excitatory designer receptor, hM3Dq, with mice expressing cre under control of the POMC promoter. When these mice are administered intraperitoneal clozapine-N-oxide (CNO), POMC neurons exhibit increased activation. We completed a comprehensive mating analysis to measure the sexual desire and erectile and ejaculatory capabilities of these male mice under CNO or saline administration. Additionally, we sacrificed the mice after injection of CNO or saline to perform immunostaining for the protein c-fos as an indicator of neural activation. As expected, activation of POMC neurons with CNO increased c-fos expression, while the impact on male sexual interest was more nuanced. These experiments emphasize the need to investigate the specific neuropeptide and transmitter output by POMC neurons that influences sexual behavior and function.

Adipose Tissue, Appetite, and Obesity
NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE

Renal (Pro)renin Receptor Contributes to High Fat Diet-Induced Obesity

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Recently we reported that (Pro)renin receptor (PRR) expression increases in the renal nephron during high fat diet intake. This study evaluated the role of renal PRR in the development of obesity. Eight-week old male mice with inducible nephron specific PRR knockout (KO) and wild type littermate (control) were fed either normal diet (ND, 12%kcal fat) or high fat diet (HFD, 45%kcal fat) for 6 months. KO Mice underwent induction of PRR KO with oral doxycycline 2mg/mL in 2% sucrose water for 12 days prior to starting diet. Compared to ND, HFD increased body weight by 40% ($p<0.05$) in control mice. In contrast, compared to control mice fed HFD, body weight of induced PRR KO on HFD was reduced by 56% ($p<0.05$). Total body fat increased by 179% ($p<0.05$) with HFD compared to ND control mice while it did not increase in PRR KO mice fed HFD. Twenty-four-hour caloric intake was not reduced in KO mice compared to controls while there were significant increases in nocturnal VO2 by 31% and respiratory exchange by 10% ($p<0.05$) in HFD PRR KO mice compared to HFD fed controls. Unexpectedly, urine glucose excretion significantly increased in PRR KO mice on both ND and HFD. Our results demonstrate that nephron specific PRR KO reduced diet induced obesity and adiposity, while increasing energy expenditure. Future investigations are warranted to elucidate the mechanisms by which renal PRR contributes to the development of obesity.

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ScRNA-seq Reveals a Role of Mammary Luminal Epithelium in Adipocyte Adaptations

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Almost four decades of research suggest a dynamic role of ductal epithelial cells in adipocyte adaptation in mammary gland white adipose tissue (mgWAT), but factors that mediate such communication are not known. Here, we identify a complex intercellular crosstalk in mgWAT revealed by single-cell RNA-seq (scRNA-seq) and comprehensive data analysis suggest that epithelial luminal cells during cold exposure undergo major transcriptomic changes that lead to the expression of an array of genes that encode for secreted factors involved in adipose metabolism such as Adropin (Enho), neuregulin 4 (Nrg4), angiopoietin-like 4 (Angptl4), lipocalin 2 (Lcn2), milk fat globule-EGF factor 8 (Mfge8), Insulin-like growth factor-binding protein 1 (Igfbp1), and haptoglobin (Hp). To define the mammary epithelial secretome, we coin the phrase "mammokines". We validated our cluster annotations and cluster-specific transcriptomics using eight different adipose scRNA-seq datasets including *Tabula Muris* and *Tabula Muris Senis*. In situ mRNA hybridization and ex vivo isolated mgWAT luminal cells show highly localized expression of mammokines in mammary ducts. Trajectory inference demonstrates that cold-exposed luminal cells have similar transcriptional profiles to lactation post-involution (PI), a phase defined by reappearance and maintenance of adipocytes in the mammary gland. Concomitantly, we found that under cold exposure female mgWAT maintains more adipogenic and less thermogenic potential than male scWAT and ex vivo removal of luminal epithelial cells from mgWAT markedly potentiates beige adipocyte differentiation. Conditioned media from isolated mammary epithelial cells treated with isoproterenol suppressed thermogenesis in differentiated beige/brown adipocytes and treatment of beige/brown differentiated adipocyte with mammokine LCN2 suppresses thermogenesis and increases adipogenesis. Finally, we find that mice lacking LCN2 show markedly higher cold-dependent thermogenesis in mgWAT than controls, and reconstitution of LCN2 in the mgWAT of LCN2 knockout mice promotes inhibition of thermogenesis. These results show a previously unknown role of mammary epithelium in adipocyte metabolism and suggest a potentially redundant evolutionary role of mammokines in maintaining mgWAT adiposity during cold exposure. Our data highlight mammary gland epithelium as a highly active metabolic cell type and mammokines could have broader implications in mammary gland physiology and lipid metabolism.

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Serotonin as a Regulator of Leptin-Mediated Food Intake Control Within a Novel Neuronal Circuit Between the Hypothalamus and Raphe Nuclei

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