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Comparison of Age-related Tyramine Concentration in the Male Mouse Reproductive System

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Erectile dysfunction is the most common disorder of the male reproductive system and plays a role in infertility, yet little is known about the signaling mechanisms responsible for this condition [1]. Although the cause of this condition can vary, erectile dysfunction is thought to occur due to an imbalance of vasoconstrictors and vasodilators within the male reproductive system [2]. Understanding the signaling pathways responsible for muscle contraction and dilation could provide insight on treatments for this prevalent condition.

The male reproductive system is a multi-organ network consisting of the penis, testes, vas deferens, and epididymis. These tissues contain smooth muscle capable of constriction or dilation which are controlled by a combination of hormones, peptides, neurotransmitters, and amines. Tyramine, a biogenic monoamine, has been found to modify peripheral vasoconstriction, increased cardiac output, and elevated blood glucose as well as modulate smooth muscle contraction in mouse uterine tissue. Previous studies have linked the induction of smooth muscle contractions with tyramine as a stimulant [3]; however, the complex interactions between tyramine, norepinephrine, and smooth muscle contractions remains to be discovered. The focus of this study was to identify the regions in the male reproductive system with the highest concentrations of tyramine and TAAR1 (trace amine associated receptor 1), a high affinity receptor for tyramine. Because male reproductive conditions, such as erectile dysfunction, increase in frequency with an individual's age this study compared tyramine and TAAR1 concentrations during the age of peak reproductivity and fully mature mice with diminishing reproductive potential.

Histological and fluorescent microscopy were used to determine the changes in tyramine and TAAR1 concentrations between young and aging male mouse reproductive systems. Aging mice used in this study were classified as mice that were older than 1 year and young reproductive mice were between 3 and 6 months. This protocol was approved through the IACUC protocol 18-1606R at Arizona State University (ASU). The male reproductive tissue was obtained from C57BL/6J wild type and a GFP LifeAct transgenic mouse line [4]. Specific antibodies used include anti-TAAR1 (Santa Cruz Biotechnology) and anti-tyramine (Millipore). Secondary labeling included Alexa 568 and 633 (ThermoFisher). Images were acquired on a Leica SP8 confocal (NIH SIG award 1 S10 OD023691-01) at ASU. Microscopy results have revealed lower concentrations of tyramine and TAAR1 receptors in older mice as compared to a younger mouse at an optimal reproductive age within the male reproductive system. This finding is being further explored using HPLC and rtPCR for quantitative results. Because tyramine is known to play a role in modulating smooth muscle contraction, this decrease in concentration may play a role in conditions like erectile dysfunction [5].

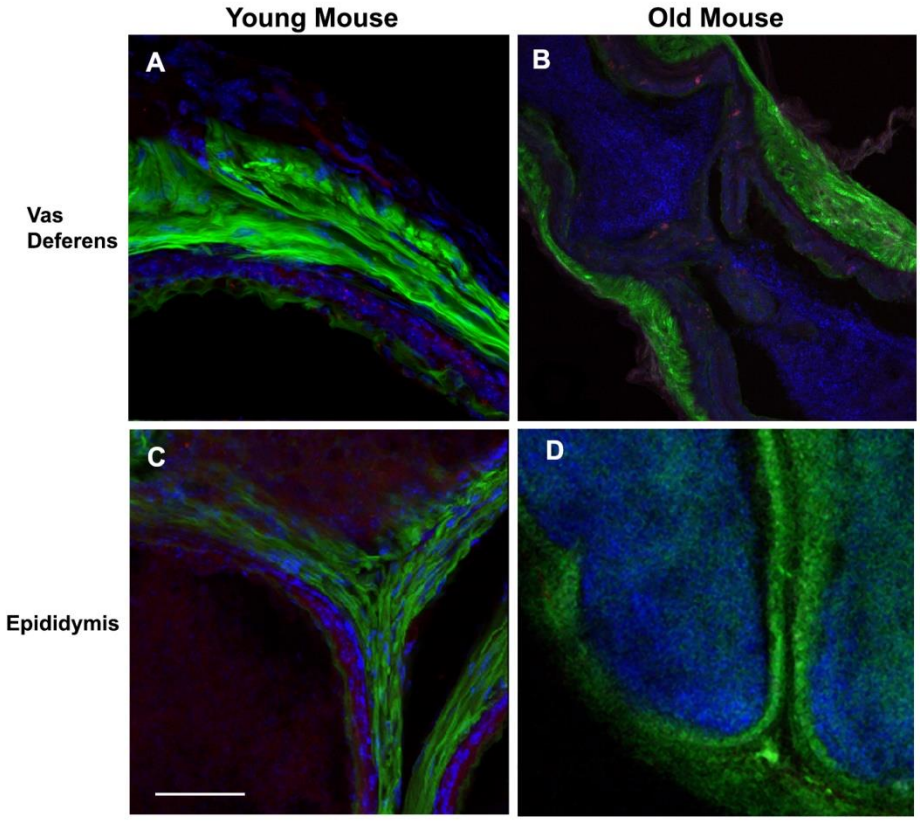

Figure 1. TAAR1 Localization in Young and Old Mice within in the Male Reproductive System. TAAR1 localization (red) is increased in young mice (A and C) as compared to older mice (B and D) within both the vas deferens and epididymis tissue. The green regions are f-actin labeled with GFP Lifeact and blue is the DNA. Scale bar is 100um.

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