EDITORIAL

What will metabolomics studies mean to endocrinology?

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Personalized medicine is a key topic for the development of future health-care provisions, even in endocrinology. The objective of personalized medicine is to use state-of-the-art diagnostics and novel therapeutic interventions that take into account the specific requirements and characteristics of the individual patient in order to optimize the effectiveness of treatments, avoid unwanted adverse reactions, and significantly reduce health-care costs. Identification of molecular pathways by integrated analysis of genetics and further molecular information by available OMICs technologies in combination with clinical phenotypes and biomarkers is the hallmark of this development. The majority of our current medical practice is based on extrapolated research in physiology, knowledge from randomized controlled trials or epidemiological studies of large cohorts, and expert experience. Most of those studies do not take into account the individual's genetic, proteomic, and metabolic characteristics. It is time to bridge this gap between knowledge accumulated from basic science, discovering molecular pathways and mechanism by new OMICs technologies, and clinical research with an implementation of personalized medicine at the patient's bedside – this can be achieved by the approach of metabolomics.

Metabolomics is a technique that provides a comprehensive assessment of small molecular mass organic compounds that are substrates or products of metabolic pathways as an individual fingerprint of metabolism. Recent advances in this field allow the acquisition of high-throughput metabolic profiles in different biofluids like plasma or urine in animal models or humans. The most common analytical platforms are mass spectrometry and nuclear magnetic resonance spectroscopy, which allow the detection of individual metabolic fingerprint (metabolic profiling) as well as untargeted quantitative or semiquantitative analysis for measurement of dynamic metabolites (metabolomics). The detected spectra contain a few hundred to thousands of signals related to both genetic and environmental contributions. Therefore, these techniques are the most promising tools for the identification of new biomarkers.

Basically all OMICs techniques, such as genome-wide association studies (GWAS), transcriptomics, proteomics as well as metabolomics are able to identify the up to now unknown pathways or underlying mechanisms for many diseases, especially in the field of endocrinology. The main limitation of current GWAS, even for clinical use in multifactorial diseases, is that this method only provides information about the genetic contribution. Recently, published proof-of-concept studies regarding the association of genome-wide datasets and metabolomics were highlighted in the thematic review by Homuth *et al.* (2012) in this issue. These investigations identified different genetic polymorphisms with large effects on the metabolic capacities of individuals and showed that genetic variation in genes is related to metabolism, leading to clearly differentiated metabolic phenotypes termed 'genetically determined metabotypes'. Most of those genes encode enzymes and transport proteins (Suhre *et al.* 2011). The thematic review by Homuth *et al.* (2012) demonstrates the technical progress in correlation of genetic variation and metabolome, reflecting the nearest OMICs approach to the phenotype as a first step of integrated OMICs analysis.

Furthermore, in this context, the rapidly growing research field of metabolomics has introduced new insights into the pathology of diabetes as well as methods to predict disease onset and has revealed new biomarkers. Diabetes is the most common metabolic disease, and its complications have a significant economic impact on the health system. Prediction of type 2 diabetes in asymptomatic patients as well as its personalized risk stratification for complications in diagnosed patients will become one of the major aims within the next years. The current literature of this endemic disease was reviewed by Friedrich (2012). The overall comparison of different animal models and pathways related to the phenotype type 2 diabetes might be a very promising basic tool for individualization of risk prediction and future therapy.

Up to now the laboratory characterization of endocrine disorders and diseases has included the measurement of

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single effector hormones, their major pituitary regulators, or dynamic testing. One of the limitations of the current biochemical characterization of endocrine diseases on the road to personalized medicine is the analytical coefficient of variation (CV) of the most relevant immunoassays. It might be doubtful that the moderate CV of our currently used automated assays is suitable to interpret individual changes against the background of biological variability as one of the key requirements for personalized medicine.

Moreover, the endocrine system is the major regulator of metabolism. Therefore, endocrine disorders and diseases affect different kinds of metabolic traits or pathways influenced by individual genetic and environmental factors, which cannot be characterized by a single measurement. Therefore, metabolic profiles of serum or urine are regarded as indicators of individual physiological or pathophysiological states to provide metabolic information as a marker tool of disease and monitoring treatment. This future perspective of metabolomics in an example of testosterone replacement is shown in the thematic review by Haring (2012). Thus, the combination of clinical (phenotype) and molecular datasets (OMICs technologies) should be integrated in a future bioinformatic platform/decision support system to be used at the point of care to bring this vision of personalized medicine in endocrinology diabetes into reality.

In summary, these three reviews introduce metabolomics as a metabolite profiling technique in individuals with metabolic or endocrine disorders. They bridge the gap between basic sciences of OMICs and current clinical knowledge of metabolism, showing a promising perspective for personalized medicine in endocrinology.

Declaration of interest

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References

Friedrich N 2012 Metabolomics in diabetes research. *Journal of Endocrinology* **215** 29–42. (doi:10.1530/JOE-12-0120)

Haring R 2012 Perspectives for metabolomics in testosterone replacement therapy. *Journal of Endocrinology* **215** 3–16. (doi:10.1530/JOE-12-0119)

Homuth G, Teumer A, Völker U & Nauck M 2012 A description of large-scale metabolomics studies – increasing value by combining metabolomics with genome-wide SNP genotyping and transcriptional profiling. *Journal of Endocrinology* **215** 17–28. (doi:10.1530/JOE-12-0144)

Suhre K, Wallaschofski H, Raffler J, Friedrich N, Haring R, Michael K, Wasner C, Krebs A, Kronenberg F, Chang D *et al.* 2011 A genome-wide association study of metabolic traits in human urine. *Nature Genetics* **43** 565–569. (doi:10.1038/ng.837)

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