56-67

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