

Characterization of the plasma membrane lipid organization in Fabry disease

Project partners
Université de Strasbourg, Universität Freiburg
Project duration / Awarded funding
01/02/2021 – 31/01/2023 / 40,000€
Short description of the project
This project in the field of biology examined the plasma membrane lipid organization in Fabry cells. The team investigated the role of alteration of lipid organization on cell surface-mediated signaling events.
Concrete implementation of the project (What was the funding used for?)
We hired an ingénieur d'études (Université de Strasbourg) and a student research assistant (HiWi, Universität Freiburg) to acquire preliminary data. We also used the funding for purchasing consumables (reagents for molecular biology experiments, fluorescence imaging and biochemical analysis). In addition, a master thesis at the Universität Freiburg was performed based on the ideas of this project.
Project result(s) and continuation of collaboration
Our major objective was to examine plasma membrane lipid organization in Fabry cells using the original lipid-specific probes (French partner). Our results indicate dramatic decrease of cell surface cholesterol in Fabry cells. In contrast, cell surface sphingomyelin distribution was not altered. The role of alteration of lipid organization on cell surface-mediated signaling events is now in progress. The German partner analyzed the abundance of the glycosphingolipid Gb3 in healthy and Fabry cells by mass spectrometry. We could also provide a detailed analysis of Gb3 species varying in fatty acyl chain length, degree of saturation and hydroxylation. By using Gb3-binding lectins and antibodies in combination with immunofluorescence and confocal microscopy, we analyzed the intracellular distribution. In addition, by flow cytometry we quantified and compared the abundance of the glycosphingolipid Gb3 at the plasma membrane of healthy and Fabry cells. The next project meeting is planned for October 2023, also to discuss about a joint ANR-DFG grant proposal.
Further information (links, articles, photos)
-Kobayashi T, Tomishige N, Inaba T, Makino A, Murata M, Yamaji-Hasegawa A, Murate M (2021) Impact of intrinsic and extrinsic factors on cellular sphingomyelin imaging with specific reporter

proteins *Contact* 4:1-13. doi: 10.1177/2515256421104245

- Neugebauer, Daniela (2022, master thesis): Characterization of Fabry fibroblasts: Subcellular localization of accumulated globotriaosylceramide, sphingolipid metabolism, and intracellular trafficking