The molecular basis of metabolic syndrome: studies in zebrafish

Nowik, N.

List of Abbreviations

AB/TL: AB/Tupfel long fin
BMI: body mass index
Cas9: CRISPR associated protein 9
CFU: colony forming units
COPAS: Complex Object Parametric Analyzer and Sorter
CRISPR: Clustered regularly interspaced short palindromic repeats
DAVID: The Database for Annotation, Visualization and Integrated Discovery
DM: diabetes mellitus
DMSO: Dimethyl sulfoxide
dpf: days post fertilization
dpi: days post infection
hpf: hours post fertilization
HRL: human recombinant leptin
lep: leptin
Mm/tb: Mycobacterium marinum/ tuberculosis
MO: morpholino
qPCR: quantitative PCR
PTPN: Tyrosine Phosphatase, Non-Receptor Type
PTPs: protein tyrosine phosphatases
T2DM: type 2 diabetes mellitus
TB: tuberculosis
Tg: transgenic
WT: wild-type

Curriculum vitae

Natalia Nowik was born in Olsztyn, Poland on August 31, 1987. After graduating from No. III High school in Olsztyn in 2006, she started a 6-years program in veterinary medicine at the Faculty of Veterinary Medicine, University of Warmia and Mazury (UWM) in Olsztyn.

In 2009, during the second year of the studies, she started a one year internship at the Laboratory of Genomics and Transcriptomics under the supervision of dr. Piotr Podlasz, where she conducted research on the role of the neuropeptide galanin using zebrafish as the model organism. She was awarded a prize for her scientific work as a young researcher in a poster session of Veterinary Medicine and Animal Based Products Section for young scientists.

After graduation in 2012, she moved to the Netherlands, where she worked as a veterinarian and a food production specialist. In 2014 she joined dr. Podlasz's group again and after a few months, in 2015, she started her scientific project, as a guest researcher, at dr. Spaink's lab. One year later she was admitted as a Ph.D. candidate at the Institute of Biology, Leiden University. In 2017 she won a grant, PRELUDIUM 11, funded by the Polish National Science Centre that is a prestigious funding opportunity intended for pre-doctoral researchers about to embark on their scientific career. The work done during her time at Leiden University is presented in this thesis.

List of Publications

Nowik N, Prajsnar TK, Przyborowska A, Rakus K, Sienkiewicz W, Spaink HP, Podlasz P. The Role of Galanin during Bacterial Infection in Larval Zebrafish. *Cells*. 2021 Aug 6;10(8):2011. doi: 10.3390/cells10082011.

Ding Y, Haks MC, Forn-Cuní G, He J, **Nowik N**, Harms AC, Hankemeier T, Eeza MNH, Matysik J, Alia A, Spaink HP. Metabolomic and transcriptomic profiling of adult mice and larval zebrafish leptin mutants reveal a common pattern of changes in metabolites and signaling pathways. *Cell Biosci*. 2021 Jul 7;11(1):126.

He J, Ding Y, **Nowik N**, Jager C, Eeza MNH, Alia A, Baelde HJ, Spaink HP. Leptin deficiency affects glucose homeostasis and results in adiposity in zebrafish. *J Endocrinol*. 2021 May;249(2):125-134.

Nowik N, Przyborowska A, Sienkiewicz W, Podlasz P. Protective Role of Galanin during Chemically Induced Inflammation in Zebrafish Larvae. *Biology* (Basel). 2021 Jan 30;10(2):99.

Podlasz P, Jakimiuk A, Chmielewska-Krzesinska M, Kasica N, **Nowik N**, Kaleczyc J. Galanin regulates blood glucose level in the zebrafish: a morphological and functional study. *Histochem Cell Biol*. 2016 Jan;145(1):105-17.

Nowik N, Podlasz P, Jakimiuk A, Kasica N, Sienkiewicz W, Kaleczyc J.Zebrafish: an animal model for research in veterinary medicine. *Pol J Vet Sci*. 2015;18(3):663-74.

Podlasz P, Sallinen V, Chen YC, Kudo H, **Fedorowska (Nowik) N**, Panula P. Galanin Gene Expression and Effects of Its Knock-Down on the Development of the Nervous System in Larval Zebrafish. *J Comp Neurol*. 2012 Dec 1;520(17):3846-62.

Acknowledgments

It would be impossible to write this thesis without help of many people that supported me in many different ways during my PhD project.

Foremost, I would like to thank my promotors prof. dr. Herman Spaink and dr. Marcel Schaaf for supporting and helping me during all this time. Thank you, Herman, for giving me this chance and supervising me through all these years. As your PhD student, I really appreciate your positive attitude and professionalism. You are not only a prominent researcher, but also a great person. Marcel, you are a really dedicated supervisor that takes all the responsibilities very serious. Thank you for all your help and mentoring. Your professionalism and friendly attitude makes coo peration with you a pleasure.

I would like to thank prof. dr. Annemarie Meijer and prof. dr. Ewa Snaar-Jagalska for their support and scientific discussions during our weekly meetings. Your suggestions and ideas had a substantial contribution to my scientific work.

When I have started my work at IBL, the first person that I met was Wouter whom I want to thank for being my mentor during the first months of my stay. Thanks to you, I have learnt all the necessary techniques that helped me to build up my scientific work presented in this thesis. Arwin, Claudia and Lanpeng, thanks to you my first days in Leiden went smoothy, and I immediately felt welcomed. I would also like to thank all the people in the lab: Shuxin, Yasuhito, Quanchi, Kelly, Hurzos, Elena, Samrah, Vincenzo, Rui, Tomek, Bjørn, Natalia, Ralf, Monica, Yufei, Radek, Salome, Gabriel, Mahmoud, Marlon, Francisco (Panchito) and Michiel. Min and Hilda thank you for our scientific and non-scientific chats when we were sitting in the same office. I still miss those days and your companionship. I cannot skip Saskia who has always been kind and helpful. I am still missing her stories about life in Uganda; I wish these memories were published one day. Thank you Retno and Cikra for our time together. It was a pleasure working with you. And finally, thank you Wanbin and Yi for being in one team with me. You are very talented young researchers, do not miss your opportunities.

I am deeply grateful for my students, I mentored during my PhD. This experience ta ught me a lot, not only about science, but also about myself. It was not an easy task as we had many ups and downs, but I hope that you all remember it as a good time. Many thanks Charlotte, Joyce, Monisha and Roxan. I wish you all the best in the future.

My scientific work could not be finished without the zebrafish team. Karin, Guus, Urlike, Michelle, Corrina you are a fantastic people. Thank you for all the fun that we had together.

My sincere thanks go to dr. Piotr Podlasz who showed me the zebrafish w orld and, without whom, I would not be where I am now.

PhD is not only about science, but also friendship. Thank you, Frida, for being there with me through all these years. You were (and still are) my mental support during hard times. I wish we could work together in the future again.

I am grateful to all members of my Promotion Committee for reviewing my manuscript. Piotr thank you very much for the extensive feedback that you provided.

Last but not least, I would like to thank those closest to me. Mom and Dad, thank you for your love and for believing in me. Pawel you are not only my husband, but also my best friend. I am grateful for your support and love, I would not achieve it without you. I would like to thank my sister Paulina for always being there for me and my daughter Lena for showing me different aspects of life.