Towards a mechanistic understanding of nanoparticle behavior using zebrafish

Arias Alpizar, G.

Biography

Gabriela Arias Alpízar was born on April 22, 1984 in San José, Costa Rica. In 2005, she obtained a Bachelor of Science in Pharmacy degree followed by a Licentiate (Master's) degree in Pharmacy in 2008, from the University of Medical Sciences (Universidad de Ciencias Médicas, UCIMED) in Costa Rica. Subsequently, she worked as a pharmacist for about 2 years and represented GlaxoSmithKline as a medical advisor for almost a year.

After moving from Costa Rica to The Netherlands and motivated to contribute as a scientific researcher, she obtained a Master's degree in "Drug Discovery and Safety" in the research track of "Target Finding" at the *Vrije* University Amsterdam in 2015. During this program, two masters internships were performed at the Amsterdam Institute for Molecules, Medicines and Systems (AIMMS), in the Division of BioAnalytical Chemistry Department and in the Division of Medicinal Chemistry Department, *Vrije* University Amsterdam. The first focused on the optimization and validation of an at-line high resolution screening methodology to separate and identify bioactive compounds from complex mixtures. In the second internship, radioligand binding assays and functional assays were optimized and validated to pharmacologically characterize zebrafish histamine3-like receptors and compare them to human orthologues.

In February 2016, she started a PhD research in the Supramolecular & Biomaterials Chemistry group in Leiden Institute of Chemistry (LIC), Leiden University under supervision of Prof. Dr. Alexander Kros, Dr. Jeroen Bussmann and in close collaboration with the Institute of Biology Leiden (IBL), under supervision of Prof. Dr. Herman Spaink. She focused on understanding the fundamental behavior of nanoparticles *in vivo* and investigating interactions associated by using the zebrafish embryo as a model, as described in this thesis. She presented parts of the work described in this dissertation in several (inter)national meetings and conferences and was awarded in two occasions with a poster prize. During her PhD, she also supervised Bachelor and Master students and was involved in teaching of practical academic courses.

Since June 2020, Gabriela has been working as a research scientist in the Leiden Academic Centre for Drug and Research (LACDR), at the Biotherapeutic Division with Prof. Dr. Wim Jiskoot and Dr. Jeroen Bussmann, where she will continue the research identifying the role of other receptors in the mechanism of nanoparticles in circulation using different *in vivo* models.

This work was presented at the following meetings:

Oral Presentations

Nanobio&Med, Barcelona **2019**. "Fundamental behavior of nanoparticles revealed in zebrafish".
CHAINS, Veldhoven **2019**. "Liposomes targeting the BBB *in vivo*"
ESM-EVBO European Vascular Biology meeting, Maastricht **2019.** "Unraveling the selective accumulation of unusual liposomes to the BBB in the zebrafish".
CHAINS, Veldhoven **2017.** "Selective blood vessel deletion through Stabilin2-dependent nanoparticle uptake *in vivo*".

Poster Presentations

CHAINS, Veldhoven **2019.**
Belgian-Dutch Biopharmacy, Ghent **2019**.
CHAINS, Veldhoven **2018**. (**Awarded**).
Germany-Dutch Microvascular biology meeting, Amsterdam **2018**. (**Awarded**).
FIGON Innovative Drug Research, Ede **2018**.
ZDM11 Zebrafish Disease Models Congress, Leiden **2018.**
FIGON Innovative Drug research, Ede **2017**.
The European zebrafish meeting, Budapest **2017.**
Annual BBBnedwork meeting "Barrier of the brain in ageing", Leiden **2017.**
Reedijk Symposium, Leiden **2017.**

List of publications

Manuscripts described in this thesis:

Arias-Alpizar, G.*; Papadopoulou, P.*; Rios, X.; Moradi, M.A.; Pattipeiluhu, R.; Bussmann, J.; Sommerdijk, N.; Llop, J.; , J.; Kros, A.; Campbell, F., Phase-Separated, "Parachute" Liposomes Hijack a Triglyceride Lipase-Mediated Lipid Transport and Metabolism Pathway to Selectively Target Endothelial Cells *in vivo*. **Manuscript in preparation.**

Pattipeiluhu, R.*; **Arias-Alpizar, G.***; Basha, G.; Bussmann, J.; Sharp, T.H.; Moradi, M.A.; Sommerdijk, N.; Cullis, P.R.; Kros, A.; Campbell, F., Anionic Lipid Nanoparticles Preferentially Deliver mRNA to the Hepatic Reticuloendothelial System. **Submitted.**

Arias-Alpizar, G.; Bussmann, J.; Campbell, F., Zebrafish as a predictive animal model to study nanoparticle behavior *in vivo*. *Bio-Protocols.* **2021,** 4173.

Arias-Alpizar, G.; Koch, B.; Hamelmann, N. M.; Neustrup, M. A.; Paulusse, J. M. J.; Jiskoot, W.; Kros, A.; Bussmann, J., Stabilin-1 is required for the endothelial clearance of small anionic nanoparticles. *Nanomedicine: Nanotechnology, Biol. Med.* **2021**, 34, 102395.

Arias-Alpizar, G.*; Kong, Li*; Vlieg, R.; Rabe, A.; Papadopoulou, P.; Meijer, M.S.; Bonnet, S.; Vogel, S.; van Noort, J.; Kros, A.; Campbell, F., Light-triggered switching of liposome surface charge directs the intracellular delivery of membrane impermeable payloads *in vivo*. *Nat Comm* **2020,** 11 (1), 3638.

Campbell, F.; Bos, F. L.*; Sieber, S*.; **Arias-Alpizar, G.***; Koch, B. E.; Huwyler, J.; Kros, A.; Bussmann, J., Directing Nanoparticle Biodistribution through Evasion and Exploitation of Stab2-Dependent Nanoparticle Uptake. *ACS Nano* **2018,** 12, 2138-2150.

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Other publications:

Saez Talens*, V.; **Arias-Alpizar, G***.; Makurat, D. M. M.; Davis, J.; Bussmann, J.; Kros, A.; Kieltyka, R. E., Stab2-Mediated Clearance of Supramolecular Polymer Nanoparticles in Zebrafish Embryos. *Biomacromolecules* **2020,** *21*, 1060-1068.

Otvos, R. A.*; Mladic, M.*; **Arias-Alpizar, G.**; Niessen, W. M.; Somsen, G. W.; Smit, A. B.; Kool, J., At-Line Cellular Screening Methodology for Bioactives in Mixtures Targeting the Alpha7-Nicotinic Acetylcholine Receptor. *J Biomol Screen* **2016,** *21*, 459-467.

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