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Editorial

Steroid profiling and analytics: Going towards sterome

This special issue gathered contributions at the-cutting-edge for steroid profiling and its applications. Advances in the routine analysis of steroid hormones were closely connected to the development of conventional radioimmunoassays and direct immunoassays over the last 40 years. During that time gas chromatography in combination with mass spectrometry (GC–MS) served as a gold standard for the quantitation of steroids and is still important for identification and determination of complete metabolic pathways. The great potential and increasingly importance of liquid chromatography–tandem mass spectrometry (LC–MS/MS) as a diagnostic tool for steroid analysis is impressively shown for different fields of clinical diagnostics, epidemiological studies, doping control, and metabolome studies. Commercial test kits for steroid hormone profiling using LC–MS/MS are now appearing on the market. These developments anticipate a change from routine direct immunoassays to LC–MS/MS in the same way we could observe 5 years ago in the field of therapeutic drug monitoring.

Ceglarek and co-workers address an often neglected aspect of steroid hormone measurements and that is biologically influencing factors that may affect these measurements, which they refer to as preclinical challenges. The major factors include sex, age, pubertal stage, phase of menstrual cycle, pregnancy and diurnal rhythm. The authors also emphasize that these factors are essential to consider in establishing valid reference intervals for steroid hormone LC–MS/MS assays that are presently being used and developed.

Improvement and standardization of steroid hormone assays using mass spectrometry assays, beginning with testosterone, is a very important ambitious challenge that has been initiated at the Center for Disease Control (CDC) in collaboration with clinical diagnostic laboratories and investigators in academic institutions. Vesper and Bothelo provide well described insights into pre- and post-analytical challenges, such as test selection, interpretation, and establishing reference intervals to improve the translation of standardized results into clinical guidelines and public health assessments.

For the analyses in target tissues the sensitivity of assays becomes an issue. The article by Penning and co-workers describes the applications of LC–MS/MS assay methodology for measurement of androgen and estrogen metabolites in plasma. This methodology is important because it may be adapted for measurement of targeted steroid metabolomes within prostate and breast tumor biopsy samples.

In the article by Honda and co-workers, the authors provide a brief review in which they describe their recently developed LC–MS/MS assay methodology for the quantitation of non-cholesterol sterols in biologic samples, such as serum and cell homogenates. The authors emphasize thorough liquid chromatographic separation of sterols to achieve high specificity, the importance of picolinyl ester derivatization to obtain enhanced sensitivity, and use of LC–MS/MS in ESI positive mode to quantify the sterols.

It is well recognized that mammalian animal models such as the mouse are an indispensible tool for investigating reproductive health, medicine and biology. Serum and reproductive tissue levels in the mouse are very low. In their article, McNamara and co-workers demonstrate that the LC–MS/MS assay method has the sensitivity, specificity and multi-analyte capability to offer accurate steroid profiling for studies using mouse serum and tissue samples.

Other manuscripts deal with perspectives, advantages and disadvantages of distinct steroid analysis methods (see contributions by Shackleton and co-workers, Stanczyk and Clarke, and Vogeser).

In several fields steroid analyses are providing new interesting insights for disease mechanisms. In the article on sex steroid metabolism in the regulation of bone health in men, Vandenput and co-workers demonstrate that estradiol plays an important role in regulating bone homeostasis, even though an important role of testosterone is not excluded. In addition, the authors show evidence to indicate that a threshold level for serum estradiol exists, which is necessary for optimal skeletal maturation and preventing bone loss as well as fractures in men.

The article by Christakoudi and co-workers describes a study in which a new urinary marker for early diagnosis of 21-hydroxylase deficiency was identified. The compound was characterized as 3β,16α,17α-trihydroxy-5α-pregnane-7,20-dione by GC–MS and GC–MS/MS and was found to be present in much higher levels than the currently used specific marker, 11-oxo-pregnanetriol, during the first days of life. It is expected that this compound will prove to be a highly useful marker of 21-hydroxylase deficiency, the most common cause of congenital adrenal hyperplasia. In pediatrics early detection of adrenal disorders is facilitated by the use of LC–MS/MS as illustrated in the contribution by Rauh. Further aspects of neonatal steroid profiling (simultaneous coverage of 69 analytes) are presented by Hill and co-workers.

Analyses of dysregulation of sterol or glucocorticoid synthesis and excretion pathways are presented by Fon Tracer et al. and Vogeser, respectively. This special issue also touches on doping and its monitoring (Parr and co-workers).

Steroid analytics is moving form single molecule quantification to mapping of whole pathways. Integrative approaches in steroid metabolomics already could be called “sterome” analytics similar to lipid analytics addressed as “lipidome”. At present the steromics is important for targeted drug development, studies on endocrine

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disruptors and disease pathophysiology, e.g., cancer and obesity. Epidemiologic studies being initiated by Ziegler and co-workers foster research on mechanisms of steroid-related diseases and support the development of diagnostics.

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