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 \geq 25 compared to women with a BMI \leq 25. AT-EVs from patients with a BMI \geq 25 induced proliferation of MCF7 cells compared to AT-EVs from patients with a BMI \leq 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 Santosh Kumar Singh, DM. Private clinic, Patna, India.

SAT-036

Redifining 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.2 Only three(3%) males had arm span 1 SD above mean(172.55 \pm 12.01 cm) and US/LS 1 SD below mean $(0.91 \pm 0.04 \text{ cm})$. 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 due to delayed puberty in Indians compared to the Western population.

References

1.Winters SJ:Clinical Disorders of the Testis.In Leslie J Degroot eds.Endocrinology.3rded. W. B. Saunders Company 1995;2377-2403.

2. Santen RJ:The Testis. In P.Felig et.al. eds.
Endocrinology and Metabolism. 2 $^{\rm nd}$ ed.McGraw Hill,
1981,821-905.

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 \leq 1.0 x ULN in response to a stable dose of 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 (average of week 34 and 36). The trial met the primary endpoint, with 58% (16/28) of patients receiving octreotide capsules maintaining IGF-I response vs 19% (5/28) receiving placebo (P=0.008). The median time to loss of response (2 criteria evaluated: IGF-I >1.0 and ≥ 1.3 x ULN for 2 consecutive visits) was 16 weeks in the placebo group, while it was not reached in the octreotide capsule group. Of the 5 patients in the placebo group who maintained their biochemical response at 36 weeks, only 2 (7% of placebo group) did not meet loss of response criteria. When IGF-I values for any 2 consecutive visits were analyzed for patients receiving placebo, 93% (26/28) lost response based on IGF-I > 1 x ULN and 79% (22/28) lost response based on IGF-I ≥ 1.3 x ULN. Irrespective of biochemical control of acromegaly, 26/28 patients receiving placebo experienced active disease-related symptoms reported as AEs of special interest (AESIs). Most common AESIs (≥ 5%) included arthralgia/arthritis (60.7%), soft tissue swelling (35.7%), headache (32.1%), hyperhidrosis (25%), carpal tunnel (14.3%), musculoskeletal pain (14.3%), weight increased (7.1%) and tongue disorders (7.1%). The 5 patients receiving placebo with controlled IGF-I at 36 weeks received active medical treatment in the open label extension by decision of their study PIs, as they were deemed to have either lost their response during the study or had continuing active acromegaly symptoms. 93% of patients receiving placebo lost response following withdrawal of injectable SRLs, with a median duration of 16 weeks. All 5 patients receiving placebo who met the primary endpoint criteria at the end of the study were assessed clinically to have active disease and were continued on oral SRL treatment in the open label extension.

Adrenal

ADRENAL PHYSIOLOGY AND DISEASE

High Salt Intake May Paradoxically Drive Autonomous Aldosterone Production

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SUN-220

Many modifiable factors contribute to the high prevalence rates of hypertension, among them is the consumption of too much salt (sodium). Another curable cause of hypertension is the excess of the hormone aldosterone. Aldosterone is normally produced by the zona glomerulosa (ZG) of the adrenal glands in response to a lack of salt and conversely suppressed by salt excess. We hypothesize that [i] suppression of aldosterone production induces apoptosis of ZG cells, as occurs following genetic deletion¹; [ii] this sets up a maladaptive response to chronic salt overload by conferring a survival advantage to cells in which mutations drive autonomous aldosterone production. To address [i], we measured apoptosis of cells in which aldosterone synthesis was inhibited; to address [ii] we undertook a cross-sectional clinical study of aldosterone and sodium excretion, hypothesising that aldosterone excretion will be highest in the outside quartiles of sodium excretion. Aldosterone was inhibited by modification, in human adrenocortical H295R cells, of either CADM1 expression (mutated in aldosterone-producing adenomas²) or intracellular calcium concentration³. Apoptosis was measured by flow cytometric analysis of annexin V conjugates. 24-hour urinary aldosterone excretion (24h-Ualdo) was correlated with 24-hour urinary sodium (24h-Usodium) in 24h-urine samples collected for a Malaysian population-based salt intake study (MyCoSS). The prevalence of autonomous aldosterone production was estimated from the proportion of subjects with serum measurement whose "SUSSPUP" ratio (= serum sodium to urinary sodium)/(serum potassium² to urinary potassium) was >5.3⁴. Modification of CADM1 in human adrenocortical H295R cells decreased aldosterone production by half compared to vector control, and this was associated with a 3 to 5-fold increase of apoptotic cells (p<0.05; n>3). Pilot investigation of a Cav1.3 inhibitor decreased aldosterone production by 70%, and increased apoptosis by 7-fold (p<0.10; n=2). In 767 subjects, 24h-urine samples from the high urinary sodium quartile (>150mmol/d) had higher urinary aldosterone (4+0.18 ug/d) than other quartiles (p=0.00001). Overall, the estimated prevalence of autonomous aldossterone production using SUSSPUP ratio was 4.5% (8 of 179 subjects). In 63 subjects with 24h-Usodium>200 mmol/day, autonomous aldosterone secretion (conventionally >10μg/d) was found in 9.5%. Our results support the hypothesis that initial suppression of aldosterone production by salt excess may create a selective advantage for cells which autonomously produce aldosterone, and hence an inappropriate long-term increase in aldosterone production.

¹Lee et al., Endocrinology. 2005;146:2650-6.

²Wu et al., 21st European Congress of Endocrinology. Vol. 63. BioScientifica, 2019.

³Xie et al., Sci Rep. 2016;6:24697.

⁴Willenberg et al., Eur J Clin Invest. 2009;39:43-50.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II

Rural India Embracing Advanced Techniques in MIS:- A Series of 20 Cases of Thyroid Surgeries by Transoral Endoscopic Thyroidectomy-Vestibular Approach (TOETVA) Technique with Respect to Acceptance of Progressive Surgeries Using Advanced Technologies, Techniques by Rural Patients and it's Safety & Feasibility in Small Setup Hospital in Rural India.

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SUN-428

Title

Rural India embracing Advanced Techniques in MIS: - A Series of 20 Cases of Thyroid Surgeries by Transoral Endoscopic Thyroidectomy-Vestibular Approach (TOETVA) Technique with Respect to an Acceptance of progressive surgeries using Advanced Technologies, Techniques by Rural patients and it's Safety & Feasibility in Small setup Hospital in Rural India.

Aims & Objectives

Transoral Endoscopic Thyroidectomy Vestibular Approach (TOETVA) an alternative surgical technique for thyroid surgery is slowly gaining widespread popularity.

Majority of *TOETVA* surgeries are performed in Tertiary Care institutes. It's safety & Feasibility in small setup