



Karsten Motzler

HMGU München

My name is Karsten Motzler, 26 years old, and I am a doctoral researcher in the group for “Endocytosis and Metabolism” of Anja Zeigerer at the Helmholtz Diabetes Center in Munich. During both, my Biology Bachelor and Drug Research Master, I focused on topics related to metabolic disease. Therefore, I started my PhD in 2020 in

a related topic for which I have just very recently submitted my thesis.

Last year, I gave a talk at the “100 years of glucagon and a hundred more” conference in Copenhagen. There, I presented a part of my PhD project on the role of ESCRT-I complex protein subunit Vps37a and its role in blood glucose homeostasis. The ESCRT-I complex is part of a machinery that regulates the sorting of membrane proteins destined for degradation at endosomes after internalization. In this highly collaborative project, we could show that depleting Vps37a from livers of mice results in increased hepatic blood glucose production, contributing to accelerated blood glucose excursions in high fat diet fed mice. These effects were due to enhanced endosomal signaling of the glucagon receptor towards the gluconeogenic cAMP/PKA/p-Creb axis. Importantly, increased endosomal signaling upon Vps37a depletion was limited to this axis, leaving glucagon receptor-mediated lipid usage unaffected.

By overexpressing Vps37a in livers, we could show that this diversion of the two signaling arms has the potential to lower blood glucose levels, without changing liver lipids. Thus, this project highlights the importance of the endosomal trafficking system for metabolic disease and offers new directions for potential glucagon-based therapies.

Sekar & Motzler et al. (2022) Vps37a regulates hepatic glucose production by controlling glucagon receptor localization to endosomes (Cell Metabolism)