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# Lipids: Metabolism, Nutrition & Health

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## Quantitative neurolipidomics

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Lipids are molecular components which play essential roles in many physiological processes and pathological conditions, including neurodegenerative, metabolic and immune diseases. The lipids serve not only a constitutive role in the cell membrane, but also as the source for downstream signaling molecules, such as endocannabinoids and eicosanoids that underscore essential neurobiological functions. In neurobiology research, lipids emerge as important candidates for biomarkers, drug targets, but also as therapeutic agents. To gain a better understanding of their specific functions and to define the signaling networks, especially under pathological conditions, accurate identification and quantification of lipids, as well as profiling of other molecular correlates such as related genes and proteins in one and the same tissue source is essential. In addition, (sub) localization of disease-associated lipid changes within and across tissue regions is essential to expedite the unravelling of disease mechanisms, as well as discovery of lipid-based drug targets and lipid-based therapeutic agents. Here, advanced lipidomic strategies, combining quantitative mass spectrometry with high-throughput sample preparation for multiplex lipid analysis in minute amount of biological matrices, that enable translation of pre-clinical features of neurological disorders into quantitative neurolipidomics will be discussed.

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## Novel approaches to study cholesterol removal from tissues

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High-density lipoproteins (HDLs) have been extensively studied and linked to various diseases including metabolic diseases. Despite expanding details in our knowledge about HDL at a molecular level, fundamental connections between HDL levels in blood and cardiovascular diseases still remain controversial: HDL levels in blood do not always represent the cardioprotective activity of HDLs. At the present time, the field is very limited because there are no existing tools/techniques to monitor in vivo dynamic HDL trafficking: How it gains access to peripheral tissues, and how it transports through lymphatics to the liver back to circulation. Our investigation presented rectifies this problem as we have created tools to study HDL transport to and from the desired tissue compartments. We created photo-activatable HDL particles wherein HDL particles can be labeled in situ by laser activation in a desired tissue at any time. ApoA1, the key and unique scaffold apo-lipoprotein to generate HDL particles, is fused with a photo-activatable green fluorescence protein (PA-GFP), which displays green fluorescence after 405nm laser activation, in its N-terminus. We have generated an AAV vector that expresses this chimera protein PA-GFP-Linker-ApoA1 (PGA1) allowing for the expression of functional HDL particles that can reconstitute WT or ApoA1 KO mice with HDLs. We have also set up a laser activation protocol that has allowed us to label HDLs in skin of mice and detect enhanced GFP in plasma over an ensuing time course. We then studied HDL transport by using a murine imiquimod (IMQ)-induced psoriasis model. We showed that IMQ treated ApoE KO mouse under high fat diet displays psoriasis-like skin lesions and exacerbates atherosclerosis. When monitoring the transport of PGA1 HDLs from the mouse skin back to plasma from WT and IMQ treated mice, IMQ treated mice display significant reduced HDL transport compared to non-treated controls, correlating defective reverse cholesterol transport with accelerating atherosclerosis. This new approach permits scientists to uncover the biological basis of HDL transport in tissues under various disease conditions.

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