**Abstract citation ID: bvac150.1480**

## Steroid Hormones and Receptors

***ODP435***

***11-Ketotestosterone is One of the Major Androgens in Pigs***

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11-ketotestosterone (11-KT) is one of the active androgens, which belongs to the novel 11-oxygenated class of androgens. Although 11-KT has been regarded as a teleost-specific androgen, it was recently demonstrated that 11-KT is a major human androgen. However, the details of its functions and dynamics remain unknown. Deficiency of proper animal model is one of the reasons for this. Although rodent models have contributed to reveal synthesis and functions of steroid hormones, only small amounts of 11-KT are synthesized in mice and rats (Yazawa et al. Endocrinology, 2008). In mammal, 11-KT is abundant in limited animal species, such as non-human primates, pig and guinea pig. This suggest that these animal species are valuable models for determining the functions of 11-KT in mammals. In the

present study, we evaluated the production and potential functions of 11-KT in pig. In previous studies, we studied human and murine steroidogenesis using steroidogenic cells-derived from mesenchymal stem cells (MSCs, Yazawa et al. Endocrinology 2006, 2009; Mol Endo, 2010; Endocrine J 2016). Therefore, we first induced steroidogenic cells from porcine subcutaneous preadipocytes (PSPA cells), which originate from MSCs. With the aid of cAMP, adenovirus-mediated introduction of SF-1/Ad4BP induced the differentiation of PSPA cells into 11-KT-producing cells. Using PSPA cell-derived steroidogenic cells and our previously established method (Yazawa et al. JSBMB, 2020), we found that porcine AKR1C1 can convert androstenedione into testosterone (T) and is expressed in adrenal, testis and ovary. In addition, we showed that HSD11B2, one of the essential genes to produce 11-KT from T was expressed in testicular Leydig cells and the adrenal cortex. 11-KT was present in the plasma of both immature male and female pigs, with slightly higher levels in males than in females. T levels were much higher in male pigs. It is noteworthy that 11-KT levels were >10-fold higher than T levels in female pigs. However, castration altered the plasma profiles of 11-KT and T in male pigs to the female-like profiles. 11-KT induced endothelial nitric oxide synthase (eNOS) in porcine vascular endothelial cells. These results indicate that 11-KT is produced in porcine adrenal glands and testes. It can potentially be involved in the regulation of cardiovascular functions through eNOS expression. In addition, these findings indicate that pigs (especially female) represent an ideal model for analyzing the functions of 11-KT in mammal.

*Presentation:* No date and time listed