

From hyperphagic rodents to diabetic complications: Targeted metabolomics in preclinical and clinical diabetology

A.C. Gruber¹, U. Lundin¹, A. Dzien² and K. M. Weinberger¹

¹BIOCRATES Life Sciences AG, Austria

²Medicalcenter Innsbruck, Austria

It is predicted that the prevalence of type 2 diabetes (T2D) will rise from 194 million (2003) to 334 million by 2025. Although T2D is a very common disease in Western countries and cheap blood and urine tests are available, it is still underdiagnosed and the lag between onset and diagnosis is several years. Additionally, the current diagnostic approaches do not lead to direct therapeutic recommendations. Therefore, markers for earlier diagnosis are needed, and a better insight into pathomechanisms is required for individualized therapy.

A targeted metabolomics platform was used to identify biomarkers in preclinical studies on diabetic rodents, e.g. db/db mice, and on clinical cohorts with metabolic conditions ranging from healthy controls to metabolic syndrome and T2D. The commercially available MetaDisIDQ™ kit and additional assays were applied to quantify amino acids, biogenic amines, acylcarnitines, glycerophospholipids, sphingolipids, sugars, free fatty acids, eicosanoids and other oxidized polyunsaturated fatty acids, bile acids and intermediates of energy metabolism using stable isotope dilution. The analysis was performed by flow injection or HPLC coupled to tandem mass spectrometry with multiple reaction monitoring with electrospray ionization. The datasets were analyzed using uni- and multivariate statistics to identify the most significant changes.

Many findings were similar in both the animal and clinical studies. Since the db/db mouse is not the perfect model for diabetes, some metabolites, like plasmalogens and glucogenic amino acids, showed different alterations. The preclinical studies could also demonstrate how targeted metabolomics can assess efficacy and off-target effects of drug candidates earlier than conventional endpoints.

Biography

Alexandra Carina Gruber, PhD, MBA, MMFin graduated in pharmacy from the University in Vienna and finished her doctoral thesis in 1997. Dr. Gruber has been working in the pharmaceutical industry for more than 15 years. Since 2009 she is working with BIOCRATES Life Sciences AG.