work was to study the expression of aldosterone synthase (CYP11B2 which catalyzes the last steps of aldosterone synthesis) and 11β-hydroxylase (CYP11B1 which catalyzes the last step of cortisol synthesis) in normal adrenal glands to address issues regarding the zonation and the fate of the cells constitutive of each zone through the expression of Ki-67 and cleaved Caspase-3. Thirty eight normal human adrenals (16 females, 22 males, ranging in age from 22 to 81 years old with a median age of 52 years old) were obtained from brain-dead organ donors (kindly provided by the Organ Transplant Clinics, University Hospital of Rouen). As early as 22 years old, we found that the histological ZG (h-ZG) does not correspond to the functional ZG (f-ZG) expressing CYP11B2. Moreover, the h-ZG CYP11B2-cells were CYP11B1+ showing that these cells ascribed to the h-ZG are in fact cortisol producing cells. The progressive replacement of CYP11B2+ cells by CYP11B1+ cells in the h-ZG might demonstrate the role of the extracellular matrix in the morphological maintenance of the adrenal cortex. Our analysis also showed that steroidogenic cells were either CYP11B1 or CYP11B2 positive. By immunofluorescence, we observed in many cases isolated or clusters of CYP11B2+ cells located deeply in the h-ZF and sometimes in the vicinity of the central vein. We were able to show that those cells were probably issued from CYP11B2+ cell clusters located in h-ZG which migrated centripetally. Ki-67 immunoreactivity was highly variable and observed throughout the entire cortex. We also found a positive correlation between the steroidogenic and endothelial cells proliferation. It is interesting to note that some Ki-67+ cells located in the h-ZG were CYP11B1+. Cortical cells positive for cleaved Caspase-3 were extremely rare but detected in all zones when present. These findings challenge the classic view of lineage conversion of differentiated ZG cells and show a new pathway where the CYP11B2+ cells migrate without changing their phenotype.

**Thyroid**

**BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II**

**Fatigue and Quality of Life Among Thyroid Cancer Survivors**

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**SUN-416**

Fatigue and quality of life among thyroid cancer survivors

**BACKGROUND** Fatigue among thyroid cancer survivors is an important issue that needs to be appreciated and managed appropriately. Although several studies have reported potential factors that might be related to postoperative fatigue, the associations have yet to be inconclusive. The purpose of the present study was to estimate the prevalence of clinical fatigue in patients with papillary thyroid carcinoma and to reveal predictive factors, including their quality of life.

**METHODS** A cross-sectional survey was conducted on patients with papillary thyroid carcinoma. Patients who underwent non-curative surgery, or those with recurrent or metastatic PTC, or those with other malignancies were excluded. The primary outcome was fatigue measured by the Cancer Fatigue Scale (CFS), and the secondary outcome was quality of life (QoL) quantified using the SF-36 v2. The following explanatory variables were collected: gender, age, employment status, marital status, co-morbidities, time since initial surgery, types of surgery, replacement of thyroid hormone, use of radioactive iodine, and the level of thyrotropin. The prevalence of clinical fatigue was estimated with the cut-off value of 18/19 of the CFS score. Correlations between the CFS score and the explanatory variables were examined using uni-variable analyses as well as multi-variable analysis.

**RESULTS** Three hundred twenty-one patients participated in the survey. Of them, 258 respondents (80%) were female. The median age was 58 years, and the median time from initial surgery was 6.4 years. The mean and the standard deviation of the CFS score were 17.9 and 9.3, respectively (range: 0-48). The prevalence of clinical fatigue was 42% [95%CI: 36-47%]. Among the variables explored, having a job and scores of the mental component summary, the physical component summary, and the role/social component summary of the SF-36 were inversely associated with the CFS score in both uni- and multivariable analyses.

**CONCLUSION** Postoperative fatigue was common in thyroid cancer survivors. Patients with a job and better QoL, in particular, those with good mental health, maybe at low-risk of developing the burden.

**Tumor Biology**

**TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS**

**Breast Adipose Tissue Extracellular Vesicles from Obese Women Increase Breast Cancer Aggressiveness - a Novel Mechanism for the Obesity-Breast Cancer Link.**

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**SAT-126**

**Background and Objectives:** Breast cancer is among the most common cancer in women with 2.1 million new cases detected each year. Numerous studies have demonstrated a connection between body mass index (BMI) and cancer incidence, with obesity (BMI ≥ 30) being responsible for the development of at least 13 types of cancer, and 15% to 20% of total cancer-related mortality. The effects of extracellular vesicles (EVs) derived from the obese adipose tissue microenvironment on breast cancer have not yet been clearly elucidated.

**Methods:** EVs were obtained from media conditioned with human breast adipose tissue from reduction mammoplasty (n=31). Women were healthy at the time of surgery and had no history of breast cancer. Patient samples were stratified based on their body mass index (BMI), with a BMI < 25 considered healthy and a BMI ≥ 25 considered overweight/obese. Breast adipose tissue-derived EVs (AT-EVs) were characterized (Quantitative Mass Spectrometry) and used to treat human breast cancer cell lines, including the ER+ MCF7 and triple...
negative breast cancer (TNBC) MDA-MB-231. Effects on cell proliferation and migration in vitro, and on tumor growth in a mouse xenograft model, were examined after long-term education with EVs. RNA sequencing was performed to investigate potential reprogramming induced by AT-EVs.

**Results:** We found a positive correlation between protein amount per AT-EV and BMI. Quantitative proteomics of AT-EVs revealed 46 proteins that were significantly higher and 54 proteins that were significantly lower in specimens from women with a BMI ≥ 25 compared to women with a BMI < 25. AT-EVs from patients with a BMI ≥ 25 induced proliferation of MCF7 cells compared to AT-EVs from patients with a BMI < 25. Obese EVs induced a more aggressive phenotype in MDA-MB-231 cells, increasing their invasiveness in vitro. Obese EVs also increased the growth of MCF7 and MDA-MB-231 cells in vivo. Ingenuity pathway analysis of RNA-Seq data identified significant differences in mTOR signaling and canonical pathways associated with altered mitochondrial function.

**Conclusion:** Our studies identify a novel mechanism to explain the obesity-breast cancer link in older women. Namely, that in obesity, the breast microenvironment produces EVs capable of reprogramming breast cancer cells to grow faster and be more aggressive. Identifying which cargo in breast AT-EV mediates these effects may provide new targets for intervention.

**Reproductive Endocrinology**

**MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES**

**Redefining Eunuchoid Body Proportions in Adults**

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**SAT-036**

Redefining Eunuchoid Body Proportions in Adults

Different population groups have different normal adult body proportions. A retrospective study was done on 100 males with age range of 20 to 58 years. Thirty (30%) males had arm span greater than height and upper segment and lower segment ratio (US/LS) below 0.9 which was a proposed criterion for eunuchoid body proportion by Winters. Moreover, sixty-three (63%) males had arm span greater than 5 cm which was greater than the 2 cm criterion of Santen. Only three (3%) males had arm span 1 SD above mean (172.55 ± 12.01 cm) and US/LS 1 SD below mean (0.91 ± 0.04 cm). Hence, eunuchoid body proportions in adults should be defined in terms of SD from mean for the particular sex and race. The body proportion could be defined in terms of SD from mean for the particular sex and race. The body proportion could be defined in terms of SD from mean for the particular sex and race.

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**Neuroendocrinology and Pituitary**

**PITUITARY TUMORS II**

Withdrawal from Long-Acting Somatostatin Receptor Ligand Injections in Adult Patients with Acromegaly: Results from the Phase 3, Randomized, Double-Blind, Placebo-Controlled CHIASMA OPTIMAL Study

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**MON-297**

Data on the impact of withdrawal from long-acting somatostatin receptor ligand (SRL) injections on disease activity in patients with acromegaly are limited. The phase 3 Octreotide capsules versus Placebo Treatment In MultinationAL centers (OPTIMAL) study assessed the efficacy and safety of oral octreotide capsules in adult patients with acromegaly responding to injectable SRL therapy. The placebo-controlled arm of this study allowed for assessment of acromegaly biochemical and disease activity in patients after withdrawal from SRL treatment. A multinational, randomized, placebo-controlled study was conducted in 56 adult patients with active acromegaly. Patients were ≥ 18 years of age, had evidence of active disease (defined as IGF-I ≥ 1.3 x ULN after last pituitary surgery), and an average IGF-I ≤ 1.0 x ULN in response to a stable dose SRL injection. Patients were randomized, 1 month following their last injection, to octreotide capsule or placebo for 36 weeks, with an option to enroll in an open-label extension. The primary aim was to determine the proportion of patients maintaining biochemical response, defined as IGF-I ≤ 1.3 x ULN after last SRL injection, to octreotide capsule or placebo for 36 weeks, with an option to enroll in an open-label extension. The primary aim was to determine the proportion of patients maintaining biochemical response, defined as IGF-I ≤ 1.3 x ULN after last SRL injection. Patients were randomized, 1 month following their last injection, to octreotide capsule or placebo for 36 weeks, with an option to enroll in an open-label extension. The primary aim was to determine the proportion of patients maintaining biochemical response, defined as IGF-I ≤ 1.0 x ULN in response to a stable dose SRL injection. Patients were randomized, 1 month following their last injection, to octreotide capsule or placebo for 36 weeks, with an option to enroll in an open-label extension. The primary aim was to determine the proportion of patients maintaining biochemical response, defined as IGF-I ≤ 1.0 x ULN in response to a stable dose SRL injection. Patients were randomized, 1 month following their last injection, to octreotide capsule or placebo for 36 weeks, with an option to enroll in an open-label extension. The primary aim was to determine the proportion of patients maintaining biochemical response, defined as IGF-I ≤ 1.0 x ULN in response to a stable dose SRL injection.