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FACULTEIT GENEESKUNDE EN FARMACIE

Doctoraat Medische Wetenschappen
Academiejaar 2010-2011

UITNODIGING

Voor de openbare verdediging van het
doctoraatsproefschrift van

Tomas BOS

dinsdag 21 december 2010

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

Tomas BOS

'Gene regulation by lentiviral vectors and epigenetic modifications in multiple myeloma'

Op **dinsdag 21 december 2010** om **17 uur**
in auditorium **P. Brouwer** van de
Faculteit Geneeskunde & Farmacie
Laarbeeklaan 103, 1090 Brussel

Situering van het proefschrift

Multiple myeloma (MM) is a devastating cancer characterized by the uncontrolled proliferation of monoclonal plasma cells in the bone marrow. There, the tumor cells are nurtured and stimulated by the microenvironment to proliferate. In this thesis, we focused on two novel techniques to study the interactions between tumor cells and the microenvironment.
Lentiviral vectors have been described as ideal shuttles to stably incorporate foreign DNA into target cells. In two projects, we aimed at optimizing the expression of multiple proteins from one single lentiviral vector. First, we pushed the lentiviral vector system by inserting increasing-sized transgenes into its 3'LTR, thus generating large double copy vectors (DCV). These DCV proved to be functional regardless the size and nature of the insert, but demonstrated a size-dependent decline in transduction efficiency. In the second project, we focused on the bicistronic lentiviral vectors. We demonstrated that the nature of this linker was responsible for the transcriptional level of the transgenes and showed that a construct containing the 2A-self-cleaving linker was superior over identical constructs containing the IRES and SIRES linkers.
In the second part of this thesis, we showed that the expression of the proapoptotic Bim-gene was directly regulated by IGF-1, one of the major growth factors involved in MM. By further dissecting the mechanisms involved in the regulation, we demonstrated that IGF-1 directly influences the post-translational histone marks at both the Bim- and FoxO3A-promoter. Finally, we showed that Bim-depletion in MM resulted in resistance to drugs commonly used to treat MM.

Curriculum Vitae

Tomas Bos (° Brussels, 30/10/1978) graduated as a Bachelor in Pharmaceutical and Biological Techniques at the 'Erasmus Hogeschool Brussel' in 2001. He obtained the degree of Master in Industrial Sciences in the field of Biochemistry and Biotechnology at the 'De Nayerinstituut', Sint-Katelijne-Waver, in 2003. During his thesis under supervision of Prof. Veerle Baekelandt at the Laboratory of Neurobiology and Gene Therapy, he was introduced and fascinated by the lentiviral vectorology. Finally, he graduated as a Master in Molecular Biology and Biotechnology at the Vrije Universiteit Brussel in 2004 and pursued a Ph.D. program at the same university with Prof. Karin Vanderkerken. His research activities focus on the development and use of lentiviral vectors and epigenetic modifications as tools to study diseases. He is author and co-author of several publications in the international scientific literature.