SAT-421
Abstract: **Context:** Graves’ orbitopathy (GO) presents with infiltrative exophthalmos due to excessive proliferation, adipogenesis and glycosaminoglycans production of orbital fibroblasts (OFs). There are few therapies potent for proptosis. Intervention in autophagy of OFs could be a potential therapy. **Objectives:** Here, our purpose was to evaluate the effects of chloroquine (CQ) and its derivative hydroxychloroquine (HCQ), as autophagy inhibitors commonly used in clinical practice, on GO-OFs from human orbit. **Design/Setting/Participants:** OFs isolated from patients with GO (n = 10) or control persons (non-GO) (n = 8) were allowed to proliferate in the proliferation medium (PM) or differentiate into adipocytes in the differentiation medium (DM), co-treated with CQ of different concentrations, and subsequently examined in vitro. **Main Outcome Measures:** CCK-8, EdU incorporation and flow cytometry were used to assess cellular viability. Adipogenesis was assessed by Western blot, real time-PCR, and Oil Red O staining. Hyaluronan was determined by real time-PCR and ELISA. Autophagy flux was detected using RFP-GFP-LC3 fluorescent staining and Western blot. **Results:** CQ (10μM) or HCQ (10μM) treatment for 48h was sufficient to block autophagy flux without exhibiting cell toxicity in OFs from either GO or non-GO participants. Cellular proliferation of GO-OFs was halted by both CQ and HCQ. Also CQ and HCQ exerted an inhibitory action on lipid accumulation of GO-OFs during differentiation as well as expression of adipogetic markers such as PPARγ and c/EBP-α/β. Moreover, hyaluronan secretion, concurrent with expression of hyaluronan synthase 2 (HAS2), was obviously decreased by CQ and HCQ. **Conclusions:** We reported the efficacies of CQ and HCQ on proliferation, adipogenesis and hyaluronan generation of GO-OFs via inhibiting autophagy, providing proof of concept that quinoline-based antimalarial (QBA) drugs like CQ and HCQ have potential to be a new treatment for GO as autophagy inhibitors.

Tumor Biology
**TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS**
**Intratumoral Expression of Steroid Receptors, CD68+ Macrophages and Mdm2 in Different Molecular-Biological Types of Endometrial Cancer**
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**SUN-133**
**Background and aims:** In Risk Classifier for Endometrial Cancer/EC (ProMisE) 4 molecular biological types of this tumor are described recently [1,2,3] and need an additional research, including evaluation of hormone-associated characteristics of both tumor tissue and patients [4]. Aim of the work was a study of estrogen (ER) and progesterone (PR) receptors in comparison with CD68+ macrophage infiltration (which promotes the invasion of tumor cells into the myometrium [5]) and expression of MDM2 protein, a negative regulator of p53 [6], in EC types presented in the ProMisE classification. **Materials and methods:** The tumor tissue of 218 EC patients included in the study (mean age 60.6 years) was assigned according to the data of genetic and immunohistochemical analysis to the types of carcinomas with gene POLE mutations, deficiency of mismatch repair proteins (MMR-D), expression (positive or diffuse) of p53 oncprotein and to the type without characteristic molecular profile, WCMP. Immunohistochemistry was used also for evaluation of ER (Ventana antibodies, clone SP1) and PR (Ventana antibodies, clone 1E2) according to Allred, MDM2 (antibodies ABCAM, dilution 1:200) and macrophage marker CD68 (DAKO antibodies, clone CD8/144B). **Results:** According to the averaged data, the highest expression of ER and PR was found in EC types MMR-D and WCMP, and the lowest, respectively, in types POLE and p53+. Most often, positive expression of MDM2 (in 93.2% and 96.9% of studied cases) was detected respectively in MMR-D and p53+ type of EC, indicating, therefore, a positive relationship between MDM2 and the presence of steroid receptors in the first of these types (MMR-D) and negative - in the second of them (p53+). Expression of CD68+ macrophages demonstrated (contrary to the EC types POLE and p53+) a tendency to the lower values in types MMR-D and WCMP (128.0 ± 8.1 and 113.5 ± 6.3 cond.un.), i.e. in tumors with potential sensitivity to estrogen. **Conclusions:** The results indicate the importance of taking into account of both - the molecular biological type of the EC as well as the role of microenvironment of tumor cells, including the colonization of the neoplasm tissue by macrophages (and possibly lymphocytes) and the features of hormonal signal transmission in it. For further analysis, it is desirable to consider also the EC histotype, as one of the factors underlying various prognostic groups of this tumor [7].

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Bone and Mineral Metabolism
**OSTEOPOROSIS AND VITAMIN D**
**Crystal Bone: Personalized, Short-Term Fracture Risk Prediction with Natural Language Processing Methods**
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**OR13-07**
Fragility fractures due to osteoporosis are common and are associated with significant clinical, personal, and economic
burden. Even after a fragility fracture, osteoporosis remains widely undiagnosed and undertreated. Common fracture risk assessment tools, such as FRAX and Garvan, confer risk over the long term but do not provide short-term risk estimates necessary to identify very high-risk patients likely to fracture in the next 1–2 years. Furthermore, these tools utilize cross-sectional data representing a subset of all available clinical risk factors for risk prediction. Thus, these methods are generalized across patient populations and may not fully utilize patient histories commonly found in electronic health records (EHRs) that contain temporal information for thousands of unique features. The Optum de-identified EHR dataset (2007–2018) provides an opportunity to use historical medical data to generate short-term, personalized fracture risk predictions for individual patients. We used the Optum dataset to develop Crystal Bone, a method that applies machine learning techniques commonly used in natural language processing to the temporal nature of patient histories in order to predict fracture risk over a 1- to 2-year timeframe. Specifically, we repurposed deep-learning models typically applied to language-based prediction tasks in which the goal is to learn the meanings of words and sentences to classify them. Crystal Bone uses context-based embedding techniques to learn an equivalent “semantic” meaning of various medical events. Similar to how language models predict the next word in a given sentence or the topic of an overall document, Crystal Bone can predict that a patient’s future trajectory may contain a fracture or that the “signature” of the patient’s overall journey is similar to that of a typical fracture patient. We applied Crystal Bone to two datasets, one enriched for fracture patients and one representative of a typical hospital system. In both datasets, when predicting likelihood of fracture in the next 1–2 years, Crystal Bone had an area under the receiver operating characteristic (AUROC) score ranging from 72% to 83% on a test (holdout) dataset. These results suggest performance similar to that of FRAX and Garvan, which have 10-year fracture risk prediction AUROC scores of 64.4% +/- 3.7%. Our results suggest that it is possible to use each patient’s unique medical history as it changes over time to predict patients at risk for fracture in 1–2 years. Furthermore, it is theoretically possible to integrate a model like Crystal Bone directly into an EHR system, enabling “hands-off” fracture risk prediction, which could lead to improved identification of patients at very high risk for fracture.

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Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS II

Primary Amenorrhea, Growth Arrest and Metabolic Syndrome Due to an Unclassified Hepatocellular Adenoma.

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MON-901

Primary Amenorrhea, Growth Arrest and Metabolic Syndrome Due to an Unclassified Hepatocellular Adenoma.

Background: Hepatocellular adenoma is a rare benign neoplasm, seldom ascribed as the cause of endocrine and metabolic derangement. We herein report a case of primary amenorrhea, growth arrest and metabolic syndrome due to huge hepatocellular adenoma. En bloc resection of the tumor normalized all the disturbances.

Clinical Case: A 16-year-old girl, who is one of the quintuplets, complained of primary amenorrhea and growth arrest for the past 2 years. Her height (150cm) and weight (40kg) was at the 3rd percentile, whereas waist circumference (75cm) was at the 90th percentile for chronological age. She was hypertensive (145/115mmHg) on admission. Plasma cholesterol (TC 6.3mmol/L, LDL-c 3.76mmol/L), triglyceride (2.66mmol/L) and uric acid (532μmol/L) were elevated. Evaluation of GH/IGF-1 axis showed normal GH (0.90–2.53 μg/L) with extremely low IGF-1 concentration (35.29–39.74 ng/mL), and the latter was unresponsive to hGH stimulation. Computer tomography identified a huge liver mass (18.2cm×13.7cm×21cm). The patient underwent an uneventful open right hepatic lobectomy and cholecystectomy, and the tumor was en bloc resected. Immunohistochemistry indicated an unclassified hepatocellular adenoma, which was confirmed by whole exome sequencing. Her menarche started 6 months later followed by regular cycles without hormone replacement. IGF-1 concentration (471 ng/mL), blood pressure (106/62mmHg), lipid profile (TC 4.2mmol/L, LDL-c 2.51mmol/L, TG 1.44mmol/L) were normal 10 months after surgery, and the girl had a reduction in waist circumference by 5cm, and a small gain in height by 2cm.

Conclusion: We provide evidence that liver-derived IGF-1 has a direct effect on skeletal and pubertal development, blood pressure, visceral adiposity and dyslipidemia. Though rare, we propose the need to look into cases with hepatocellular adenoma, for the existence of IGF-1 deficiency and its impact on endocrine and metabolic derangement.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Rapid Decompensation from Complications of Severe Hypercortisolism in an Unusual Presentation of an Ectopic ACTH-Secreting Neuroendocrine Tumor

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SAT-118

Background: Ectopic Cushing’s syndrome from an ACTH-secreting neuroendocrine tumor (NET) is a rare condition whose onset and disease progression is often more aggressive than other forms of Cushing’s syndrome due to complications from severe hypercortisolism.

Clinical Case: A 75-year-old woman presented with profound proximal muscle weakness, severe hypokalemia,