

calcium/vitamin D in musculoskeletal health). Importantly, a significant proportion of the aging population does not meet the recommended intake of many micronutrients.<sup>17</sup> Clinical trials on the benefits of micronutrient supplementation have not been conclusive, but adequate intake should be considered an essential component of comprehensive healthcare for older adults.

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## Reproductive Endocrinology

### REPRODUCTIVE ENDOCRINOLOGY: REPRODUCTIVE FUNCTION AND DYSFUNCTION ON DEVELOPMENT

#### *A Gene Expression Profile of the Adolescent Breast and the Impact of Obesity*

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#### MON-031

Environmental exposures that occur early in life affect breast development and breast cancer (BC) risk in adulthood. Puberty is one such developmental 'window of susceptibility' when estrogen (E) stimulates breast adipocytes and stromal and epithelial cells to proliferate at an exponential rate, making them vulnerable to carcinogens. Excess adiposity during adulthood may increase BC risk through obesity-associated inflammation and/or aromatase activity, which increases local E levels. While obesity during puberty might be expected to also increase future BC risk, epidemiological studies suggest that pediatric obesity may actually be protective. The current studies investigated the gene expression profile of the normal adolescent breast and how early life factors such as obesity may influence these profiles.

We performed RNA-seq in 62 histologically-normal breast tissue samples from adolescent girls and young women (mean age 17.8 yrs) who underwent breast reduction surgery. Twenty-nine patients were normal weight (NW; mean BMI 23.2 kg/m<sup>2</sup>) and 33 were overweight/obese (OB; BMI 31.7). Comparison of our adolescent dataset with published mammary RNAseq datasets from pubertal mice, rats, macaques, and adult women (mean age 38 yrs) revealed relatively poor (~30%) overlap with other species, but 88% overlap with adults for the 500 most highly expressed genes in each dataset. The small gene set (n=43) common to all groups was enriched for extracellular matrix components. We used DESeq2 to identify differentially-expressed (DE) genes in NW vs OB samples. To avoid confounding due to differences in the cellular composition of NW and OB samples, we first used CIBERSORT to computationally estimate the adipocyte fraction of each sample and included this estimate as a covariate. We identified 74 up-regulated and 73 down-regulated genes in NW vs. OB ( $p_{\text{adj}} < 0.05$ ). We used Ingenuity Pathway Analysis (IPA) to determine whether the DE genes might reflect activation or inhibition of upstream transcriptional regulators in OB samples. IPA identified the cytokines CSF1 and CSF2 and the chemokine receptor CCR2 as the most highly activated upstream regulators, suggesting a signature of increased inflammation in OB samples. While classical E receptor (ER) targets (e.g., PR, AREG) were not DE'd, IPA identified ESR1, 17- $\alpha$ -ethinyl estradiol, genistein, and PR, as well as growth factors/receptors (EGF, IGF-1, HGF, HER3) and kinases (AKT1, ERK) involved in hormone-independent ER activation, as activated upstream regulators in OB samples. These studies represent the first investigation of the human breast transcriptome during late puberty and demonstrate that in adolescents, as in adults, OB is associated with increased inflammation which may augment E action in the breast microenvironment.

## Pediatric Endocrinology

### PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY

#### *Seasonal Variations of 25-Hydroxy Vitamin D3, Parathyroid Hormone, and Alkaline Phosphatase in School-Aged Children*

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#### SUN-099

Background: The central role of Vitamin D is the homeostasis of calcium and phosphorus, affecting bone metabolism directly. The principal source of Vitamin D is the synthesis by the skin in response to its exposure to ultraviolet B radiation.

The synthesis of vitamin D by the skin is affected by different factors such as age, pigmentation, use of sunscreen, and clothing. The low sun exposure, especially in extreme