

XII JCET LECTURE, 16.11.2012, 9.00:

Novel therapeutic approaches for shock and ischaemia-reperfusion injury

Christoph Thiernemann, MD PhD FBPharmacolS FRCP FMedSci

Professor of Pharmacology (Tenure, since 1998), William Harvey Research Institute (WHRI), Barts & the London School of Medicine, Queen Mary University of London

Head of Centre of Translational Medicine & Therapeutics, WHRI (since 2007)

Member of the Management Committee of the William Harvey Research Foundation (since 2000)

Chief Executive Officer, William Harvey Research Limited (since 2003) www.williamharvey.co.uk

The presentation outlines the effects of erythropoietin (EPO) in ischaemia-reperfusion injury of the kidney (and other organs) as well as in trauma-haemorrhage. Preclinical data will demonstrate both beneficial and adverse effects of EPO in rodents, and in patients with critical illness. In order to overcome potential adverse effects of EPO, we have recently developed non-erythropoietic, but tissue-protective, analogues of EPO. The pharmacology of these analogues will be discussed and efficacy data in preclinical models of ischaemia-reperfusion injury and trauma will be reported. Finally, the presentation will discuss the signalling events which underly the reported beneficial effects of EPO and its analogue ARA-290.

RE: **CURRICULUM VITAE** (SUMMARY)

School of Medicine and Dentistry
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Friday, 09 November 2012

Name: Christoph **Thiemermann**, MD PhD FBPharmacoS FRCP FMedSci
Date of Birth: June 14, 1960

Education & Degrees:

1979 - 1986: Medical School, University of Cologne, Germany
1986: Graduation and Registration as Physician
1987: Medical doctorate (summa cum laude – with distinction), University of Cologne, Germany
1991: Doctor of Philosophy, William Harvey Research Institute, Bart's College, University of London
2003: Fellow of the Academy of Medical Sciences (FMedSci) of the United Kingdom
2005: Fellow of the British Pharmacological Society (FBPharmacoS) of the United Kingdom
2008: Fellow of the Royal College of Physicians (FRCP)

Present Positions:

Professor of Pharmacology (Tenure, since 1998), William Harvey Research Institute (WHRI)
Barts & the London School of Medicine, Queen Mary University of London
Head of Centre of Translational Medicine & Therapeutics, WHRI (since 2007)
Member of the Management Committee of the William Harvey Research Foundation (since 2000)
Chief Executive Officer, William Harvey Research Limited (since 2003) www.williamharvey.co.uk

Achievements & Awards

1997: University Award of the University of Cologne (Best Doctorate Degree of all Faculties)
1991: John Vane Award for Prostaglandin Research
1991: Annual Prize of the German Society of Angiology
1994: Sandoz Prize of the British Pharmacological Society (best pharmacologists under the age of 40)
1997: Young Investigator Award, Surgical Infection Society
2001: Research Award for most Innovative Research by EUPHAR
2001: Menarini Award for Basic Science (for best cardiovascular research in the UK)

Visiting Professorships:

Contract Professor of Pharmacology, University of Florence, Italy (1995-2003)
Professor of Pharmacology, University of Lisbon, Portugal (1999-today)
Professor of Experimental Medicine, University of Messina, Italy (since 2000)
Professor of Pharmacology, University of Oslo, Norway (2001)
Professor of Pharmacology, University of Belgrade, Serbia (2003)
Professor of Pharmacology, National University of Singapore (2004 - 2005)

Current Editorial Board Positions:

Shock, Senior Associate Editor for Europe (since 2002)
Critical Care Medicine (Editorial Board, since 2006)
Critical Care (Editorial Advisor) since 2006
Pharmacological Research, Member of the Editorial Board (since 2009)

Research Interests (both basic science and translational studies):

Pathophysiology and therapy of shock and multiple organ failure (in particular acute respiratory distress syndrome (ARDS), cardiac dysfunction and acute kidney injury (AKI))

Pathophysiology and experimental treatment of acute myocardial infarction and AKI

Publications: 359 publications (listed in PubMed), 45 invited chapters in books.

Metric Data (according to www.isiknowledge.com on 26th Jan 2012)

Papers captured by Web of Science on which metrics below are based: 276

Sum of the Times Cited: 14,466 (Sum of Times Cited without self-citations: 13,369)

Citing Articles: 10,157 (Citing Articles without self-citations: 9,890)

Average Citations per Item: 52.41

h-index: 62

Invited Lectures: I have presented 187 invited lectures at scientific meetings or universities, organised 10 scientific conferences and edited 1 scientific film.

Institute of Scientific Information (ISI): I am listed by the ISI as (i) one of the 100 most cited pharmacologists in the Word (based on citations in the past 20 years), and (ii) one of the 25-most cited pharmacologists (based on citations in the period from 1994-2004).

Academic Achievements:

Past-President of the European Shock Society (2006-2009)

Member of the **Council of the World Federation of Shock Societies** (since 2005)

Congress Chair – 13th Congress of the ESS in Lisbon 2009 (www.shock09.com)

Member of the **Academy of Sciences of Lisboa** (Academy of Sciences in Portugal) (May 2002) Lisboa

Member of the **Fellowships Committee of the NIHR** (2008-today).

Referee for Nature, Nature Medicine, Science, AJRCCM, Circulation, Circulation Research, Kidney International, JASN and many other scientific journals. In the last two years, I have acted as referee for many grant giving bodies (e.g. BHF, Wellcome Trust, Science Foundation Ireland, DFG-Germany, AStar-Singapore, Institut Pasteur, NIHR)

Other Achievements:

Chief Executive (in the Chair) of William Harvey Research Limited (the '*profits*' of this company are covenanted to the WHR Foundation as a gift aid to support research within the WHR Institute) (since November 2003). Since 2003, the total gift aid payment amounted to approximately £1 Million. (see www.williamharvey.co.uk)

Member of the Institute of Directors (IoD) (since 2003).

Active Funding:

2012-2015: Barts and The London Charity Programme (PI: Prof Karim Brohi), "Centre for Trauma Sciences", £3,000,000

2012: William Harvey Research Foundation Project Grant, "Development of a murine model of renal fibrosis following ureter-ligation"; £29,650.

2012-2017: NIHR-BRU Programme (Director: Prof Mark Caulfield), Research Lead for "Vascular Inflammation and Regenerative Medicine"; £1,500,000 out of £6,557,380.

2011-2012: AztraZeneca Project Grant, "Testing novel candidate compounds for ischaemia/reperfusion and shock"; £181,365.

2011-2012: British Heart Foundation Project Grant, "Pathophysiology and therapy of the cardiac dysfunction in experimental sepsis"; £51,762.

2010-2012: German Research Council Training Fellowship for Dr Sina Coldewey, "New therapeutic strategies for prevention of multiple organ dysfunction associated with shock of various aetiologies"; €80,000.

2010-2013: Medical Research Council (non-clinical PhD Studentship), "Novel therapeutic strategies for the amelioration of multiple organ dysfunction in severe sepsis"; £90,610.

2010-2013: Barts & The London Charity Project Grant (PI: Prof Magdi Yaqoob), "Mechanisms underlying the development of chronic kidney disease"; £350,000.

2010-2012: British Heart Foundation Project Grant (PI: Prof Yuti Chernajovsky), "Development of EPO latent peptides for protection of the infarcted heart"; £103,477.

2010-2013: British Heart Foundation (non-clinical PhD studentship), "Novel therapeutic approaches for haemorrhagic shock"; £108,000.

2009-2012: Kidney Research UK Fellowship for Dr Nimesh Patel, "Tissue-protective, but non-haematopoietic, analogues of erythropoietin for the treatment of acute kidney injury"; £178,185.

Patron: Her Majesty The Queen

Incorporated by Royal Charter as Queen Mary & Westfield College, University of London

Selected Publications

Byrne CJ, McCafferty K, Kieswich J, Harwood S, Andrikopoulos P, Raftery M, Thiernemann C, Yaqoob MM: Ischemic conditioning protects the uremic heart in a rodent model of myocardial infarction. *Circulation* 2012, 125:1256-1265.

Patel NS, Nandra KK, Brines M, Collino M, Wong WF, Kapoor A, Benetti E, Goh FY, Fantozzi R, Cerami A, Thiernemann C. A nonerythropoietic peptide that mimics the 3D structure of erythropoietin reduces organ injury/dysfunction and inflammation in experimental hemorrhagic shock. *Mol Med.* 2011 Sep-Oct;17(9-10):883-92. doi: 10.2119/molmed.2011.00053.

Collino M, Benetti E, Miglio G, Castiglia S, Rosa AC, Aragno M, Thiernemann C, Fantozzi R. Peroxisome proliferator-activated receptor β/δ agonism protects the kidney against ischemia/reperfusion injury in diabetic rats. *Free Radic Biol Med.* 2011 Jan 15;50(2):345-53.

Lovell MJ, Yasin M, Lee KL, Cheung KK, Shintani Y, Collino M, Sivarajah A, Leung KY, Takahashi K, Kapoor A, Yaqoob MM, Suzuki K, Lythgoe MF, Martin J, Munroe PB, Thiernemann C, Mathur A. Bone marrow mononuclear cells reduce myocardial reperfusion injury by activating the PI3K/Akt survival pathway. *Atherosclerosis.* 2010 Nov;213(1):67-76. 4.PMID: 20810112.

Kapoor A, Shintani Y, Collino M, Osuchowski MF, Busch D, Patel NS, Sepodes B, Castiglia S, Fantozzi R, Bishop-Bailey D, Mota-Filipe H, Yaqoob MM, Suzuki K, Bahrami S, Désvergne B, Mitchell JA, Thiernemann C. Protective Role of Peroxisome Proliferator-Activated Receptor- β/δ in Septic Shock. *Am J Respir Crit Care Med.* 2010 Aug 6.

Kumar S, Allen DA, Kieswich JE, Patel NS, Harwood S, Mazzon E, Cuzzocrea S, Raftery J, Thiernemann C, Yaqoob MM. Dexamethasone ameliorates renal ischemia-reperfusion injury. *J Am Soc Nephrol.* (2009) 20:2412-25.

Collino M, Aragno M, Castiglia S, Tomasinelli C, Thiernemann C, Boccuzzi G, Fantozzi . Insulin reduces cerebral ischemia/reperfusion injury in the hippocampus of diabetic rats: a role for glycogen synthase kinase-3 β . *Diabetes* (2009) 58:235-42.

Murch O, Abdelrahman M, Collino M, Gallicchio M, Benetti E, Mazzon E, Fantozzi R, Cuzzocrea S, Thiernemann C. Sphingosylphosphorylcholine reduces the organ injury/dysfunction and inflammation caused by endotoxemia in the rat. *Crit Care Med.* (2008) 36:550-9.

Brines M, Patel NS, Villa P, Brines C, Mennini T, De Paola M, Erbayraktar Z, Erbayraktar S, Sepodes B, Thiernemann C, Ghezzi P, Yamin M, Hand CC, Xie QW, Coleman T, Cerami A. Nonerythropoietic, tissue-protective peptides derived from the tertiary structure of erythropoietin. *Proc Natl Acad Sci U S A.* (2008) 105:10925-30.

Cartwright N, Murch O, McMaster SK, Paul-Clark MJ, van Heel DA, Ryffel B, Quesniaux VF, Evans TW, Thiernemann C, Mitchell JA. Selective NOD1 agonists cause shock and organ injury/dysfunction in vivo. *Am J Respir Crit Care Med.* (2007) 175:595-603.

Tripatara P, Patel NS, Webb A, Rathod K, Lecomte FM, Mazzon E, Cuzzocrea S, Yaqoob MM, Ahluwalia A, Thiernemann C. Nitrite-derived nitric oxide protects the rat kidney against ischemia/reperfusion injury in vivo: role for xanthine oxidoreductase. *J Am Soc Nephrol.* (2007) 18:570-80.

Dugo L, Collin M, Allen DA, Murch O, Foster SJ, Yaqoob MM, Thiernemann C. Insulin reduces the multiple organ injury and dysfunction caused by coadministration of lipopolysaccharide and peptidoglycan independently of blood glucose: role of glycogen synthase kinase-3 β inhibition. *Crit Care Med.* (2006) May;34(5):1489-96. PMID: 16557150

Yours sincerely,