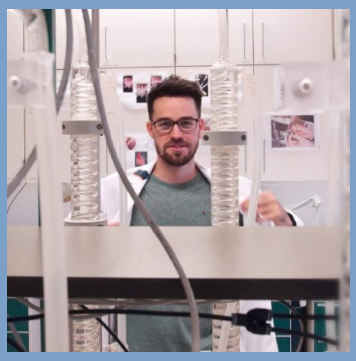


DALIBOR NAKLADAL

Comenius University
Science park

Project number
3333/03/02

Project duration
9/2022 - 8/2025

BIOGRAPHY

Dalibor Nakládal was born in Benešov near Prague, Czechoslovakia. He studied Pharmacy at the Comenius University in Bratislava, and completed an internship at Nova Southeastern University in Florida, United States. For his US-based master thesis employing computational approaches to identify a blood-based genomic signature for autism spectrum disorders, the fellow won recognition from the rector of Comenius University in Bratislava. After graduating in 2015, he began a sandwich-PhD track at two institutions. Namely at the Department of Clinical Pharmacy and Pharmacology at the University Medical Center Groningen (UMCG), The Netherlands, and at the Department of Pharmacology and Toxicology, Comenius University in Bratislava, Slovakia, where he was supervised by professor Ján Kyselovič. The combined arrangement yielded two dissertation theses, and the fellow defended his first PhD thesis in 2019 in Bratislava, and second in 2022 in Groningen. Between 2020-2022 the fellow completed a postdoc project focused on public-private drug development that was funded by the UMCG, the Health~Holland Top Consortia for Knowledge and Innovation, and the Dutch companies Sulfateq and Symeres. In 2022 he started working as an expert for technology transfer and intellectual property at the Slovak Centre of Scientific and Technical Information, and at the Comenius University Science Park in Bratislava with the goal to build a robust research environment with re-usable drug development pipelines for phenotypic screening and target-based drug discovery. In the awarded SASPRO2 project, he will strive to develop new drugs for the treatment of diabetic kidney disease.

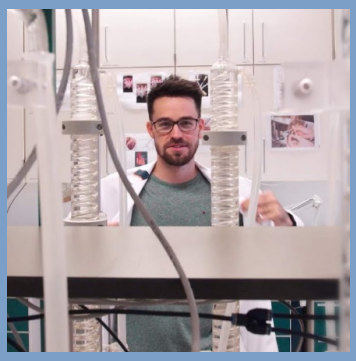
PROJECT SUMMARY

Discovery and development of new drugs for treatment of diabetic kidney disease: counteracting transsulfuration deficiency to improve defense against oxidative stress

Despite leaps in control of glycemia, patients with diabetes of types 1 and 2 still face damage to major organs with costly and debilitating injuries to heart, eyes, and kidneys. Especially kidney injury (diabetic nephropathy; DN) often progresses into chronic kidney disease, driving the ever-increasing global requirement for renal replacement therapy (dialysis, transplantation). Organ dysfunction in diabetes is rooted in excess oxidative stress and consequent vascular dysfunction. Notably, DN patients have deficient production of the antioxidant glutathione. In addition, decreased production of the antioxidant hydrogen sulfide (H_2S) contributes to the pathogenesis of DN. Both glutathione and H_2S are synthesized by the transsulfuration pathway, an amino-acid metabolic route controlled by the enzyme Cystathionine-β-synthase (CBS). Importantly, CBS activity is increased by binding of some endogenous compounds in a process called allosteric modulation. The current proposal aims to discover and develop novel drugs that exploit allosteric activation of CBS (hence the project acronym CBSAA) to boost transsulfuration, endogenous synthesis of glutathione and H_2S, and ultimately protect diabetic patients from DN.

To achieve the goals of the project, a pre-existing drug development pipeline will be transferred from University Medical Center Groningen (UMCG), The Netherlands, to the Comenius University Science Park (CUSP) in Bratislava, Slovakia. The applying researcher has hands-on experience with the technology to be transferred, in fact he has coordinated the development of a drug discovery infrastructure in the UMCG whilst operating within a Dutch academic-industrial consortium consisting of one hospital, two university departments, and two small-to-medium-size companies.

Together, the project is set to establish a collaborative drug development infrastructure at the CUSP and to leverage the technology for the discovery of novel treatments for diabetic nephropathy.



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