

MEETING ABSTRACT

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# GW501516, a PPAR-BETA/DELTA agonist, improves inflammatory pathways in the kidney of high-fructose fed mice

D'Angelo Carlo Magliano, Isabele Bringhenti Sarmiento, Vanessa de Souza Mello\*, Carlos Alberto Mandarim de Lacerda, Marcia Barbosa Aguila

From 20th Brazilian Diabetes Society Congress  
Porto Alegre, Brazil. 11-18 November 2015

## Background

Angiotensin-II type 1 receptor (AT1r) high activation is closely linked to a low-grade inflammation and oxidative stress that yield impaired renal function and, consequently, chronic kidney disease (CKD).

## Objectives

Therefore, the aim of this study was to verify if GW501516 could improve damage in the kidney of mice with high activation of AT1r.

## Materials and methods

To induce high activation of this receptor, mice were fed a high-fructose diet for eight weeks. The control group only received standard-chow (SC). After, the animals were randomly divided into four groups and the administration of GW501516 started and lasted three weeks. Morphological variables and urinary and plas-matic determinations were assessed. Renin and angio-tensin converting enzyme (ACE)/AT1r axis protein and gene expression were evaluated as well as inflammatory cytokines and proteins. Also, the protein and gene expression of the antioxidant enzymes were verified.

## Results

GW501516 activated PPAR-beta/delta and its target genes PDK4 and CPT-1. Despite showing no effects either on ACE/AT1r axis or renin expression, GW501516 improved the inflammatory state in the kidney. It elicits an expres-sive reduction in the expression of inflammatory genes such as IL-1 $\beta$ , IL-6, MCP-1 and Cd68, irrespective of AT1

downregulation. However, no differences were found in oxidative stress.

## Conclusions

We conclude that GW501516, a PPAR-beta/delta agonist, acts downstream AT1r activation, improving inflammatory pathways in the kidney of high-fructose fed model.

Published: 11 November 2015

doi:10.1186/1758-5996-7-S1-A121

**Cite this article as:** Magliano *et al.*: GW501516, a PPAR-BETA/DELTA agonist, improves inflammatory pathways in the kidney of high-fructose fed mice. *Diabetology & Metabolic Syndrome* 2015 **7**(Suppl 1):A121.

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\* Correspondence: [v.souzamello@gmail.com](mailto:v.souzamello@gmail.com)  
Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil