Short Curriculum Vitae

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Education and Professional career

2016-present Director research school Cancer Stem cells & Developmental biology (CS&D), Utrecht Graduate School of Life Sciences, Utrecht University.

2016-present Head Department Molecular Cancer Research, University Medical Center Utrecht.

2014-present Visiting professor Second College of Clinical Medicine of Guangzhou University of TCM, Guangdong Provincial Hospital of Chinese Medicine,

Guangdong Provincial Academy of Traditional Chinese Medicine, China

2011-present Collaborative Science Chair, Institute for Stem Cell Biology and Regenerative Medicine (inStem), Bangalore, India.

2011-present Head Research Department Metabolic Diseases, University Medical Center Utrecht.

2003-present Professor in the Signal transduction, Department Molecular Cancer Research University Medical Center Utrecht.

1996-2003 Assistant Professor Laboratory Physiological Chemistry-University Medical Center Utrecht

1991-1996 Post-doctoral fellow with Prof. Dr. J.L.Bos , Laboratory Physiological Chemistry-University Medical Center Utrecht

1986-1991 PhD at the Laboratory Medical Biochemistry, Leiden Title thesis: The role of p21ras in signal transduction Promoter: Prof. Dr. A.J. van der Eb and Prof. Dr. J.L.Bos

1985-1985 New York State Department of Health, Albany (NY) Dr. D. Flaherty, Molecular cloning of Qla genes

1977-1985 Landbouwhogeschool Wageningen (Agricultural University

Wageningen) Study: Molecular Sciences (cum laude)

1971-1977 Gymnasium B, Vught

Other

2011-present Reviewer ERC grants, Brussels, Belgium

2004 Elected Member Dutch consortium on Cancer Research (CGC.nl

formerly known as CBG)

2004-2010 Member Research Council Dutch Cancer Foundation (KWF)

2002 elected member EMBO

Reviewer

Nature; Nature Cell Biology; Cell; EMBO Journal; Genes & Development; Molecular and Cellular Biology; Science

Advisory Board and Memberships

2011 – Nature Communications (Nature Publishing Group) editorial Advisory Panel Member

2012 – ERC Scientific Council member and the coordinator for the Life Science domain

Organization of national and international meetings

1998 Organizer EMBO course signal transduction, Weizmann Institute, Israel

Description of Research (projects)

The PI3K/PKB(AKT)/FOXO signaling pathway

The signaling emanating from the lipid kinase PI3K is involved in a number of interesting and important cellular and organismal functions. In insulin signaling PI3K signaling drives important metabolic features and is the major pathway deregulated in insulin-dependent diabetes, when insulin signaling and hence PI3K signaling is impaired. On the other hand hyperactive PI3K signaling acts to drive many types of cancer. Diabetes and cancer are two main age-related diseases and interestingly deregulated insulin/ PI3K signaling towards the FOXO/DAF16 class of transcription factors also impacts lifespan or ageing of various model organisms. We are trying to understand this pivotal role of PI3K signaling in connecting age to disease and thus to understand how age contributes to disease in particular cancer. To this end we focus on

- (-) Transcriptional regulation of FOXO-dependent target genes
- (-) Regulation of FOXO activity by Post-translational modifications and interactions with co-factors
- (-) Biological consequences of normal and derailed PI3K/PKB(AKT/FOXO signaling
- (-) Redox control by and of FOXOs

Metabolic regulation in cancer and differentiation

We study the interaction between protein signaling networks with that of metabolic pathways. To this end we make use of various model systems and at present this is predominantly the organoid culture system. Small intestinal organoids are studied amongst others at the signal cell level by using various sensors that can monitor various aspects of metabolism. We use also all kinds of genetic perturbations in order to understand how metabolism and signaling within a single cell type contribute to the life of this cell type in the context of other cell types.

In the area of metabolism we are strongly collaborating with the MRI imaging group in the UMCU hospital, which uses 7Tesla MRI imaging to detect metabolism of cancer in patients.

All projects are highly technology driven and therefore we make use in house of all modern day technology including mass-spectrometry for proteomics and metabolomics, microscopy for live imaging etc.

Publications 2012-2016 selected

Targeted inhibition of metastatic melanoma through interference with Pin1-FOXM1 signaling.Kruiswijk F, Hasenfuss SC, Sivapatham R, Baar MP, Putavet D, Naipal KA,

van den Broek NJ, Kruit W, van der Spek PJ, van Gent DC, Brenkman AB, Campisi J, Burgering BM, Hoeijmakers JH, de Keizer PL.

Oncogene. 2015 Aug 17. doi: 10.1038/onc.2015.282. [Epub ahead of print]

FOXO target gene CTDSP2 regulates cell cycle progression through Ras and p21(Cip1/Waf1). Kloet DE, Polderman PE, Eijkelenboom A, Smits LM, van Triest MH, van den Berg MC, Groot Koerkamp MJ, van Leenen D, Lijnzaad P, Holstege FC, Burgering BM.

Biochem J. 2015 Jul 15;469(2):289-98.

FOXOs support the metabolic requirements of normal and tumor cells by promoting IDH1 expression. Charitou P, Rodriguez-Colman M, Gerrits J, van Triest M, Groot Koerkamp M, Hornsveld M, Holstege F, Verhoeven-Duif NM, Burgering BM. EMBO Rep. 2015 Apr;16(4):456-66.

Evolutionary acquisition of cysteines determines FOXO paralog-specific redox signaling. Putker M, Vos HR, van Dorenmalen K, de Ruiter H, Duran AG, Snel B, Burgering BM, Vermeulen M, Dansen TB. Antioxid Redox Signal. 2015;22(1):15-28.

The expression of the tumour suppressor HBP1 is down-regulated by growth factors via the PI3K/PKB/FOXO pathway. Coomans de Brachène A, Bollaert E, Eijkelenboom A, de Rocca Serra A, van der Vos KE, Burgering BM, Coffer PJ, Essaghir A, Demoulin JB.

Biochem J. 2014;460(1):25-34.

FOXO3 selectively amplifies enhancer activity to establish target gene regulation. Eijkelenboom A, Mokry M, Smits LM, Nieuwenhuis EE, Burgering BM. Cell Rep. 2013 26;5(6):1664-78.

FOXP1 acts through a negative feedback loop to suppress FOXO-induced apoptosis.van Boxtel R, Gomez-Puerto C, Mokry M, Eijkelenboom A, van der Vos KE, Nieuwenhuis EE, Burgering BM, Lam EW, Coffer PJ. Cell Death Differ. 2013 Sep;20(9):1219-29.

The small GTPase RALA controls c-Jun N-terminal kinase-mediated FOXO activation by regulation of a JIP1 scaffold complex. van den Berg MC, van Gogh IJ, Smits AM, van Triest M, Dansen TB, Visscher M, Polderman PE, Vliem MJ, Rehmann H, Burgering BM.

J Biol Chem. 2013 Jul 26;288(30):21729-41.

Genome-wide analysis of FOXO3 mediated transcription regulation through RNA polymerase II profiling. Eijkelenboom A, Mokry M, de Wit E, Smits LM, Polderman PE, van Triest MH, van Boxtel R, Schulze A, de Laat W, Cuppen E, Burgering BM. Mol Syst Biol. 2013;9:638.

Redox-dependent control of FOXO/DAF-16 by transportin-1. Putker M, Madl T, Vos HR, de Ruiter H, Visscher M, van den Berg MC, Kaplan M, Korswagen HC, Boelens R, Vermeulen M, Burgering BM, Dansen TB. Mol Cell. 2013;49(4):730-42.

FOXOs: signalling integrators for homeostasis maintenance. Eijkelenboom A, Burgering BM.

Nat Rev Mol Cell Biol. 2013;14(2):83-97.

Modulation of glutamine metabolism by the PI(3)K-PKB-FOXO network regulates autophagy. van der Vos KE, Eliasson P, Proikas-Cezanne T, Vervoort SJ, van Boxtel R, Putker M, van Zutphen IJ, Mauthe M, Zellmer S, Pals C, Verhagen LP, Groot Koerkamp MJ, Braat AK, Dansen TB, Holstege FC, Gebhardt R, Burgering BM, Coffer PJ.

Nat Cell Biol. 2012 Aug;14(8):829-37.

Group members

Ing Lydia Smits technician
Ing. Miranda van Triest technician
Ing Pauline Polderman technician
Drs Maaike Meerlo technician
Ing Robert van Es technician
Ing Yuen Fung Tan technician

Dr Edwin-Stigter Senior Scientist Dr. HarmJan Vos Senior Scientist Dr Sasha de Henau Post-doc Dr Maria Rodriguez-Colman Post-doc

Drs Marten Hornsveld PhD Drs Sabina van Doeselaar PhD Drs Loes van Dam PhD