Journal of Steroid Biochemistry & Molecular Biology 122 (2010) 1–2

Contents lists available at ScienceDirect

Journal of Steroid Biochemistry and Molecular Biology

journal homepage: www.elsevier.com/locate/jsbmb

Editorial

Special issue on *Steroids in Obesity and Diabetes*

Over the last 20 years, western societies have witnessed a notable increase in the prevalence of metabolic disorders including dyslipidemia, insulin resistance, hypertension, overweight and obesity [1]. From a population perspective, it is predicted that this trend will inevitably result in unprecedentedly high incidences of type 2 diabetes and cardiovascular disease worldwide [2,3]. As a major underlying factor to this phenomenon, our sedentary lifestyles coupled with increased consumption of omnipresent, low-cost, energy-dense foods [4,5]. Within these population trends however, individual responses to this sometimes called 'toxic environment' remain highly variable. As a consequence, metabolic features are extremely heterogeneous, leading to significant challenges in the study of this condition, but also in the identification and treatment of high risk subpopulations [6,7]. Attention to metabolic disorders from the medical and scientific community also has followed a rising trend, and, as a result, the medical literature now presents a multitude of original studies, of reviews, and consensus opinions aimed at and sometimes succeeding in providing new information, original angles or novel approaches to what has been called the 'civilization syndrome' [8].

Steroid hormones from all the major classes have been the basis of numerous studies on metabolic disorders over the years. In this special issue of the *Journal of Steroid Biochemistry and Molecular Biology* entitled **Steroids in Obesity and Diabetes**, we present a series of review articles and original studies that dissect the complex relationship between steroid hormones and metabolic disorders. The array of populations and conditions examined as well as the number of models and methodological approaches included in this special issue truly reflect the pleiotrophic nature of steroid hormones. The breadth of the research interest, together with the urgency with which we need to address the clinical problem of the rapidly escalating prevalence of metabolic disease highlights the timely nature of this special issue.

Form our very earliest age, exposure to glucocorticoids can be detrimental to foetal growth and development. However, these effects may extend far beyond the womb into adult life and may program metabolic phenotype. These hypotheses, reviewed by Rebecca Reynolds in this issue [9], appear to stand up to scrutiny in animal models, but are clearly more challenging to tease out in clinical studies. However, robust associations in large clinical cohorts are well described.

Animal models have considerably enhanced our understanding of almost all aspects of steroid hormone biology and action. The review by Rose et al. [10] highlights this specifically with regards to the glucocorticoid receptor. It emphasises the role that state-of-the-art molecular biological techniques can play, in particular when examining tissue specific effects of steroid hormones.

Peripheral glucocorticoid metabolism has received a tremendous amount of scientific attention in recent years. Gathercole and Stewart present a review article on this topic, with a specific emphasis on the promising avenue of selective 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitors [11]. This is complemented by an original study examining adipose tissue depot-specific expression of 11β-HSD1 which demonstrates that omental adipose 11β-HSD1 expression is an independent predictor of adiposity (albeit in women only) and further endorses 11β-HSD1 as a therapeutic target that may have the potential to decrease central obesity [12]. Dysregulation of corticosteroid hormone production and metabolism are well described in metabolic diseases including obesity and insulin resistance. However, in this special issue, a report by Simunkova and colleagues shows that a quarter of young adults with type 1 diabetes also present with evidence of subclinical hypocorticalism [13] which has not previously been reported.

Whilst glucocorticoids have a potent impact upon metabolic phenotype, sex steroids almost certainly have an equally important role to play. Two review articles address the critical role of estrogens in metabolic homeostasis. A paper by Brown and Clegg first provides an overview of the role of estrogen signalling in the brain as it relates to body fat accretion and distribution [14]. A second article by Foryst-Ludwig and Kintscher then focuses on the impact of estrogen receptor alpha and beta signalling on glucose and lipid metabolism [15]. The well-studied topic of insulin and hyperandrogenism in the polycystic ovary syndrome is also summarized in detail in a review article by Baptiste and collaborators [16]. Two original papers examine the impact of estrogen [17] and dihydrotestosterone [18] upon skeletal muscle and adipose tissue gene expression. Both studies identify novel gene targets that are regulated by sex steroids although the functional significance of these observations remains to be determined.

An original study by Alexanderson and colleagues performed in rats shows that a single, early postnatal estradiol injection has long-lasting effects on both the ovary and adipose tissue of the animals, again emphasizing the potential impact of sex hormones in the fetal programming of metabolic and endocrine function [19]. Finally, the additive effects of physical activity and estradiol treatment in rats are explored by Zoth et al. [20].

Overall, the diversity of studies and reviews that are presented in this special issue reflect the fundamental role that steroid hormones have in the etiology and pathogenesis of metabolic disorders including obesity, diabetes and insulin resistance. As well

0960-0760/$ – see front matter
doi:10.1016/j.jsbmb.2010.08.002

as enhancing our understanding of the mechanism underpinning disease processes, they are also potentially exciting and novel therapeutic targets and with the ever increasing disease burden that we are facing, this is becoming an urgent clinical priority.

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