Newsletter

4-2023

December 2023 edition:

We would like to continue our tradition of dedicating our last Newsletter of the year to research articles applying QconCATs from PolyQuant.

In 2023 our QconCATs were mainly used for targeted proteomics studies with a medical and pharmacological focus in different sample types (e.g. serum, cell lines, tissue biopsies….)

ADVANCED HEALTHCARE MATERIALS

Targeting Ligand Independent Tropism of siRNA-LNP by Small Molecules for Directed Therapy of Liver or Myeloid Immune Cells

Lin C, Mostafa A, Jans A, Wolters JC, Mohamed MR, Van der Vorst EPC, Trautwein C, Bartneck M.
Adv Healthc Mater. 2023 Jan 8

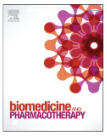
During the SARS-CoV-2 pandemic, mRNA vaccines were developed. These vaccines require lipid nanoparticles (LNPs) for stability and to ensure intracellular delivery. To study the mechanism of LNP distribution in the body, Lin et al performed untargeted proteomics analysis of serum to detect alterations of protein abundance upon siRNA-LNP administration and targeted proteomics for more in-depth analysis of selected proteins using QconCATs from PolyQuant's CVDQuant Kit.

frontiers in Oncology

Proteomic quantification of receptor tyrosine kinases involved in the development and progression of colorectal cancer liver metastasis.

Vasilogianni AM, Al-Majdoub ZM, Achour B, Peters SA, Rostami-Hodjegan A, Barber
J. Front Oncol. 2023 Feb 20;13:1010563.

Vasilogianni et al. assessed protein abundance of 21 receptor tyrosine kinases (RTKs) in 15 healthy and 18 cancerous liver samples using a QconCAT to validate protein abundance. Their work allowed identification of proteins with reduced protein levels in cancerous liver samples, but also proteins whose protein levels were increased.



Pharmacological inhibition of MEK1/2 signaling disrupts bile acid metabolism through loss of Shp and enhanced Cyp7a1 expression.

Verzijl CRC, van de Peppel IP, Eilers RE, Bloks VW, Wolters JC, Koehorst M, Kloosterhuis NJ, Havinga R, Jalving M, Struik D, Jonker JW.
Biomed Pharmacother. 2023 Mar;159:114270.

Verzijl et al., tested the effect of a MEK inhibitor on mouse and human hepatocyte cell lines. After transcriptome analysis, they evaluated whether the observed changes in transcription of genes involved in bile acid metabolism also affected protein abundance. To determine protein levels, they analyzed 13 proteins involved in bile acid metabolism using targeted proteomics and a QconCAT reference standard.

BMC Biology

Personalised modelling of clinical heterogeneity between medium-chain acyl-CoA dehydrogenase patients

Odendaal C, Jager EA, Martines AMF, Vieira-Lara MA, Huijkman NCA, Kiyuna LA, Gerding A, Wolters JC, Heiner-Fokkema R, van Eunen K, Derks TGJ, Bakker BM
BMC Biol. 2023 Sep 4;21(1):184.

In this study, Odendaal et al., built and validated, a kinetic model of the human liver mitochondrial fatty acid oxidation (mFAO). As proteome remodeling can adapt for enzyme deficiencies, they performed targeted proteomics in HepG2 MCAD knockout cell lines and in patient fibroblasts. Using QconCATs from PolyQuant as reference standard to determine the absolute quantities of 9 key proteins, they were able to observe a clear distinct pattern of the SCAD protein in the asymptomatic patient. Their data underlines that kinetic models are powerful tools, complementing models based on genomic data.

European Journal of Pharmaceutics and Biopharmaceutics

Quantification of drug metabolising enzymes and transporter proteins in the paediatric duodenum via LC-MS/MS proteomics using a QconCAT technique

Goelen J, Farrell G, McGeehan J, Titman CM, J W Rattray N, Johnson TN, Horniblow RD, Batchelor HK
Eur J Pharm Biopharm. 2023 Oct:191:68-77.

In this study, Goelen et al., employed mass spectrometry to study intestinal proteins from gut, using a QconCAT reference standard to simultaneously quantify 21 proteins of the three key intestinal Drug Metabolising Enzymes and Transporter (DMET) protein families (transporters, CYP and UGT-enzymes). They developed a simplified method for studying intestinal proteins using pinch biopsies from the paediatric duodenum and demonstrated the feasibility of this novel method. Their work provides the basis for future research to develop appropriate predictive models for physiologically-based pharmacokinetic (PBPK) modelling in pediatric populations.

Effects of lysine deacetylase inhibitor treatment on LPS responses of alveolar-like macrophages

Russo S, Kwiatkowski M, Wolters JC, Gerding A, Hermans J, Govorukhina N, Bischoff R, Melgert BN.
J Leukoc Biol. 2023 Oct 9:qiad12.

Russo et al., investigated if the anti-inflammatory effect of lysine deacetylase inhibitors correlated with metabolic changes in macrophages. Though a first exploratory proteome analysis indicated changes in metabolism of alveolar-like macrophages by inhibition of LPS and/or KDAC, a targeted proteomic analysis of 59 proteins, encoded on QconCATs from PolyQuant, involved in the major metabolic pathways showed no significant alterations of their proteins levels. However, their data indicates that protein ubiquitination may be the driver of the anti-inflammatory effects of lysine deacetylase inhibitors, requiring further studies.

Species-specific metabolic reprogramming in human and mouse microglia during inflammatory pathway induction.

Sabogal-Guáqueta AM, Marmolejo-Garza A, Trombetta-Lima M, Oun A, Hunneman J, Chen T, Koistinaho J, Lehtonen S, Kortholt A, Wolters JC, Bakker BM, Eggen BJL, Boddeke E, Dolga A.
Nat Commun. 2023 Oct 13;14(1):6454.

In this study Sabogal-Guáqueta et al., investigated the effects of lipopolysaccharides (LPS) on mouse microglia and human microglia-like cells at the protein level, performing both label-free and targeted proteomics. They quantitatively determined expression levels of 11 TCA cycle enzymes, using QconCAT reference standards. The targeted approach enabled them to observe an increased abundance of the isoforms PFKM and PFKP in human but not mouse microglia.

A Kinase Interacting Protein 1 regulates mitochondrial protein levels in energy metabolism and promotes mitochondrial turnover after exercise

Kirsten T. Nijholt, Pablo I. Sánchez-Aguilera, Belend Mahmoud, Albert Gerding, Justina C. Wolters, Anouk H. G. Wolters, Ben N. G. Giepmans, Herman H. W. Silljé, Rudolf A. de Boer, Barbara M. Bakker, B. Daan Westenbrink
Sci Rep. 2023; 13: 18822. Published online 2023 Nov 1.

Nijhoult et al., studied the influence of A Kinase Interacting Protein 1 (AKIP1) on mitochondrial function and adaptation in response to exercise *in vivo*. They could show that levels of proteins in mitochondrial energy metabolism and related pathways was changed in hearts from mice with cardiomyocyte-specific overexpression of AKIP1 by performing quantitative proteomics with QconCATs from PolyQuant targeting 38 proteins involved in fatty acid β-oxidation, tricarboxylic acid cycle (TCA), oxidative phosphorylation (OXPHOS), substrate transport and antioxidant activity.

Loss of hepatic SMLR1 causes hepatosteatosis and protects against atherosclerosis due to decreased hepatic VLDL secretion

van Zwol W, Rimbert A, Wolters JC, Smit M, Bloks VW, Kloosterhuis NJ, Huijkman NCA, Koster MH, Tharehalli U, de Neck SM, Bournez C, Fuh MM, Kuipers J, Rajan S, de Bruin A, Ginsberg HN, van Westen GJP, Hussain MM, Scheja L, Heeren J, Zimmerman P, van de Sluis B, Kuivenhoven JA.
Hepatology. 2023 Nov 1;78(5):1418-1432.

Van Zwol et al studied the role of SMLR1 in the liver by silencing *Smlr1* in hepatocytes. In their study they used a targeted proteomics approach to measure protein levels of 11 apolipoproteins using a mix of QconCATs and isotopically labeled standard peptides. In *Smlr*-KO mice, they observed a drop in plasma HDL cholesterol, reflected by a 56% reduction of apoA1 when fed a chow diet, indicating that loss of hepatocyte SMLR1 reduced VLDL secretion.

Hepatic ChREBP orchestrates intrahepatic carbohydrate metabolism to limit hepatic glucose 6-phosphate and glycogen accumulation in a mouse model for acute Glycogen Storage Disease type Ib

Krishnamurthy KA, Rutten MGS, Hoogerland JA, van Dijk TH, Bos T, Koehorst M, de Vries MP, Kloosterhuis NJ, Havinga H, Schomakers BV, van Weeghel M, Wolters JC, Bakker BM, Oosterveer MH.
Mol Metab. 2023 Nov 22;79:101838.

Krishnamurthy et al., studied the role of hepatic ChREBP as a mediator of the immediate responses to hepatic G6P accumulation in a mouse model for acute hepatic glucose storage disease (GSD) type Ib. They performed immunoblot analysis investigating protein levels of key proteins and confirmed their results by complementary targeted proteomic analysis using heavy labeled reference peptides, encoded on QconCATs from PolyQuant.