

CHAPTER 9

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Authors' Affiliations

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Karn Wejaphikul, Prapai Dejkhamron, Kevalee Unachak

List of Publications and Manuscripts

Wejaphikul K, Groeneweg S, Dejkhamron P, Unachak K, Visser WE, Chatterjee VK, Visser TJ, Meima ME, Peeters RP. Role of Leucine 341 in Thyroid Hormone Receptor Beta Revealed by a Novel Mutation Causing Thyroid Hormone Resistance. *Thyroid* 2018;28(12):1723-1726.

Wejaphikul K, Groeneweg S, Hilhorst-Hofstee Y, Chatterjee VK, Peeters RP, Meima ME, Visser WE. Insight into molecular determinants of T3 vs T4 recognition from mutations in thyroid hormone receptor α and β . *J Clin Endocrinol Metab* 2019;104(8):3491-3500.

Wejaphikul K, Van Gucht ALM, Groeneweg S, Visser WE, Visser TJ, Peeters RP, Meima ME. The *in vitro* functional impairment of thyroid hormone receptor alpha 1 isoform mutants is mainly dictated by reduced ligand-sensitivity. *Thyroid* 2019 (*in press*).

Wejaphikul K, Visser WE, Leeuwenburgh S, Van IJcken WFJ, Peeters RP, Meima ME. The effect of thyroid hormone receptor truncating mutants on gene transcription in neuronal cells. *Manuscript in preparation*

Meima ME, **Wejaphikul K**, Leeuwenburgh S, Van Gucht ALM, Zeneyedpour L, Dekker LJM, Visser WE, Luider TM, Peeters RP. Human liver and neuronal interactomes reveal novel binding partners for the T3 receptor isoform $\alpha 1$. *Submitted*

Wejaphikul K, Zeneyedpour L, Visser WE, Leeuwenburgh S, Luider TM, Peeters RP, Meima ME. Coregulatory protein recruitment by thyroid hormone receptors in neuronal cells. *Manuscript in preparation*

Publications not in this Thesis

Dejkhamron P, **Wejaphikul K**, Mahatumarat T, Silvilairat S, Charoenkwan P, Saekho S, Unachak K. Vitamin D deficiency and its relationship with cardiac iron and function in patients with transfusion dependent thalassemia at Chiang Mai University Hospital. *Pediatr Hematol Oncol* 2018;35(1):52-59.

Choeyprasert W, Yansomdet T, Netesirinilkul R, **Wejaphikul K**, Charoenkwan P. Adverse effects of imatinib in children with chronic myelogenous leukemia. *Pediatr Int* 2017;59(3):286-292.

Wejaphikul K, Cho SY, Huh R, Kwun Y, Lee J, Ki CS, Jin DK. Hypoparathyroidism in a 3-year-old Korean Boy with Sotos Syndrome and a Novel Mutation in NSD1. *Ann Clin Lab Sci* 2015;45(2):215-8.

PhD Portfolio

PhD Student: Karn Wejaphikul

Erasmus MC Department: Internal Medicine, Academic Center for Thyroid Diseases

Research School: Molecular Medicine

PhD period: 2015-2019

Promotor: Prof.dr. Robin P. Peeters

Co-promoters: Dr. Marcel E. Meima

Dr. W. Edward Visser

PhD Training	Year	Workload	ECTs
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Courses & Workshops

Stralingsbeschermings-deskundigheidsniveau 5B	2015	3 days	1.0
Introduction to GraphPad Prism	2015	1 day	0.3
The Basic Human Genetic course: Genetics for Dummies	2015	2 days	0.5
The Course Biomedical Research Techniques XIV	2015	5 days	1.5
The Annual Course on Molecular Medicine	2016	2 days	0.7
Biostatistic course CCO2A 2016	2016	4 days	2.0
The 6 th course Basic and Translational Endocrinology: "Emerging Technologies in Endocrine Research"	2016	3 days	1.0
Research Integrity	2017	1day	0.3
The Workshop on Photoshop & Illustrator CS6 for PhD-students and other researchers	2017	1 day	0.3
The SNP Course XIV: SNPs and Human Diseases	2017	5 days	2.0
The course in English Biomedical Writing and Communication	2017	10 weeks	3.0
The Ensembl Workshop	2018	2 days	0.6
The Workshop on NCBI & other open source software	2018	3 days	1.0
The Workshop on InDesign CC 2019 for PhD-students and other researchers	2019	1 day	0.3

Oral presentations

Dutch Endocrine Society Meeting 2016, Noordwijkerhout, The Netherlands: <i>The Activity of T3 Receptor Mutants on Different T3 Response Elements</i>	2016		0.7
39 th Annual Meeting of the European Thyroid Association (ETA), Copenhagen, Denmark: <i>Variably Defective Transcriptional Activity of T3 Receptor TRα1 Mutants in Different Thyroid Hormone Response Elements</i>	2016		0.7

PhD Training	Year	Workload	ECTs
9 th Biennial Scientific Meeting of the Asia Pacific Pediatric Endocrine Society (APPES): <i>Comprehensive Steroid Profile in Classic 21-Hydroxylase Deficiency: Clinical and Hormonal Correlation</i>	2016		0.7
3 rd JNVE conference 2016, Leiden, The Netherlands: <i>A Novel L341V Mutation of the Thyroid Hormone (TH) Receptor β Gene in a Girl with Resistance to TH</i>	2016		0.7
Wetenschapsdagen (Science Day) 2017, Antwerp, Belgium: <i>A Novel L341V Mutation of the Thyroid Hormone (TH) Receptor β Gene in a Girl with Resistance to TH</i>	2017		0.7
Dutch Endocrine Society Meeting 2017, Noordwijkerhout, The Netherlands: <i>A Novel L341V Mutation of the Thyroid Hormone (TH) Receptor β Gene in a Girl with Resistance to TH</i>	2017		0.7
The Internal Medicine Research Symposium: <i>Diverse Functional Impairment of Thyroid Hormone Receptor Alpha (TRα) Mutations</i>	2017		0.4
40 th Annual Meeting of the European Thyroid Association (ETA), Belgrade, Serbia: <i>Diverse Functional Impairment of Thyroid Hormone Receptor Alpha Mutations</i> (Topic Highlight)	2017		0.7
4 th JNVE conference 2017, Leiden, The Netherlands: <i>Diverse Functional Impairment of Thyroid Hormone Receptor Alpha Mutations</i>	2017		0.7
33 rd Workshop on Experimental Thyroid Research (Arbeitstagung Experimentelle Schilddrüsenforschung, AESF), Berlin, Germany: <i>How to Study Functions of Mutated Thyroid Hormone Receptors (TRs)?</i> (invited speaker)	2018		0.7
13 th International Workshop on Resistance to Thyroid Hormone (IWRTH) Meeting 2018, Doorn, The Netherlands: <i>Naturally Occurring Mutations in Thyroid Hormone Receptors Highlight T3 versus T4 Recognition</i>	2018		0.7
41 st Annual Meeting of the European Thyroid Association (ETA), Newcastle, United Kingdom: <i>A Novel THRA M256T Mutation in Resistance to Thyroid Hormone Alpha Highlights T3 versus T4 Recognition of Thyroid Hormone Receptors</i>	2018		0.7
10 th Asia Pacific Paediatric Endocrine Society (APPES) Scientific Meeting, Chiang Mai, Thailand: <i>A Resistance to Thyroid Hormone α Patient with a Novel THRA M256T Mutation Lacking T3 versus T4 Discrimination</i>	2018		0.7
Dutch Thyroid Club Meeting, Nijmegen, Rotterdam: <i>Coregulatory Protein Recruitment by Thyroid Hormone Receptors in Neuronal Cells</i>	2019		0.7
Dutch Endocrine Society Meeting 2019, Noordwijkerhout, The Netherlands: <i>Coregulatory Protein Recruitment by Thyroid Hormone Receptors in Neuronal Cells</i>	2019		0.7

PhD Training	Year	Workload	ECTs
<u>Poster presentations</u>			
Wetenschapsdagen (Science Day) 2016, Antwerp, Belgium: <i>The Activity of T3 Receptor Mutants on Different T3 Response Elements</i>	2016		0.7
20 th Molecular Medicine Day 2016: <i>The Activity of T3 Receptor Mutants on Different T3 Response Elements</i>	2016		0.7
12 th International Workshop on Resistance to Thyroid Hormone (IWRTH), Colorado, USA: <i>Diverse Transcriptional Activation Patterns of Thyroid Hormone Receptor Alpha Mutations on Different Thyroid Response Elements</i>	2016		0.7
86 th Annual Meeting of the American Thyroid Association (ATA), Denver, USA: <i>A Novel L341V Mutation of the Thyroid Hormone (TH) Receptor β Gene in a Girl with Resistance to TH</i> (Basic poster award winner)	2016		0.7
9 th Biennial Scientific Meeting of the Asia Pacific Pediatric Endocrine Society (APPES): <i>GnRH-independent Precocious Puberty in a Thai Boy with NR0B1 Novel Mutation Causing X-linked Adrenal Hypoplasia Congenita</i>	2016		0.7
The 10 th Benelux Nuclear Receptor meeting, Leuven, Belgium: <i>Variably Defective Functional Properties of Thyroid Hormone Receptor Alpha Mutations</i>	2017		0.7
Wetenschapsdagen (Science Day) 2018, Antwerp, Belgium: <i>Resistance to Thyroid Hormone due to Novel THRA M256T Mutation</i>	2018		0.7
10 th Asia Pacific Paediatric Endocrine Society (APPES) Scientific Meeting, Chiang Mai, Thailand: <i>Clinical Features and Genetic Analysis of Patients with Resistance to Thyroid Hormone β: A single-center experience</i>	2018		0.7
Wetenschapsdagen (Science Day) 2019, Sint-Michielsgestel, the Netherlands: <i>Coregulatory Protein Recruitment by Thyroid Hormone Receptors in Neuronal Cells</i>	2019		0.7
<u>Conferences</u>			
54 th Annuals European Society for Paediatric Endocrinology (ESPE) Meeting, Barcelona, Spain	2016	3 days	
The 8 th Benelux Nuclear Receptor meeting, Leiden, The Netherlands	2016	1 day	
Wetenschapsdagen (Science Day) 2016, Antwerp, Belgium	2016	2 days	
Dutch Endocrine Society Meeting 2016, Noordwijkerhout, The Netherlands	2016	2 days	
20 th Molecular Medicine Day 2016	2016	1 day	
39 th Annual Meeting of the European Thyroid Association (ETA), Copenhagen, Denmark	2016	4 days	

PhD Training	Year	Workload	ECTs
12 th International Workshop on Resistance to Thyroid Hormone (IWRTH), Colorado, USA	2016	4 days	
86 th Annual Meeting of the American Thyroid Association, Denver, USA	2016	5 days	
9 th Biennial Scientific Meeting of the Asia Pacific Pediatric Endocrine Society (APPES)	2016	4 days	
3 rd JNVE conference 2016, Leiden, The Netherlands	2016	2 days	
Wetenschapsdagen (Science Day) 2017, Antwerp, Belgium	2017	2 days	
Dutch Endocrine Society Meeting 2017, Noordwijkerhout, The Netherlands	2017	2 days	
40 th Annual Meeting of the European Thyroid Association, Belgrade, Serbia	2017	4 days	
4 th JNVE conference 2017, Leiden, The Netherlands	2017	2 days	
The 10 th Benelux Nuclear Receptor meeting, Leuven, Belgium	2017	1 day	
Wetenschapsdagen (Science Day) 2018, Antwerp, Belgium	2018	2 days	
33 rd Workshop on Experimental Thyroid Research (Arbeitstagung Experimentelle Schilddrüsenforschung, AESF), Berlin, Germany	2018	3 days	
13 th International Workshop on Resistance to Thyroid Hormone (IWRTH) Meeting 2018, Doorn, The Netherlands	2018	4 days	
41 st Annual Meeting of the European Thyroid Association, Newcastle, United Kingdom	2018	4 days	
10 th Asia Pacific Paediatric Endocrine Society Scientific Meeting, Chiang Mai, Thailand	2018	4 days	
Wetenschapsdagen (Science Day) 2019, Sint-Michielsgestel, the Netherlands	2019	2 days	
Dutch Thyroid Club Meeting, Nijmegen, Rotterdam	2019	½ day	
Dutch Endocrine Society Meeting 2019, Noordwijkerhout, The Netherlands	2019	2 days	
<u>Seminars and Meetings</u>			
Thyroid Laboratory Meeting	2015-2019		1.0
Annual Symposium of the Dutch Thyroid Research Foundation	2015-2019		0.7
The Internal Medicine Research Symposium	2016-2019		0.4
<u>Teaching Activities</u>			
6 th course Basic and Translational Endocrinology: "Emerging Technologies in Endocrine Research" (Lecturing: Thyroid Hormone Resistance due to Mutations in Thyroid Hormone receptors)	2016	1 day	0.3

PhD Training	Year	Workload	ECTs
<u>Other Academic Activities</u>			
Co-chair of oral presentation session in Wetenschapsdagen (Science Day) 2018, Antwerp, Belgium	2018		
Judging committee for poster-prize in Wetenschapsdagen (Science Day) 2019, Sint-Michielsgestel, the Netherlands	2019		
<u>Grants and Awards</u>			
ETA Travel Award Grant (for Young Investigator) 2016 (500€)	2016		
ATA Travel Grant 2016	2016		
ATA Trainee Poster Award 2016 (The winner of Basic Poster)	2016		
ETA Travel Award Grant 2017 (500€)	2017		
ETA Travel Award Grant 2018 (500€)	2018		

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The completion of my PhD would not have been possible without the support of my co-promotor and daily supervisor, **Dr. M.E. Meima**. Dear Marcel, how can I find enough words to thank you for all the things you have done for me? I have learned a lot from you, especially the laboratory skills that I had no experience before. Not only that, you always be there to support me whenever I want, which made me feel very secure. You also helped me to improve my writing and presenting skills, which are vital for my future career. Thank you for your patient guidance and all of your brilliant ideas and suggestions. I also appreciate your sense of humor and easy-going personality, which made me (and everybody in the lab) feel very comfortable to work with you. It was very fortunate for me to have you as my supervisor.

I am also extremely grateful to my second co-promotor, **Dr. W.E. Visser**. Dear Edward, thank you very much for your significant contribution to my research. It was an excellent opportunity for me to work with you. Thanks also for your kindness and your profound belief in my work. I really appreciate it.

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Four and a half years in Rotterdam would have been worse than this if I had not had these lovely Thai people around. Dear **Aung**, you were such a fantastic roommate. I believe it was a destiny that brought us to reunite and had memorable moments together. It was always fun to talk nonsense and watch Toey-Taew-Thai (and so on) together. You were also the one who dragged me to the gym and built my exercise habits. Thanks for sharing with me all the good and the bad. Thanks also for the beautiful thesis cover. I wish you all the best in your PhD. Keep in touch and see you in CM soon. Dear **P'Ann**, thank you so much for all of your help and practical advice since my first day in R'dam. Although we did not hang out together so much afterward (because you were always super busy), you still kept concerning about me and all Thai students. See you in CM very soon. Dear **Keng**, I was so lucky to have you on the same floor and extremely happy to have you as a paronymph. You were very supportive and always tried your best to help me and everybody to solve all the issues we have, which I very much appreciate. Now you are approaching the finish line, and I am sure you will do great. Good luck with that. Dear **Dew**, thank you so much for being a kind and supportive sister. I have to congratulate you as well for your magnificent achievement. Next chapter now officially begins. I wish you lots of success. Dear **Utt**, although we had hardly talked when we were in med school together, we managed to be very close now. It is brilliant to see you are doing

better and better in your PhD trajectory. Do not give up. You will rock it. Dear **Nook, Jan, Kib,** and **Ply**, you guys made my days in R'dam more enjoyable. I wish you all the best for your PhD and your future career. Please stay in touch and see you again in Thailand.

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About the Author

Karn Wejaphikul was born on 6 May 1983 in Chiang Mai, Thailand. In 2001, he graduated from Chiang Mai University Demonstration School in his home town. He started his Medical Training at Faculty of Medicine, Chiang Mai University and obtained his medical degree (First-Class Honors, Gold Medal) in 2007. After that, he completed a four-year Pediatrics training at Chiang Mai University Hospital, Chiang Mai, Thailand and obtained the Thai Board of Pediatrics in 2011. He then attained a two-year Pediatric



Endocrinology training at King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand and received his Thai Subboard of Pediatric Endocrinology in 2013. Afterward, he started working as an instructor in Pediatric and Pediatric Endocrinologist at Chiang Mai University Hospital. During that time (2014), Karn was awarded a scholarship from Samsung Medical Center to be a visiting fellow in Pediatric Endocrinology and Medical Genetics for three months at Samsung Medical Center, Seoul, Republic of Korea. In 2015, he started his PhD project at the Academic Center for Thyroid Diseases, Erasmus MC, under the supervision of Prof.dr. Robin P. Peeters, Dr. Marcel E. Meima, and Dr. W. Edward Visser. The results of his research are presented in this PhD thesis entitled "Complexity of genomic actions controlled by thyroid hormone receptors".

