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**Prof. Ilse Smolders, co-promotor**

Department of Pharmaceutical and Pharmacological Sciences, Center for Neurosciences  
Vrije Universiteit Brussel

**Prof. Richard Wainford, co-promotor**

Department of Pharmacology  
Boston University School of Medicine

PhD in Medical Sciences  
2014-2015

INVITATION to the Public defence of

**Sofie BROUWERS**

To obtain the academic degree of '**DOCTOR IN MEDICAL SCIENCES**'

**The AT<sub>2</sub>-receptor: role in central regulation of blood pressure and renal hemodynamics****Monday 8 June 2015**

Auditorium **P. Brouwer**, 17:00  
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:

<http://www.vub.ac.be/english/infoabout/campuses>



Vrije Universiteit Brussel

## Summary of the dissertation

Hypertension, contributing to cardio- and cerebrovascular morbidity and mortality, is the leading risk factor for global burden of disease. The renin-angiotensin-aldosterone system (RAAS) is one of the most important physiological pathways regulating arterial blood pressure.

Angiotensin II is the main mediator exerting its actions mainly through the angiotensin II type 1 receptor (AT1 receptor) and the angiotensin II type 2 receptor (AT2 receptor). The AT2 receptor is part of the protective arm of the renin-angiotensin-aldosterone-system, counter-regulating the cardiovascular unfavourable effects mediated by AT1 receptor stimulation. Besides the well known circulating RAAS, a local tissue RAAS was more recently discovered in different organs, including the kidney and the brain, fine-tuning the system's actions on a smaller scale. The research presented in this thesis focused on the role of the AT2 receptor in the two main blood pressure regulating organs, namely the kidney and the brain. The present results support the role of the AT2 receptor as an important element in the protective arm of the renin-angiotensin system. This receptor indeed mediates renal vasodilator effects in the hypertensive state possibly as part of a renal adaptive mechanism. In contrast with the lack of hypotensive response to peripheral AT2 receptor stimulation, we provide the first evidence for a marked depressor effect of central AT2 receptor stimulation using local administration of a specific and selective AT2 receptor agonist and conclude that the brain AT2 receptor might be a new target for the development of new antihypertensive agents providing they can pass the blood brain barrier.

## Curriculum Vitae

Sofie Brouwers was born on December 1<sup>st</sup> 1986 in Jette (Brussels). After completing her secondary education at the Koninklijk Atheneum Vilvoorde she enrolled as a student in Medicine at the Vrije Universiteit Brussel in September 2004. During this seven years education she did several international internships (Bordeaux, South Africa, Montpellier) and published her first scientific paper. She graduated with *summa cum laude* and was the 2011 'Nedeljkovitch Price' laureate, awarded to the best graduating student in the Faculty of Medicine. Her passion for internal medicine and science led her to start a PhD in hypertension research, for which she obtained a PhD grant from the 'Fonds Wetenschappelijk Onderzoek' (FWO). The project, focussing on the role of AT2 receptors in the kidney and the brain was conducted under the supervision of Prof. Dr. A. Dupont and Prof. Dr. I. Smolders. Prof. Dr. R. Wainford invited her to conduct part of her research at his laboratory at the Boston University (USA). Sofie was the 2013 laureate of the prestigious Horlait-Dapsens grant, which, together with a FWO travel grant, financed her stay in Boston from August 2013 to August 2014. The work she realized during these 4 years was summarized in 6 publications (2 as first author) and presented at many conferences, leading to several awards and grants. As a PhD candidate she combined her scientific work partly with her clinical training in the UZ Brussel. She will proceed her residency in cardiology in the coming years and intends to also continue her scientific career.