Compared with the U to U group, the U to B group showed opposite results. Whether to use ACTH stimulation during adrenal venous sampling (AVS) for the subtype diagnosis of PA remains unresolved. **Objectives:** Our purpose of this study is to evaluate the clinical implications of ACTH stimulation during AVS in terms of surgical outcomes. **Design and settings:** Among JRAS cohort, we allocated 314 patients with both basal and ACTH-stimulated AVS data who underwent adrenalectomy to 3 groups: basal laterazation index (LI) ≥ 2 with ACTH-stimulated LI ≥ 4 on the ipsilateral side (Unilateral (U) to U Group, n=245); basal LI < 2 with ACTH-stimulated LI ≥ 4 (n=15); basal LI ≥ 2 with ACTH-stimulated LI < 4 (U to Bilateral (B) Group, n=54). We compared surgical outcomes among the groups. **Results:** Compared with the U to U group, the U to B group had poor clinical and biochemical outcomes and low rates of adrenal adenoma as a pathological finding. All patients in the U to B group had clinical and biochemical benefits however had adrenal adenoma as a pathological finding and could be well differentiated from those with poor surgical outcome via basal LI, but not ACTH-stimulated LI. A receiver operating characteristic curve analysis demonstrated that the cut-off value of 8.3 showed the specificity of 84% for the prediction of good surgical outcome in U to B group. These results were similar even when we defined each group based on a cut-off value of 4 for basal LI. Although, the basal plasma aldosterone concentration (PAC) in the adrenal veins on both dominant and non-dominant sides among patients with better surgical outcome in the U to B group were not significantly different from those in the U to U group, there was a significant difference in the ACTH-stimulated PAC on the dominant side. **Conclusions:** We demonstrated novel findings showing that patients in the U to B group were shown to be comprised of 2 groups with good and poor surgical outcomes, and basal LI was useful in identifying PA patients with good surgical outcome in U to B group. The low expression level of MC2R receptor on aldosterone-producing adenoma (APA) might be the explanation of the weak response in aldosterone level in a proportion of surgically curable APA cases. These findings point to the important fact that ACTH stimulation on AVS obscure surgically curable cases of PA.
capacity of these stem cell-derived neurons to fully mature and integrate into existing neural circuits of physiological relevance is unknown. This study systematically tested whether Pomc mRNA-positve cells newly generated from tanycyte precursors can differentiate into melanocortin-secreting POMC neurons, integrate into the normal anatomical projection pathways of these cells and rescue the obesity phenotype caused by the loss of Pomc expression in ArcPomc<sup>neo/fneo</sup> mice. We generated an inducible compound genetic mouse model by crossing RaxCreERT2 with the Cre-dependent ArcPomc<sup>neo/fneo</sup> and LSL-syp-tdTomato alleles. Rax is expressed exclusively in postnatal tanycytes, thereby limiting tamoxifen-induced recombination of the two floxed alleles by CreERT2 to tanycytes. As expected, tamoxifen treatment of the mice at age 4–5 wk recapitulated endogenous Rax expression 16 wk later as observed by red fluorescent tdTomato expression in all tanycytes. In addition, Cre recombinase-mediated deletion of the floxed-neomycin cassette from the neuronal enhancer region of the ArcPomc<sup>neo</sup> alleles relieved their constitutive transcriptional silencing. Consequently, tamoxifen treatment consistently generated a significant number of newly generated POMC neurons from tanycytes (~10% of the POMC neurons in a WT mouse), identified by Pomc FISH and POMC/α-MSH immunofluorescence in the soma and established terminal projections to hypothalamic nuclei including the PVH and DMH involved in energy homeostasis. A subpopulation of these neurons also expressed the synaptophysin-tdTomato reporter. We performed serial body weight, food intake, body composition, oral GTT and insulin measurements with the RaxCreERT2/+, ArcPomc<sup>neo/fneo</sup> mice and found no significant differences in any of these metabolic variables compared to untreated obese ArcPomc<sup>neo/fneo</sup> mice. These data are consistent with previous studies from our lab suggesting that Pomc expression has to be at least ~30% of normal to mitigate the obesity phenotype in Pomc-null mice. In conclusion, we demonstrated that tanycytes are capable of generating mature Pomc-expressing neurons in the hypothalamus of adult mice. However, we propose that determining the underlying mechanisms involved in the generation of hypothalamic POMC neurons from tanycytes and interventions to increase their number, might lead to a novel approach to treat obesity. Nothing to Disclose: SG, GW, RML, MJL.

Tumor Biology
TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS

Distinct Molecular Phenotypes of Non-Diseased Breast Adipose Tissue of Pre-Menopausal Obese and Non-Obese Women May Underlie Differing Breast Cancer Risks
Iiad Alhallah, BSc, Keith G. Wolter, MD, PhD, Frank A. Simmen, PhD, Richard Jon Ward, BSc, Stacy A. Petty, APRN, Rosalia CM Simmen, PhD. Univ of Arkansas for Med Sciences, Little Rock, AR, USA.

SUN-126
Obesity is a major risk factor for many chronic diseases including postmenopausal breast cancer. Paradoxically, breast cancer susceptibility is inversely linked to obesity in pre-menopausal women. Adipose tissues are active endocrine organs that play major roles in tumor development and progression; however, fat depots at different anatomical sites are biologically and functionally distinct and their singular influence on breast epithelial biology remains unclear. To study the early events by which breast adiposity may provide a microenvironment predisposing normal breast epithelial cells to tumorigenesis, we collected breast tissue from pre-menopausal (n=10/group) non-obese (NO, BMI=27.6±0.8) and obese (O, BMI=44.5±2.8) women of comparable ages (NO: 36.1±3.3; O: 40.4±2.0) with no breast cancer and undergoing elective breast reduction surgery. Breast adipose tissue and corresponding glandular cells were analyzed histologically and evaluated for expression of genes (adipokines, cytokines, steroid hormone signaling) by QPCR and proteins (proliferation, apoptosis, inflammation) by IHC. Adipocyte size distributions from NO and O breasts did not differ (P<0.9). However, adipose mRNA levels for pro-inflammatory cytokines (IL-6, IL-8, CSF-1, MCP-1) and adipokines (LEP, CFD) were higher for O than NO (P<0.05). AdipoQ, ER-α, and ER-β transcript levels were lower for O than NO (P<0.05), while those for CYP19 and PTGS2 showed reverse trends (O>NO, P<0.05). In the corresponding glandular cells, NO had higher mRNA levels for IL-6, IL-8, ER-α, and ER-β than O (P<0.05). Immunostaining with anti-Ki67 antibodies indicated that O glandular cells were 3-fold less proliferative than those for NO, consistent with their lower Cyclin D1 mRNA levels (P<0.05). Galectin-1, a pro-fibrotic protein, showed predominant myo- vs. luminal epithelial localization, with staining intensities for O tending to be higher (P=0.07) than for NO. Perilipin immunostaining was specific for adipocytes and did not differ for O and NO. A non-targeted approach using a Human Cytokine Array (R&D Systems) was employed to further evaluate the inflammation status of O vs. NO adipose. The analyses confirmed the higher expression of IL-8, Leptin and CFD (by QPCR) in O vs. NO and identified C-reactive protein, EMMPRIN, Trefoil Factor-3, Cystatin-3 and Macrophage Migration Inhibitory Factor-1 as greater in O than NO (~2-fold). Our findings demonstrate marked differences in gene and protein expression patterns of O and NO breast adipose tissue, which were accompanied by a suppression of proliferation of O relative to NO breast epithelium. We speculate that early exposure of the breast epithelium to a highly inflammatory environment fueled by breast adiposity may promote a senescent state that confers protection from pre-menopausal breast cancer.

Bone and Mineral Metabolism
OSTEOPOROSIS: DIAGNOSIS AND CLINICAL ASPECTS

Denosumab Preserves Bone Mineral Density at the Knee in Persons with Subacute Spinal Cord Injury
William Alan Bauman, MD<sup>1</sup>, Christopher M. Cirnigliaro, MS<sup>1</sup>, Michael F. La Fontaine, EdD<sup>2</sup>, Josh Hobson, MS<sup>2</sup>, Steven C. Kirshblum, MD<sup>2</sup>, Christin McKenna, MD<sup>1</sup>, Ann M. Spungen, EdD<sup>1</sup>.

<sup>1</sup>James J. Peters VA Medical Center, Bronx, NY, USA. <sup>2</sup>Kessler Institute for Rehabilitation, East Orange, NJ, USA, <sup>3</sup>Kessler Institute for Rehabilitation, Bronx, NJ, USA.