GESELLSCHAFT DEUTSCHER CHEMIKER

KOLLOQUIUM

Sommersemester 2025

Titel

„Metabolic dysfunction-associated steatotic liver disease (MASLD): Hepatic and extrahepatic consequences“
"Glycerophospholipid metabolism in cancer - targeting the glycerophosphodiesterase EDI3 in HER2+ breast cancer"

Vortragender

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Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the most common chronic liver disease in the world. Mainly driven by chronic overnutrition, MASLD is characterized by the excessive accumulation of lipids within the liver. Individuals with MASLD are at risk of developing a more serious liver condition as well as extrahepatic complications that can cause mortality. Our research at IfADo aims at understanding mechanisms that drive disease progression and complications in other organs. Among the multiple epigenetic and expression changes in the fatty liver, we have identified loss of the expression of the alanine-glyoxylate aminotransferase (Agxt), a key enzyme catalyzing the detoxification of glyoxylate to glycine. Because Agxt prevents the excessive conversion of glyoxylate to oxalate, Agxt deficiency results in hepatic overproduction of oxalate, a waste product with harmful effects in renal and cardiovascular diseases. This mechanism provides a potential explanation for the higher risk of renal and cardiovascular diseases in MASLD patients. Our ongoing research links Agxt deficiency with further metabolic complications.

Cellular metabolism refers to the multitude of controlled chemical reactions regulated by networks of genes, proteins and metabolites needed for cellular homeostasis. Disruption of these pathways has been linked to various pathologic states, including cancer. Our group discovered the glycerophosphodiesterase, EDI3 (GPCPD1; GDE5; GDPD6), an enzyme that hydrolyses the phosphodiester, glycerophosphocholine to glycerol-3-phosphate and choline. Both metabolic products are intermediates in several metabolic pathways, including phospholipid, triglyceride, and glucose metabolism, all of which when altered can disrupt cellular homeostasis leading to disease. Indeed, we have shown that manipulating EDI3 expression changes the cellular metabolome, with consequences to cell function. We were also the first to link EDI3 to cancer, reporting an association between high EDI3 expression and worse prognosis in endometrial and ovarian cancer, and more recently showing that EDI3 is a potential therapeutic target in HER2+ breast cancer. In our ongoing projects, we continue to investigate the role of EDI3 and other enzymes in choline and glycerophospholipid metabolic pathways in cancer, particularly breast and ovarian, using in vitro 2D and 3D cell and in vivo mouse models of these diseases.

Ort

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Zeit

Dienstag, 01.07.2025, 17:15 Uhr

gez. Professor Dr. Andreas Steffen
Gesellschaft Deutscher Chemiker Ortsverband Dortmund