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Time is of the essence - investigating kinetic interactions between drug, endogenous neuropeptides and receptor

Nederpelt, I.

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List of publications

From receptor binding kinetics to signal transduction; a missing link in predicting in vivo drug-action. I. Nederpelt, M. Kuzikov, P. Schnider, B. Tuijt, A.P. IJzerman, E.C.M. de Lange, L.H. Heitman. *Manuscript in preparation*

Kinetic Profile of Neuropeptide-Receptor Interactions. I. Nederpelt, J. Bunnik, A.P. IJzerman, L.H. Heitman. *Trends in Neurosciences* **2016** 39 (12): 830–839

Kinetic binding and activation profiles of endogenous tachykinins targeting the NK1 receptor. I. Nederpelt, D. Bleeker, B. Tuijt, A.P. IJzerman, L.H. Heitman. *Biochemical Pharmacology* **2016** 118: 88-95

Persistent GnRH receptor activation in pituitary α T3-1 cells analyzed with a label-free technology. I. Nederpelt, R.D. Vergroesen, A. P. IJzerman and L.H. Heitman. *Biosensors and Bioelectronics* **2016** 79: 721-727

Characterization of 12 GnRH peptide agonists – a kinetic perspective. I. Nederpelt, V. Georgi, F. Schiele, K. Nowak-Reppel, A.E. Fernández-Montalván, A.P. IJzerman and L.H. Heitman. *British Journal of Pharmacology* **2016** 173 (1): 128-41

Kinetics for Drug Discovery – An industry driven effort to target drug residence time. D.A. Schuetz, W.E.A. de Witte, Y.C. Wong, B. Knasmueller, L. Richter, R. Bosma, D. Kokh, S. Kashif, I. Nederpelt, E. Segala, M. Amaral, D. Guo, D. Andres, L.A. Stoddart, S. Hill, R.M. Cooke, R. Leurs, M. Frech, R. Wade, E.C.M de Lange, A.P. IJzerman, A. Müller-Fahrnow, G.F. Ecker. *Drug Discovery Today* in press

Mechanistic models enable the rational use of in vitro drug-target binding kinetics for better drug effects in patients. W.E. de Witte, Y.C. Wong, I. Nederpelt, L.H. Heitman, M. Danhof, P.H. van der Graaf, R.A. Gilissen, E.C. de Lange. *Expert Opinion in Drug Discovery* **2016** 11 (1): 45-63

Multiple binding sites for small-molecule antagonists at the CC chemokine receptor 2. A.J. Zweemer, I. Nederpelt, H. Vrieling, S. Hafith, M.L. Doornbos, H. de Vries, J. Abt, R. Gross, D. Stamos, J. Saunders, M.J. Smit, A.P. IJzerman, L.H. Heitman. *Molecular Pharmacology* **2013** 84 (4): 551-61

Curriculum Vitae

Indira Nederpelt was born in Rotterdam, The Netherlands on October 4th, 1988. After graduating high school at the IJsselcollege in Capelle aan den IJssel, she studied Biopharmaceutical Sciences at Leiden University starting in 2006. During her studies she performed two research internships under supervision of Dr. Annelien Zweemer, Dr. Laura Heitman and Prof. Dr. Ad IJzerman. These internships were both focused on designing and validating kinetic binding assays for the GnRH receptor and CCR2 receptor. Her contribution to the CCR2 project resulted in a co-publication in Molecular Pharmacology. Subsequently she moved to San Diego, CA, USA to perform a third internship at Vertex Pharmaceuticals under supervision of Akiko Nakatani and Dr. Julie Selkirk. She studied ligand selectivity at the extracellular and intracellular binding site of a tyrosine receptor kinase in an industrial setting. Upon her return to The Netherlands she finished her MSc. degree *cum laude* in 2012.

In 2013, Indira started her PhD study at Leiden University at the Department of Medicinal Chemistry, under supervision of Dr. Laura Heitman and Prof. Dr. Ad IJzerman. Her PhD research was part of an Innovative Medicine Initiative (IMI) project named Kinetics for Drug Discovery (K4DD) (grant number 115366) in collaboration with 20 partners throughout Europe in academia, small and medium-sized enterprises (SMEs) and pharmaceutical companies. This project was founded to improve measurement techniques and the understanding of ligand-receptor binding kinetics. Indira's research was focused on two G protein-coupled receptors, the GnRH receptor (a continuation of the project from her research internship) and the NK1 receptor. Throughout her PhD studies she presented the work described in this thesis at numerous national and international conference. In 2014 she was awarded the Young Investigator Award at the 11th international symposium on GnRH for best oral presentation. Later that year she was awarded for the best oral presentation at the Dutch Medicine Days in the section medicinal chemistry.

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