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Androgen Metabolism and Homeostasis in the Lateral Nasal Gland and the Olfactory Mucosa of Male Mice: Potential Function of the Lateral Nasal Gland As a Paracrine Organ for Testosterone

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Circulating sex steroid hormones are known to modulate the structure and function of the mammalian olfactory chemosensory system; yet detailed mechanisms of hormone action, including mechanisms of regulation of hormone bioavailability in various nasal organs or tissue compartments, are still poorly understood. It has been proposed that levels of steroid hormones in the nasal tissues are controlled by nasal P450 enzymes. The aim of this study was to determine whether tissue levels of the major androgen, testosterone (T), are altered in the olfactory mucosa (OM) and the lateral nasal gland (LNG), the largest anterior gland in the nasal cavity, of a Cyp2g1-null/Cyp2a5-low mouse model. CYP2G1 is expressed only in the OM, whereas CYP2A5 is expressed in both OM and LNG; both enzymes are highly active in T hydroxylation in vitro. We found that T level in the LNG of adult male mice was ~10 times higher than that in the OM. In fact, the level of T in the LNG was the highest among all non-endocrine organs examined. On the other hand, microsomal T-hydroxylase activity was ~40 times lower in the LNG than in the OM. The T level was increased by ~3 times in the LNG, but not in the OM, of the Cyp2g1-null/Cyp2a5-low mouse, which had ~75% and ~50% decreases in microsomal T-hydroxylase activities in the LNG and OM, respectively, compared to wild-type mouse. The tissue-selective increase in T level was accompanied by increased gene expression in the LNG for two proteins capable of binding T, the salivary androgen binding protein (sAbp) and the lipocalin-type prostaglandin D2 synthase (L-PGDS). Based on these findings, we conclude that nasal P450 enzymes play a critical role in the maintenance of androgen homeostasis in the LNG. We propose that the levels of T in the OM and LNG are controlled by the counteracting activities of androgen-binding proteins and androgen-metabolizing enzymes. Furthermore, we hypothesize that the remarkably high level of T in the LNG, a secretory gland, may have a paracrine function in the male olfactory system, a situation that can have a significant impact on our understanding of the peri-receptor events that influence pheromone/odorant signal transduction in mammals.