Role of CGI-58 in Skin Lipid Metabolism

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In mammals, energy is stored in form of triacylglycerol (TG) in adipose tissue. In times of energy demand the stepwise breakdown of TG is initiated by the activity of adipose triglyceride lipase (ATGL). This results in the release of free fatty acids and diacylglycerol (DG) which is furthermore consecutively catabolized by hormone-sensitive lipase (HSL) and monoglyceride lipase (MGL) to free glycerol and two free fatty acids. Furthermore the activity of ATGL is highly increased by its activator protein comparative gene identification 58 (CGI-58).

ATGL and CGI-58 knock out mice as well as patients carrying mutations in one of these enzymes display very distinct phenotypical appearances. Mutations in *ATGL* lead to an accumulation of TG in almost all tissues and especially in the heart the accrual of neutral lipids leads to a premature death. In contrast mutations in *CGI-58* cause a severe skin defect characterized by an impaired permeability barrier and result in postnatal death due to dehydration. This indicates an yet unidentified ATGL-independent role of CGI-58 in skin lipid metabolism. It is reasonable that CGI-58 stimulates another lipase specifically in skin or assists the transport of lipid intermediates arising during the lipolytic cascade. However so far the specific role of CGI-58 in skin lipid metabolism is matter of speculations.

This study is an attempt to elucidate the ATGL-independent function of CGI-58 in skin. Hence skin preparations obtained from genetically different mouse lines i.e. wildtype, ATGL, and CGI-58 deficient mice are assayed for non-ATGL lipase activity stimulated by CGI-58. For this purpose protein separation and activity assays as well as inhibitor studies and mass-spectrometric analysis are initially performed.