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The role of PPARβ/δ nuclear receptors as innovative drug target in the management of insulin resistance and its associated cardiovascular complications

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The association between insulin resistance and cardiovascular diseases raises important questions about the underlying pathological processes, especially for designing targeted therapeutic interventions. The Peroxisome Proliferators Activated Receptors (PPARs) are ligand-activated transcription factors that control lipid and glucose metabolism. PPARs regulate gene expression by binding with RXR as a heterodimeric partner to specific DNA sequences, termed PPAR response elements. In addition, PPARs may modulate gene transcription also by directly interfering with other transcription factor pathways in a DNA-binding independent manner. To date, three different PPAR isoforms, designated α, β/δ and γ, have been identified. PPARα and PPARγ are the most extensively examined and characterized, mainly because they are activated by compounds, such as fibrates and thiazolidinediones, that are in clinical use for the treatment of hypertriglyceridemia and insulin resistance, respectively. In contrast the role of PPARβ/δ in metabolism has been less investigated. The recent availability of specific PPARβ/δ agonists revealed that PPARβ/δ plays a crucial role in fatty acid metabolism in several tissues. Our research group has recently demonstrated that PPAR activation exerts beneficial effects against organ-related ischemic events, such as myocardial, renal and cerebral infarction, which are among the most critical cardiovascular complications evoked by metabolic dysregulation. The most recent evidence from our lab have clearly demonstrated beneficial effects of PPARβ/δ against diet-induced obesity and insulin resistence. Overall, recent developments relating to the potential therapeutic effects of PPARβ/δ agonists in the treatment of insulin resistance and its associated cardiovascular risk factors will be comparatively discussed.

Biography

Massimo Collino, male, pharmacologist, Bachelor Degree in Pharmaceutical Chemistry and Technology at the University of Turin, (summa cum laude) in 1998 and Ph. D. in "Pharmacology and Toxicology" in 2002. Visiting Scientist at The William Harvey Research Institute, Centre for Experimental Medicine, Nephrology & Critical Care, Barts and The London, Queen Mary's School of Medicine and Dentistry, London (UK) in 2003-2004. Now,

Assistant Professor of Pharmacology and Toxicology at the Faculty of Pharmacy, University of Turin (Italy). Member of the Editorial Boards of the World Journal of Diabetes, the World Journal of Pharmacology and the Journal of Diabetes & Metabolism. Invited reviewer for several peer-reviewed scientific journals, including Diabetes; Stroke; Diabetes, Obesity and Metabolism; British Journal of Pharmacology; Biochemical Pharmacology; Journal of Cellular and Molecular Medicine, etc. Invited participant to the FRENZ Diabetes and Obesity Sandpit organized by the European Commission (5-8 July 2011, Rotorua, New Zealand). Authors of more than 35 article on the topic of the pathophysiology and experimental therapy of insulin resistance and related cardiovascular diseases.

The paper by Collino et al. (Eur. J. Pharmacol., 530: 70-80, 2006) was awarded as top-cited research paper published in 2006 by Eselvier, a leading publisher of health science books and journals.

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