loss of the proximal row of carpal bones. His mother was followed as an adolescent with presumed juvenile rheumatoid arthritis. Genetic testing confirmed MAFB gene mutation (c.206C>T,p.Ser69Leu) in both patient and mother. At 7y, skeletal survey showed diffuse osteopenia and mild height loss in T1. DXA (L1-4) Z-score was -0.7. Calcium phosphate metabolism indices were within reference ranges. Bone Specific Alk Pi was modestly increased and C-telopeptide markedly increased.He received Denosumab (0.5-0.75 mg/Kg) 4-monthly for two years and experienced less pain and increased daily activities with improved R wrist function. Osteolysis stabilized and none was noted in the L wrist or ankles. BMD Z-score was -0.2. A year following treatment (2016) he received two more injections of Denosumab following pain and movement restriction of R elbow, R knee and L ankle. In 2019 (13y) he fell and radiology showed, R knee osteopenia, R wrist almost complete destruction of the carpal bones. Neither ankle nor L wrist showed osteolysis. R upper limb musculature was wasted when compared with the left. Shoulder and elbow strength were preserved. BMD Z-score was -1.2. Serum calcium, 25(OH)Vitamin D and PTH were normal. Bone specific alkaline phosphatase and C-Telopeptide were elevated. Serum creatinine was normal, eGFR 150 ml/min/1.73m2, ACR (6.6 [normal< 3.5] mg/mmol)) with no hypercalciuria or nephrocalcinosis. He was normotensive.High resolution peripheral quantitative computerized tomography (HRpQCT) of the L distal radius and distal tibia compared with 7 age-matched healthy males showed reduced total volumetric BMD (186.4;198.2-306.4), normal trabecular volumetric BMD and markedly reduced cortical volumetric BMD (320.4;636.5-792.5). Cortical thickness was below the expected range. HRpQCT measurements of the R wrist and tibia were similar. sRANKL, 6 weeks after Denosumab were markedly increased in both undiluted (35.4 pmol/L) and averaged diluted samples (83.73 pmol/L) when compared with healthy age-matched children (0.21-0.41pmol/L).

**Conclusions/Clinical Lessons:**MCTO (MAFB, mutation c.206C>T,p.Ser69Leu), has a generalized high turnover skeletal phenotype (osteoporosis), likely driven by very high levels of sRANKL. Denosumab is a targeted treatment for the osteoporosis, which may help stabilize the osteolysis.

# Neuroendocrinology and Pituitary

## ADVANCES IN NEUROENDOCRINOLOGY

### *Chronic Exposure to Predator Odour Stress Disrupts LH Pulsatility and Delays Puberty While Activation of Amygdala Kisspeptin Advances Puberty*

*Deyana Ivanova, MS, BS[1], Xiao Feng Li, PhD[2], Caitlin McIntyre, BS[3], Kevin Thomas O'Byrne, BSC,PhD[4].*

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**SUN-LB49**

Chronic exposure to predator odour stress disrupts LH pulsatility and delays puberty whileactivation of amygdala kisspeptin advances pubertyDeyana Ivanova MS[1], Xiao Feng Li MD/PhD[1], Caitlin Mcintyre BS[1], and Kevin O'Byrne PhD[1];[1]Department of Women and Children's Health, Faculty of Life Science and Medicine, King'sCollege London, UKPost-traumatic stress (PTSD) is associated with altered pubertal timing and predator odourexposure is a classical rodent PTSD model. Kisspeptin neurones in the posterodorsal sub-nucleus of the medial amygdala (MePD) are thought to modulate pubertal timing and anxiety.We test the hypothesis that psychosocial stress, processed by the MePD, is relayed to theGnRH pulse generator to delay puberty. Female mice were exposed to predator odour, 2,4,5-Trimethylthiazole (TMT), for 14 days from postnatal day (pnd) 21 and pubertal onset wasmonitored. Anxiety was tested using the Elevated Plus Maze (EPM), Light/Dark Box (LDB) andsocial interaction (SI). The effect of TMT on luteinizing hormone (LH) pulses was measured,on pnd 26 and 29. Additionally, kisspeptin-cre mice were bilaterally injected with hM3Dq-DREADD AAV in the MePD at pnd 13. From pnd 21, CNO was administered via drinking waterfor 14 days and pubertal onset was monitored. The TMT-mice showed a significant delay offirst estrous (FE; TMT: 38.1 ± 0.5 vs. control: 33.3 ± 0.6 days; $p<0.0001$; n=10-14) withoutaffecting body weight (BW; $p=0.9$; n=10-14). TMT-mice spent less time exploring the openarm of the EPM (TMT: 13 ± 3 vs. control: 32 ± 5 secs; $p<0.05$; n=10-14) and in the lightcompartment of the LDB (TMT: 117 ± 12 vs. control: 162 ± 15 secs; $p<0.05$; n=10-14), whileengaging less in SI (TMT: 26.8 ± 2.8 vs. control: 47.7 ± 8.8 secs; $p<0.05$; n=10-14) during TMT-exposure compared to controls. The TMT group exhibited a reduction in LH pulse frequencyon pnd 26 (TMT: 0.2 ± 0.2 vs. control: 1.7 ± 0.4 pulses/2 h; $p<0.05$; n=6-9) and 29 (TMT: 0.6 ±0.2 vs. control: 2.6 ± 0.4 pulses/2 h; $p<0.001$; n=6-9). DREADD activation of kisspeptinneurones in the MePD advances FE (DREADD: 30 ± 1 vs. control 34.67 ± 0.82 days; $p<0.05$;n=6) without affecting BW ($p=0.9$; n=6). Predator odour stress reduces GnRH pulse generatorfrequency, delays puberty and enhances anxiety-like behaviour, while selective chemogeneticactivation of kisspeptin neurones in the MePD advances puberty in female mice.

# Adipose Tissue, Appetite, and Obesity

## OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

### *Treat: A Randomized Controlled Trial Examining the Effects of Time Restricted Eating on Weight Loss and Metabolic Markers*

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**MON-LB107**

**Background:** Studies indicate that time-restricted eating (TRE) can prevent weight gain and/or lead to weight loss [1,2]. The few human studies to date are small and/or non-randomized

[3,4]. This is a prospective and randomized study in humans who are overweight and obese designed to determine if TRE leads to weight loss and to characterize the metabolic effects of TRE. **Methods:** 140 overweight and obese males and females with a body mass index between 27-43 kg/m$^2$ were enrolled in the study. 100 participants completed the 12-week protocol. The study was conducted on a custom mobile study app on the Eureka Research Platform. Participants were given a Bluetooth weight scale to use daily, which was connected through the study app. Subjects were randomized to one of two eating plans and received daily reminders about their eating windows through the app. The control group was instructed to eat three structured meals per day. The TRE group was instructed to eat *ad libitum* from 12:00 pm until 8:00 pm and completely abstain from caloric intake from 8:00 pm until 12:00 pm the following day (16h fast:8h eat). Participants who lived within 60 miles of the study site were eligible to undergo extensive in-person metabolic testing. **Results:** Weight change in the TRE group was -1.3 kg compared to -0.6 kg in the control group (p=0.22). 46 (TRE n=22; control=24) of 50 participants who opted into the "in-person" visits completed all 4 visits. In that cohort, weight change in the TRE group was -1.62 kg compared to -0.57 kg in control (p=0.09). There were no significant differences in the changes in total fat mass, visceral or subcutaneous fat mass, waist or hip measurements, or resting metabolic rate. However, there was a trend towards reduced fat-free mass in the TRE group (-1.10kg) compared to controls (-0.35kg) (p=0.09). There was a significant change in the appendicular fat-free mass index of the TRE subjects compared to controls (p=0.011). This change in appendicular fat-free mass index was not associated with significant differences in strength measures. No changes were observed in plasma ketones, insulin, or glucose between treatment groups. **Conclusion:** These results indicate that TRE may lead to reductions in body weight in individuals who are overweight or obese. However, the majority of weight loss is attributed to reductions in fat-free mass rather than fat mass. Future analyses will determine if TRE leads to changes in metabolic blood markers or the plasma metabolome. **References:** 1.Hatori et al. Cell Metab. 2012 Jun 6;15(6):848-60. doi: 10.1016/j.cmet.2012.04.019. Epub 2012 May 17.2.
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# Tumor Biology

## ENDOCRINE NEOPLASIA CASE REPORTS III

### *Inoperable, Metastatic Pheochromocytoma & Paraganglioma Tumor Size Reduction After Lu-177-dotatate (Lutathera®) Treatment Trial: The Role of Nursing*

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**SAT-LB311**

Tumor Size Reduction after Lu-177-DOTATATE (Lutathera®) Treatment in Patients with Inoperable Metastatic Pheochromocytoma and Paraganglioma: The Role of NursingAssumpta Ude, Frank I. Lin, Karel Pacak, Ejigayehu Demissie. Clinical Center Nursing Department, Molecular Imaging Program NCI, Endocrine Service Program, Eunice Kennedy Shriver National Institute of Child Health & Human Development.**Background:** Nursing management of patients with metastatic pheochromocytoma (PCC) and paraganglioma (PGL) undergoing treatment trial with radiopharmaceutical medication has unpredictable clinical outcomes. **Clinical Case:** A 52-year old woman with inoperable metastatic PCC/PGL was admitted into protocol 17-C-0087 after poor response to various chemotherapies. Patient was treated in the endocrine nursing unit with 200 mCi of Lu-177-DOTATATE (Lutathera®) intravenous infusion given by a radionuclide specialist every eight weeks for a total of four doses. Prior to admission, various members of the endocrine clinical nursing leadership team reviewed protocol with the medical and radiation safety team and a clinical research nurse (CRN) to ensure CRNs understand their roles and expectations to ensure patient safety during procedures and treatment. The patient was admitted on the day preceding the treatment and monitored for 48 hours afterwards. The CRN obtained comprehensive diet and medication history to determine if there is anything that may falsely elevate plasma/urinary catecholamines/metanephrines. The
CRN ensured correct placement of intravenous (IV) line and proper collection of blood from IV line to increase the reliability of results. The CRN ensured that IV amino acid (Clinisol 15 %) infusion was administered 30 minutes prior to dosing to diminish renal issues. This patient had minimal side effects and no adverse events to therapy. The research team followed up the patient in clinic every month while she was on treatment, then every 3 months in the follow-up period. Recent evaluation showed this patient had stable vital signs, impalpable supraclavicular lymph node, returned to baseline physical activity with significant decrease in the size of the PCC/PGL, and reduction in serum catecholamine/metanephrine levels. **Conclusion**: The endocrine CRN team is critical in the assessment, monitoring, observation and education of patients and families regarding expectations during therapy which played a significant role in minimizing the patient's side effects to therapy. Working collaboratively with other members of the multidisciplinary research team also contributed to patient's favorable outcome.

# Diabetes Mellitus and Glucose Metabolism

## DIABETES DIAGNOSIS, TREATMENT AND COMPLICATIONS

### *Efficacy & Safety After Switchover to Remogliflozin in Indian T2DM Patients - a Real World Study*

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**SUN-LB112**

**INTRODUCTON:** Remogliflozin is new SGLT2i recently approved in India, but more economical than the previously