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Cardiolipin and its Role in Ageing and Oxidative Stress on Biomimetics of the Inner Mitochondrial Membrane

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Cardiolipin (CL) represents a unique tetra-acyl phospholipid and is almost exclusively found in the inner mitochondrial membrane (IMM), comprising ~15-20 mol% of the overall phospholipid content. CL supporting the optimal function of most enzymes involved in the cellular energy metabolism (e.g. complexes I-IV in the respiratory chain). Besides its functional importance, CL modulates due to its inverse-cone shape the membrane fluidity and osmotic stability of the membrane.[1] Furthermore, it anchors signalling molecules and proteins electrostatically, playing an important role in events linked to ageing and apoptosis.[2] In cases of mitochondrial dysfunction, changes in the CL content and/or its fatty acid composition can be a dominant cause, leading to neurodegenerative and cardiac diseases.[3]

In this project, we aim to unravel the role of CL in biological membranes by mimicking the composition of the IMM in liposomes, focusing on the integrity of CL-containing membranes under oxidative stress conditions due to the presence of reactive oxygen species (ROS). One of the main emphasis lies on correlating morphology-based changes of these vesicles (e.g. size, charge, membrane fluidity) due to exposure towards various ROS such as superoxide radicals, hydrogen peroxide and hydroxyl radicals. Proof of concept is given in studies where respiratory complex I was successfully incorporated into CL-containing liposomes and changes in the enzyme's activity due to the membrane composition and presence of ROS.[4,5] Based on these promising results, we want to gain a better fundamental understanding of the importance of CL in both biomimetics as well as in biological membranes.

[1] J. Dudek, *Front. Cell Dev. Biol.* **2017**, *5*, 90.
[2] A. J. Chicco, G. C. Sparagna, *American Journal of Physiology-Cell Physiology* **2007**, *292*, C33–C44.
[3] Z. Liang, M. W. Schmidtke, M. L. Greenberg, *Front. Mol. Biosci.* **2022**, *9*, 915301.
[4] J. Eisermann, J. J. Wright, J. D. E. T. Wilton-Ely, J. Hirst, M. M. Roessler, *RSC Chem. Biol.* **2023**, *4*, 386–398.
[5] J. Eisermann, Y. Liang, J. J. Wright, E. Clifford, J. D. E. T. Wilton-Ely, M. Kuimova, M. Roessler, *Chemistry A European J* **2024**, e202402035.