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Vrije Universiteit Brussel

FACULTEIT GENEESKUNDE EN FARMACIE

Doctoraat Medische Wetenschappen

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UITNODIGING

Voor de openbare verdediging van het
doctoraatsproefschrift van

Eduardo Linck M. Guimarães

Donderdag 28 juni 2012

U wordt vriendelijk uitgenodigd op de openbare verdediging van het proefschrift van

Eduardo Linck M. Guimarães

'Investigation of mechanisms involved in hepatic stellate cell activation in vitro'

Situering van het proefschrift

Hepatic stellate cells (HSCs) are the main contributors to the deposition of collagens during liver fibrosis. HSCs go through a process denominated activation during liver injury, where it differentiates from a quiescent lipocytic phenotype to a myofibroblastic activated one. This phenotype display high rates of proliferation, migration and expression of collagens. The study of HSC activation is therefore key in order to develop an efficient treatment for liver fibrosis.

We focused on different aspects of HSC activation and first show that advanced glycation end products, glucose-protein adducts formed in pathologies such as diabetes, can activate HSCs through NADPH-dependent reactive oxygen species production. In a subsequent study we demonstrate that autophagy is increased during activation and its inhibition hinders cell transdifferentiation. In a third part, we explore the role of mitochondria during HSC activation. Mild mitochondrial uncoupling of HSCs inhibits activation without affecting cell survival. In the final part we show that the expression of the gene P311 increases following HSC activation and its knockdown decreases HSC migration induced by different chemokines.

The inefficiency of today's therapeutic approaches against liver fibrosis may reflect the complexity of HSC biology and the fact that most treatments tackle single molecules or pathways that participate in this process. Perhaps the combination of different approaches, i.e. modulating different aspects of HSC activation simultaneously, may be more successful against disease progression.

Curriculum Vitae

Eduardo Linck M. Guimarães was born on the 22nd of January, 1980 in Porto Alegre, Brazil. After completing his bachelor in biology and master in biochemistry in the Federal University of Rio Grande do Sul, he joined the LIVR group and started a PhD under the supervision of prof. Leo van Grunsven. His work focused on molecules and pathways involved in hepatic stellate cell activation, such as advanced glycation end products and autophagy. These studies resulted in three first author publications in peer reviewed journals.

Op **donderdag 28 juni 2012** om **15 uur** in auditorium **3** van de Faculteit Geneeskunde & Farmacie Laarbeeklaan 103, 1090 Brussel