Ginsenosides as selective glucocorticoid drugs: agonists, antagonists, and prodrugs

Halima, M.

Curriculum Vitae

Mahmoud Halima was born on October 15th, 1981, in Al Nabek, a suburb of Damascus, Syria. After graduating from Alsaada School, he started a Doctor of Veterinary program at the Faculty of Albaath University in 1999. He obtained his degree in 2003 and worked in the Pathological Diagnostic Laboratory until 2005. Subsequently, he worked in an Arab Qatar company for poultry production until 2006. After this, he joined the Pharmacology lab of the Higher Institute for Science and Applied Technology in Damascus until 2012. During this period, he worked on developing an antidote against snake venom and a novel oxime for treating nerve agent poisoning. During the same period, he followed a Doctor of Medicine program and a Ph.D. program in toxicology at Damascus University. He obtained a degree as a Doctor in Medicine in 2010. Unfortunately, he submitted his thesis, but could not get a Ph.D. certificate due to the start of the war in Syria. He escaped to Jordan in 2012 as a political refugee. He worked in a Medical Center treating Syrian refugees until 2013. Then, he traveled to Turkey and worked as Consultant-Scientific Director at the Ultra Group for Veterinary Medicine until September 2014. He traveled to the Netherlands in the same year, studied Dutch, and volunteered at 's Heeren Loo Noordwijk Center, introducing services for disabled patients. He started an MSc program in Biomedical Sciences at Utrecht University in February 2017 and graduated in September 2018. During his MSc study, he performed a research project under the supervision of Dr. Hamed el Azzouzi in the Heart and Lung Department at the University Medical Center Utrecht. He studied the effects of BLU-554 as a specific inhibitor for FGFR4 in cardio-renal syndrome in mice. Subsequently, he performed a research project at Leiden University in the Institute of Biology Leiden (IBL) under the supervision of Dr. Mei Wang. Here, he studied the anti-inflammatory effects of ginsenoside Rg1 in the zebrafish model. In March 2019, he started his Ph.D. program at IBL under the supervision of Prof. Dr. Annemarie Meijer, Dr. Marcel Schaaf, and Dr. Mei Wang. In his project, he studied the mechanisms-of-action of ginsenosides using a combination of cellular, zebrafish, and mouse models. The results presented in this thesis show how an increased understanding of the effects of ginsenosides has opened the door to the development of more selective glucocorticoid drugs.

List of Publications

1. Sun, M.; He, M.; Korthout, H.; **Halima, M**.; Kim, H.; Yan, Y.; Wijk, E.; Wijk, R.; Guo, C.; Wang, M. Characterization of ginsenoside extracts by measuring delayed luminescence, high- performance liquid chromatography and bioactivity tests. *Photochem. Photobiol. Sci.* **2019**, *18*, doi:10.1039/C8PP00533H.

2. He, M.; **Halima, M***.; Xie, Y.; Schaaf, M.J.M.; Meijer, A.H.; Wang, M. Ginsenoside Rg1 Acts as a Selective Glucocorticoid Receptor Agonist with Anti-Inflammatory Action without Affecting Tissue Regeneration in Zebrafish Larvae. *Cells* **2020**, *9*, doi:10.3390/cells9051107. *Shared first author

3. Xiong, Y.; **Halima, M***.; Che, X.; Zhang, Y.; Schaaf, M.J.M.; Li, M.; Gao, M.; Guo, L.; Huang, Y.; Cui, X.; et al. Steamed Panax notoginseng and its Saponins Inhibit the Migration and Induce the Apoptosis of Neutrophils in a Zebrafish Tail-Fin Amputation Model. *Front. Pharmacol.* **2022**, *13*, 946900, doi:10.3389/fphar.2022.946900. *Shared first author

4. Kroos, S.; **Halima, M***.; Kroon, J.; van der Woude, D.; Meijer, O.C.; van de Wal, M.D.; Verhave, P.S.; Schaaf, M.J.M.; Toes, R.E.M.; Kampstra, A.S.B. Tramadol/paracetamol treatment attenuates the development of collagen antibody-induced arthritis and interferes with prednisolone treatment in mice. *Lab. Anim.* **2023**, 00236772231166029, doi:10.1177/00236772231166029. *Shared first author

5. **Halima, M**.; Schaaf, M.J.M.; Meijer, A.H.; Wang, M. Ginsenosides as promising anti-inflammatory drugs: past and future. *Submitted*.

6. **Halima, M**.; Al Ayed, K.; Kroos, S.; Kampstra, A.S.B.; Lelieveld, L.T.; Narayanan, A.; Mujumdar, S.; Štravs, A.; Sunil Kumar, S.; He, Y.; Harms, A.C.; Hankemeier, T.; Van der Woude, D.; Wang, M.; Aerts, J.M.F.G..; Toes, R.E.M.; Martin, N.I.; Meijer, A.H.; Schaaf, M.J.M. The enzyme Glucosylceramidase Beta 2 targets glycosylated glucocorticoid prodrugs to inflamed tissue. *Submitted*.

Patent

Schaaf, M.J.M.; Meijer, A.H.; **Halima, M**.; Wang, M.; Aerts, J.M.F.G.; Martin, N.I.; Al Ayed, K. International Application No. PCT/NL2022/050621. Glycosylated Prodrugs. *Leiden University.* 02-11-**2022**.