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Newsletter

4-2021

December 2021 edition:

In this edition we highlight research articles published in 2021 using QconCATs by PolyQuant.

The QconCATs were used in various fields of research involving absolute protein quantification of dozens of proteins but also individual proteins, studying disease mechanisms, effects of therapeutic intervention, development of transgenic mouse models and disease diagnostics.

HEPATOLOGY

Modeling Phenotypic Heterogeneity of Glycogen Storage Disease Type 1a Liver Disease in Mice by Somatic CRISPR/CRISPR-associated protein 9–Mediated Gene Editing

Martijn G.S. Rutten, Terry G.J. Derks, Nicolette C.A. Huijkman, Trijnie Bos, Niels J. Kloosterhuis, Kees C.W.A. van de Kolk, Justina C. Wolters, Mirjam H. Koster, Laura Bongiovanni, Rachel E. Thomas, Alain de Bruin, Bart van de Sluis, and Maaike H. Oosterveer

HEPATOLOGY, VOL. 74, NO. 5, 2021

Rutten et al. generated a hepatocyte-specific GSD-1a mouse model using somatic CRISPR/CRISPR-associated protein 9 (Cas9)–mediated gene editing. To characterize the mouse model, Rutten et al. also used a QconCAT reference standard for targeted proteomics to quantify G6PC and proteins related to glycolysis and glycogen metabolism in homogenized liver tissue.

Original Article

The hepatocyte IKK:NF-κB axis promotes liver steatosis by stimulating de novo lipogenesis and cholesterol synthesis

Andries Heida, Nanda Gruben, Leen Catrysse, Martijn Koehorst, Mirjam Koster, Niels J. Kloosterhuis, Albert Gerding, Rick Havinga, Vincent W. Bloks, Laura Bongiovanni, Justina C. Wolters, Theo van Dijk, Geert van Loo, Alain de Bruin, Folkert Kuipers, Debby P.Y. Koonen, Bart van de Sluis

MOLECULAR METABOLISM 54 (2021)

Heida et al. identified that the hepatocyte IKK:NF-κB axis plays a critical role in the initiation and progression of Metabolic Associated Fatty Liver Disease (MAFLD) by controlling lipogenesis and cholesterol synthesis. The IKK:NF-κB axis might thus contribute to cardiovascular disease risk in MAFLD patients. They used QconCAT-assisted targeted proteomics to measure the levels of ApoB in plasma reflecting the levels of low density lipoprotein (LDL).

BMC Bio

Age-related susceptibility to insulin resistance arises from a combination of CPT1B decline and lipid overload

Marcel A. Vieira-Lara, Marleen B. Dommerholt, Wenxuan Zhang, Maaike Blankestijn, Justina C. Wolters, Fentaw Abegaz, Albert Gerding, Ydwine

ACS Publications MOLECULAR PHARMAC

Non-uniformity of Changes in Drug-Metabolizing Enzymes and Transporters in Liver Cirrhosis: Implications for Drug Dosage Adjustment

Eman El-Katheeb, Brahim Achour, Zubida M. Al-Majdoub, Jill Barber and Amin Rostami-Hodjegan

Mol Pharm. 2021 Sep 6; 18(9): 3563-3577

BJCP British Journal of Clinical Pharmacology

Proteomics of Colorectal Cancer Liver Metastasis: a Quantitative Focus on Drug Elimination and Pharmacodynamics Effects

T. van der Veen, Rachel Thomas, Ronald P. van Os4, Dirk-Jan Reijngoud, Johan W. Jonker, Janine K. Kruit and Barbara M. Bakker

BMC Biology (2021) 19:154

Vieira-Lara et al. combined lipidomics, proteomics, mitochondrial function analysis and computational modelling to investigate the combined effects of age and diet on skeletal muscle lipid handling and its implications for insulin resistance (IR). The key enzyme in this process could be identified through targeted and quantitative mass spectrometry.

El-Katheeb et al. used QconCAT-based targeted proteomics to determine the absolute abundance of 51 drug-metabolizing enzymes and transporters in human liver microsomes across the three degrees for cirrhosis severity to determine their impact on the predictive performance of PBPK (physiologically based pharmacokinetic) models. Their work demonstrates the utility of proteomics-informed PBPK modeling for drug-specific dose adjustments in liver cirrhosis.

Areti-Maria Vasilogianni, Zubida M. Al-Majdoub, Brahim Achour, Sheila Annie Peters, Amin Rostami-Hodjegan, Jill Barber

British J Clin. Pharm. October 1, 2021

Vasilogianni et al. detected substantial alterations in protein abundance for receptor tyrosine-kinases (RTK), drug-metabolising enzymes, transporters and cancer-specific protein markers using QconCATs. They also performed physiologically based pharmacokinetic (PBPK) simulations to assess the contribution of altered abundance of drug-metabolising enzymes and transporters to changes in pharmacokinetics.

analytical chemist

Pipelines and Systems for Threshold-Avoiding Quantification of LC−MS/MS Data

Alejandro Sánchez Brotons, Jonatan O. Eriksson, Marcel Kwiatkowski, Justina C. Wolters, Ido P. Kema, Andrei Barcaru, Folkert Kuipers, Stephan J. L. Bakker, Rainer Bischoff, Frank Suits, and Péter Horvatovich

Anal. Chem. 2021, 93, 11215−11224

Sánchez Brotons et al. present the pipelines and systems for threshold-avoiding quantification (PASTAQ) LC–MS/MS preprocessing toolset, which allows highly accurate quantification of data-dependent acquisition LC–MS/MS datasets. They used QconCATs to study the effect of the dynamic range of compounds on the quantitative performance.

JIMD SSIEM WIL

Impaired Very-Low-Density Lipoprotein catabolism links hypoglycemia to hypertriglyceridemia in Glycogen Storage Disease type Ia

Joanne A. Hoogerland, Fabian Peeks, Brenda S. Hijmans, Justina C. Wolters, Sander Kooijman, Trijnie Bos, Aycha Bleeker, Theo H. van Dijk, Henk Wolters, Albert Gerding, Karen van Eunen, Rick Havinga, Amanda C. M. Pronk, Patrick C. N. Rensen, Gilles Mithieux, Fabienne Rajas, Folkert Kuipers, Dirk-Jan Reijngoud, Terry G. J. Derks, Maaike H. Oosterveer

J Inherit Metab Dis. 2021;44:879–892.

Hoogerland et al. performed a systematic analysis of whole-body triglyceride (TG) metabolism in normoglycemic (fed) and in hypoglycemic (fasted) hepatocyte-specific G6pc knockout (L-G6pc−/−) mice. For their comparative measurements of hepatic and plasma protein levels they used targeted proteomics. The reference peptides were encoded on a QconCAT standard.

cmgh GASTROENT

Cholangiopathy and Biliary Fibrosis in Cyp2c70-Deficient Mice Are Fully Reversed by Ursodeoxycholic Acid

Jan Freark de Boer, Hilde D. de Vries, Anna Palmiotti, Rumei Li, Marwah Doestzada, Joanne A. Hoogerland, Jingyuan Fu, Anouk M. La Rose, Marit Westerterp, Niels L. Mulder, Milaine V. Hovingh, Martijn Koehorst, Niels J. Kloosterhuis, Justina C. Wolters, Vincent W. Bloks, Joel T. Haas, David Dombrowicz, Bart Staels, Bart van de Sluis, and Folkert Kuipers

Cell Mol Gastroenterol Hepatol 2021;11:1045–1069

“Humanization” of bile acid (BA) metabolism in mice by knocking out Cyp2c70 can facilitate translation of murine data while preserving the benefits of the mouse as a preclinical model. DeBoer et al. assessed the (patho)physio-logical consequences of Cyp2c70-deletion in mice in an age-and gender-dependent manner. As a parameter of lipoprotein metabolism, plasma apolipoprotein B (ApoB) levels were determined using targeted proteomics and a QconCAT as reference standard.

ASPET | DRUG METAB AND DISPOSITI

Proteomic Quantification of Changes in Abundance of Drug-Metabolizing Enzymes and Drug Transporters in Human Liver Cirrhosis: Different Methods, Similar Outcomes

Eman El-Khateeb, Zubida M. Al-Majdoub, Amin Rostami-Hodjegan, Jill Barber, and Brahim Achour

Drug Metabolism and Disposition May 27, 2021

El-Khateeb et al. examine disease effects on the abundances of key drug-metabolizing enzymes and drug transporters and compare absolute – targeted – quantification methods to relative quantification.

ACS Publications
Most Trusted. Most Cited. Most Read.

Cov-MS: A Community-Based Template Assay for Mass-Spectrometry-Based Protein Detection in SARS-CoV-2 Patients

Bart Van Puyvelde, Katleen Van Uytfanghe, Olivier Tytgat, Laurence Van Oudenhove, Ralf Gabriels, Robbin Bouwmeester, Simon Daled, Tim Van Den Bossche, Pathmanaban Ramasamy, Sigrid Verhelst, Laura De Clerck, Laura Corveleyn, Sander Willems, Nathan Debunne, Evelien Wynendaele, Bart De Spiegeleer, Peter Judak, Kris Roels, Laurie De Wilde, Peter Van Eenoo, Tim Reyns, Marc Cherlet, Emmie Dumont, Griet Debyser, Ruben t'Kindt, Koen Sandra, Surya Gupta, Nicolas Drouin, Amy Harms, Thomas Hankemeier, Donald J. L. Jones, Pankaj Gupta, Dan Lane, Catherine S. Lane, Said El Ouadi, Jean-Baptiste Vincendet, Nick Morrice, Stuart Oehrle, Nikunj Tanna, Steve Silvester, Sally Hannam, Florian C. Sigloch, Andrea Bhangu-Uhlmann, Jan Claereboudt, N. Leigh Anderson, Morteza Razavi, Sven Degroeve, Lize Cuypers, Christophe Stove, Katrien Lagrou, Geert A. Martens, Dieter Deforce, Lennart Martens, Johannes P. C. Vissers, and Maarten Dhaenens

JACS Au 2021, 1, 6, 750–765

Van Puyvelde et al. developed a diagnostic test detecting proteolytically digested SARS-CoV-2 proteins using mass spectrometry to provide an alternative to the current standard method (reverse transcription polymerase chain reaction – RT-PCR). Their alternative method requires different reagents and instruments and allows detection of viral proteins instead of RNA at levels comparable to PCR. The QconCAT produced by PolyQuant serves as reference standard for peptide detection and control of sample quality.

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