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Geneeskunde & Farmacie

GF

PhD in Pharmaceutical Sciences
2014-2015

INVITATION to the Public defence of

## Robim MARCELINO RODRIGUES

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

# Human skin-derived precursors as a novel cell source for the in vitro prediction of drug-induced liver injury

**Friday 22 May 2015**
Auditorium **Brouwer**, 17:30
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

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## Summary of the dissertation

In this dissertation postnatal stem cells isolated from human skin (hSKP) have been evaluated for their potential applicability in predicting drug-induced liver injury *in vitro*. Highly proliferative multipotent hSKP were efficiently differentiated towards hepatic cells (hSKP-HPC). These cells exhibit a mixed phenotype of mature hepatocytes and immature hepatocyte precursor cells. Characteristic hepatotoxic responses were observed upon exposure of the cells to acetaminophen (acute liver failure), sodium valproate (steatosis) and amiodarone (steatosis and phospholipidosis). The results obtained using transcriptomics analysis and functional read outs, provided convincing proof-of-principle that hSKP-HPC represent an interesting new human-based cellular model that should be further explored for the prediction of DILI *in vitro*. In the context of the examined molecules, hSKP-HPC performed similarly to primary human hepatocytes and HepaRG cells and better than the often used HepG2 cells. The presented results must, however, be confirmed by testing a more exhaustive number of hepatotoxic compounds known to induce different types of DILI.

## Curriculum Vitae

Robim Marcelino Rodrigues was born on 16th July 1976 in Luanda, Angola. He obtained a bachelor degree in chemistry from the Ghent University in 1999 and a master degree in biotechnology in 2001 from the same university.

Before starting his PhD, Robim worked for several private and public organizations. He was shortly employed as a research associate by Kline Europe, prior to moving to Mozambique to engage in humanitarian work at the United Nations-World Food Programme for almost 2 years. Hereafter, he took a position as a research associate at Beta-Cell NV, a spin-off company from the Vrije Universiteit Brussel focusing on the isolation and culturing of porcine pancreatic cells for cell therapy in diabetes. After 2.5 years, he moved to the Institute of Health and Consumer Protection of the European Commission's Joint Research Center (JRC) in Ispra, Italy where he stayed 3 years.

Robim started his doctoral studies in November 2010 at the department of In Vitro Toxicology and Dermato-cosmetology (IVTD) of the Faculty of Medicine and Pharmacy of the Vrije Universiteit Brussel under promotership of Prof. Vera Rogiers, Prof. Tamara Vanhaecke and Prof. Joery De Kock. Robim authored 15 scientific publications in international peer-reviewed journals, out of which 7 as first author. He is also first author of two book chapters and co-author of one. The results obtained during his doctoral research work were presented at several national and international scientific congresses.

Robim recently received, together with his promoters, the prestigious German research award "Forschungspreises zur Förderung methodischer Arbeiten mit dem Ziel der Einschränkung und des Ersatzes von Tierversuchen" for the work on the application of human skin-derived stem cells in hepatotoxicity screening of pharmaceuticals.