undiagnosed health problems, we performed a systematic health screening among adults with PWS.
**Methods:** We systematically screened 115 adults with PWS (mean age 31.4 ± 12.1 y, mean BMI 31.8 ± 9,5 kg/m$^2$) for the presence of undiagnosed health problems and cardiovascular risk factors. Based on a medical questionnaire, medical file search, extensive interview, thorough physical examination and biochemical measurements we made an overview of the undiagnosed health problems in adults with PWS. If possible, we performed polygraphy to test for sleep apnea.
**Results:** Undiagnosed health problems (hypertension, DM, hypercholesterolemia, sleep apnea, hypothyroidism and hypogonadism) were present in 50% of the patients. 10% had multiple undiagnosed health problems simultaneously. All males and 94% of females had hypogonadism and 15% had hypothyroidism. Hypertension and / or hypercholesterolemia were present in 20% and DM was present in 16%. One third of patients was not on a diet and 22% exercised less than 30 minutes a day. Sleep apnea was present in 17 of 26 patients tested.
**Conclusion:** We detected a striking number of undiagnosed health problems among adults with PWS which, if left untreated, can pose a serious health threat. Systematic screening is needed to detect these problems in an early phase. This will prevent burdensome and expensive complications and might even reduce mortality in this vulnerable patient population.

# Reproductive Endocrinology

## OVARIAN FUNCTION — FROM OLIGOMENORRHEA TO AMENORRHEA

### *Single-Cell Profiling of Adult Human Ovarian Cortex Reveals Six Main Cell Types but No Germline Stem Cells*

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**OR31-03**
The human ovary orchestrates sex hormone production and undergoes monthly structural changes to release mature oocytes. The outer lining of the ovary (cortex) has a key role in defining fertility in women as it harbors the ovarian reserve. It has been suggested that oogonial stem cells exist in the ovarian cortex and that these can be captured by DDX4 antibody isolation. Our study aimed at comprehensive characterization of all cell types present in the ovarian cortex, including the previously reported oogonial stem cells. We developed methods to dissociate human ovarian cortex to a viable single cell solution allowing subsequent analysis by single cell transcriptomic profiling and cell surface antigen screening. In all analyses, cells captured by DDX4 antibodies (DDX4 Ab+) were included as a reference. High quality ovarian cortex tissue from gender reassignement and caesarean section patients was used in the analyses. Our single cell transcriptomic analyses based on >24,000 cells revealed the presence of six main cell types in ovarian cortex; oocytes, granulosa cells, immune cells, endothelial cells, perivascular cells, and stromal cells. Surface marker screening showed robust expression of 43 cell surface antigens in ovarian cortex cells. With the help of transcriptomic and cell surface antigen profiles, the DDX4 Ab+ cells were identified as perivascular cells. This finding was validated by immunostaining of ovarian tissue showing DDX4 Ab+ cells lining CD31 positive endothelial cells of blood vessels. To search for germline stem cells on a broader front, we compared our data with human fetal ovary cells including pre-meiotic germ cells (Li et al. 2017) and found no evidence for the presence of germ line stem cells of any kind in adult human ovarian cortex. In summary, we provide the first cell map of human ovarian cortex. Our results demonstrate six main cell types, but cannot provide support to the existence of oogonial stem cells. This dataset will be a valuable tool for studying the role of specific cell populations in ovarian biology, dissecting causes of infertility, and developing novel assisted reproductive technologies or even contraceptives.

# Adrenal

## ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

### *ACTH-Derived Peptide Antagonists as an Alternative Treatment Strategy for Congenital Adrenal Hyperplasia*

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**MON-185**
Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder caused by different enzyme deficiencies in the steroid hormone synthesis leading to a disturbed cortisol biosynthesis. The medical treatment of CAH includes suboptimal ACTH-suppressing high glucocorticoid doses to reduce adrenal hyperplasia and overproduction of androgens. These inappropriate corticoid substitutions are often associated with undesirable side effects such as arterial hypertension, growth failure and obesity. Since the current therapy of patients with CAH is often unsatisfactory, innovative treatment options are required.
The aim of our study was to specifically block the melanocortin 2 receptor (MC2R) signaling pathway as an alternative treatment strategy for CAH. We tested ACTH-derived selective peptides with incorporation of various synthetic non-natural amino acids in the activation motif of ACTH. To study the antagonistic activity of the peptides, cAMP production of MC2R/MRAP stably transfected human embryonic kidney (HEK) 293 cells were measured. All new synthesized peptide antagonists reduced ACTH-stimulated MC2R activity as competitive inhibitors indicated by a reduced *in vitro* cAMP response. Cells pre-incubated with peptide LNP009 showed the most

efficient blockade of the MC2R and the highest shift of $EC_{50}$ of ACTH (33.8 nM ± 0.08 vs. 7.3 nM ± 0.09). LNP009 was additionally tested for specificity concerning the other known melanocortin receptors and showed no antagonistic effect up to 1 μM on MC3, MC4 or MC5 receptor transiently transfected HEK 293 cells. To further investigate the inhibitory effect of our most potent antagonist peptide LNP009 on the steroid hormone response, we assessed steroidogenic enzyme expression of the human adrenocortical tumor cell line NCI-H295RA and performed mass spectrometry analyzes of steroids in the cell culture supernatant. Preincubation with LNP009 reduced the expression of the genes CYP21A2, CYP11B1 and HSD3B2 in NCI-H295RA cells and significantly reduced the synthesis of aldosterone (P=0.046; n=3), cortisol (P=0.020; n=3) and corticosterone (P=0.035; n=3).

With the successful blocking of the ACTH binding and signal transduction by our antagonistic peptides, we anticipate an alternative approach for optimizing the treatment of CAH patients lacking the side effects of the currently used ACTH-suppressing corticoid therapy.

# Adipose Tissue, Appetite, and Obesity

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

### *The Impact of Bariatric Surgery on the Risk of Non-Alcoholic Fatty Liver Disease in Morbidly Obese Patients*

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**MON-592**

**Introduction**: Non-alcoholic fatty liver disease (NAFLD) is strongly associated with obesity, and the prevalence of both diseases is increasing notably. The lack of effective treatment options for NAFLD is leading to a great consideration towards the identification of new approaches.

**Aim**: We aimed to evaluate the change one year after bariatric surgery of parameters of hepatic function and in the hepatic scores, *Fatty Liver Index* (FLI, predictor of hepatic steatosis), and BARD, *BMI, AST/ALT ratio and DM*, (predictor of hepatic fibrosis).

**Methods**: Observational retrospective cohort study in morbidly obese patients that underwent bariatric surgery between January 2010 and July 2018. We excluded patients missing hepatic function parameters before or one year after the surgical procedure. We used two linear regression models: 1) unadjusted; 2) adjusted for surgery type (gastric sleeve, gastric band and gastric bypass), sex, age, body mass index, diabetes and dyslipidaemia.

**Results**: The included population (n=1955) had an average age of 43.1±10 years and 85.8% were female. We observed a relevant decrease in transaminases (pre-operative AST and ALT, 24.8±12.4 and 29.5±19.5U/L, *vs* 22.4 ± 11.1 and 22.2±14.7 post-operatively, respectively, p<0.01) and gamma-glutamyltransferase (36.9±35.4 *vs* 21.4±22.0U/L, p<0.01), and an increase in alkaline phosphatase (77.8±23.5 *vs* 80.8±25.4U/L, p<0.01) and total bilirubin (0.56±0.23 *vs* 0.68±0.24mg/dL, p<0.01). Both FLI and BARD markedly decrease one year after surgery (p<0.01). Comparing the surgical procedures, gastric sleeve was associated with a greater reduction of hepatic enzymes and of both FLI and BARD comparing with gastric band. Comparing with gastric bypass, sleeve was associated with a greater reduction of transaminases and alkaline phosphatase, but a smaller reduction of FLI and BARD.

**Conclusion**: Bariatric surgery is associated with a reduction of the hepatic enzymes and an improvement of FLI and BARD. Bariatric surgery may represent an effective therapeutic approach to NAFLD.

# Bone and Mineral Metabolism

## PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

### *Baseline Characteristics from the Observational PARADIGHM Registry of Patients with Chronic Hypoparathyroidism*

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**SAT-399**

PARADIGHM is an actively recruiting, prospective, observational registry (NCT01922440/EUPAS16927). The primary objective is to evaluate the safety and effectiveness of recombinant human parathyroid hormone, rhPTH(1-84), treatment in patients with chronic hypoparathyroidism