and silent corticotroph tumor and SST5 expression or USP8 mutation status. To describe SST5 expression and the response to pasireotide in 5 patients.
Design. Retrospective cohort study.
Setting. University hospitals of Lyon.
Patients. 62 patients operated for a corticotroph tumors between 2013 and 2017.
Intervention. None.
Main Outcome Measure. Clinical, biological, radiological and pathological data were evaluated depending on SST5 expression measured by immunohistochemistry (rabbit monoclonal antibody, clone UMB-4, Abcam). Membrane immunepositivity with an IRS>1 was considered positive. USP8 analysis was performed by Sanger sequencing in 50 tumors.
Results. SST5 expression was positive in 26 (41.9%) pituitary tumors. A moderate or strong IRS was found in 24.2% of the cohort and in 32.5% of the functioning pituitary tumors. Compared to SST5-negative pituitary tumors, those expressing SST5 were more frequent in women (92.3% vs 55.6%; p=0.002), fewer were silent (7.7% vs 58.3%; p<0.001), smaller (7 vs 19mm; p=0.001) and less invasive (15.4% vs 44.4%; p=0.03).
USP8 mutations were identified in 26% of the cohort and more frequent in functioning (n=11/30, 36.7%) compared to silent corticotroph tumors (n=2/20, 10%; p=0.05). SST5 expression was more frequent in USP8mut vs USP8neg tumors (58.8% vs 7.7%; p<0.001).
Among treated patients, normal urinary free cortisol (UFC) levels were obtained in 3 patients (IRS 0, 2, and 6) and a 4-fold decrease of UFC in one patient (IRS 4).
Conclusion. SST5 expression seems to be associated with functioning, well-differentiated pituitary tumors and USP8 mutation. However, a correlation between SST5 expression or USP8mut and response to pasireotide treatment remains to be confirmed.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Cooperative Mechanism of SREBP-Dependent Cholesterol Synthesis Pathway and P53 on Malignant Formation in Breast Cancer

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SAT-144

p53 is mutated more than half of human cancers, and mutant p53, a gain of function, can actively have functional consequences with tumorigenesis. However, its action of molecular mechanisms, particularly *in vivo* conditions, has not been fully are clarified. Here, we generated KO and KI (R280K) breast cancer cell lines for p53 using CRISPR/Cas9 system, and then performed a three-dimensional culture model. We found that the introduction of mutant p53 was solely able to mediate the transformation to poor architectural structure. Interestingly, our findings in statin-effect along with cholesterol synthesis pathway, especially isoprenoid dependency, revealed that this pathway is necessary and sufficient for the regulation of malignant architecture in SREBP2-dependent manner with cooperatively being controlled by mutant p53 on 3D-cultured breast cancer. Furthermore, in accordance with the malignancy progresses, SREBP2 was accumulated in nuclear and nuclear membrane portion with enhancement in malignant formation. In addition, we found that mutant p53 interacts with SREBP2, and consistently mutant p53 was associated with DHCR7 promoter in parallel with binding pattern of SREBP2. Thus, our results provide the novel insight into the mutant p53, a gain of function, and its linkage to poor architectural structure in 3D-cultured breast cancer cells via SREBP2-dependent isoprenoids regulation as potential therapeutic targets.

Adrenal

ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

CAH-X Syndrome in a German Cohort of Patients with Congenital Adrenal Hyperplasia

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MON-177

Congenital adrenal hyperplasia due to 21-hydroxylase deficiency (CAH) is encoded by the CYP21A2 gene. The CYP21A2 gene is flanked and partially overlapped by the TNXB gene encoding an extracellular matrix protein called Tenascin-X. Deficiency of Tenascin X can cause the Ehlers-Danlos Syndrome (EDS). Deletions of CYP21A2 extending into TNXB rarely cause CAH combined with EDS. Heterozygosity of TNXB mutations causing haploinsufficiency of TNX, however, have been described in about 5-7% in a patient cohort from the US and has been named CAH-X syndrome, CAH associated with mild hypermobility form of EDS.
We genetically investigated a cohort of 81 adult patients (31 males, mean age 37,8 years +/- 9,8) with classic CAH for CAH-X. Patients genetically positive for CAH-X and unaffected CAH control patients matched for sex, age and BMI underwent a thorough clinical investigation including joint examination by Beighton 9-point scale, skin and neurological examination, by a standardised protocol of thransthoracic echocardiography and muscle ultrasound. In addition serum tenascin-X has been measured.
In our cohort we identified one patient with CAH and EDS and 4 patients with CAH-X syndrome. All CAH-X patients had serum concentrations of tenascin-X below the normal range, however, not different from 35 unaffected CAH patients with regard to serum concentration. All 4 patients with CAH-X syndrome showed some associated clinical symptoms. Two had joint hypermobility detected by Beighton 9-point score. Two of four CAH-X patients showed cardiac abnormalities (mild mitral regurgitation in one patient and a surgically corrected common arterial trunk type I A in the other patient). The patient with CAH and EDS showed cardiac abnormalities in addition to typical EDS symptomatology. All 5 affected patients complained about back pain and showed foot malposition. Profound changes in muscle ultrasound were found in 60 % of patients with CAH-X syndrome (3/5) and in none of the controls (0/5).

In conclusion, our data confirm the previously described prevalence of CAH-X. Beighton-score seems to be a quick and cheap screening instrument for CAH-X and should be performed in all patients with classic CAH, since protein level in serum cannot be used for screening for CAH-X-Syndrome. A stronger focus needs to be made on back pain and foot malposition as symptoms of CAH-X and echocardiography should be performed in all CAH-X patients. Therapy should depend on clinical symptoms in patients.

Diabetes Mellitus and Glucose Metabolism

CLINICAL STUDIES IN OBESITY, DIABETES RISK, AND CARDIOVASCULAR OUTCOMES

Framingham Cardiovascular Disease 10-Year-Risk Score Is Associated with Myocardial Perfusion in Asymptomatic Diabetic Patients

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SAT-621

Framingham Cardiovascular Disease 10-year-risk Score is associated with Myocardial Perfusion in Asymptomatic Diabetic Patients Background: Even without atherosclerosis, diabetes increases the risk of death from coronary heart disease and heart failure. Myocardial perfusion dysfunction may occur in the early stage of diabetic cardiomyopathy, but its examination method is relatively complex. It is very important to carry out targeted cardiac screening to find the factors related to diabetic myocardial perfusion in the early stage.
Methods: We enrolled 77 patients with diabetes and 30 controls, performed anthropometric and laboratory tests such as blood glucose and lipids, and calculated Framingham Cardiovascular Disease 10-year-risk Score (FRS). All participants underwent cardiac magnetic resonance examinations and recorded their cardiac structure, functional indicators (such as ejection fraction (EF), end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume(SV), peak filling rate (PFR),myocardial perfusion index (maximum upslope (Slope), half time to maximum signal intensity (Time50Max (s)), time to maximum signal intensity (TimeMax (s)), the maximum signal intensity (MaxSI),, basic signal intensity (Baseline),the ratio of MaxSI and Baseline ((MaxSI (BL) %), the difference value between MaxSI and Baseline (MaxSI (BL))).
Results: Compared with normal group, no cardiovascular symptoms of left ventricular and right ventricular systolic function in patients with diabetes and end-diastolic and end systolic volume had no obvious difference, left ventricular PFR is lower than normal (279.65 + 57.62 vs. 322.57 + / - 78.29, p = 0.02), in the subgroup analysis we found that
the FRS high-risk groups, ventricular septal thickening tend to, and Slope, MaxSI, MaxSI BL (%), MaxSI (BL) were significantly lower than the high risk group, Time50Max and TimeMax were significantly longer than the non-high-risk group, and FRS was negatively correlated with Slope, MaxSI(%BL) and positively correlated with TimeMax(s) and Time50Max(s), with statistical significance.
Conclusion: Systolic function remains and diastolic function decreases in asymptomatic diabetic patients. Moreover, the patients with high risk of FRS had significant decreased perfusion function, and the quantitative indexes of perfusion function were closely related to FRS. It is of great value to pay attention to the changes of FRS score for early screening and diagnosis of diabetic heart disease.

Reproductive Endocrinology

FEMALE REPRODUCTION: BASIC MECHANISMS

Estradiol Triggering Extracellular Matrix Degradation Leading Signalling Cascades Succeeding a Feedback Loop as Contributing Factor to Develop Endometriosis in Females of Reproductive Age

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MON-026

INTRODUCTION: Endometriosis is common gynaecological disorder that leads to infertility in females of reproductive age. It is characterized by endometrial glands and stromal tissues outside the wall of uterus. Upregulation of estradiol is responsible for the cell proliferation, adhesion and invasion in endometriosis. It enhances prostaglandins (PGE-2) that triggers the formation of matrix metalloproteinases (MMPs), Tumor necrosis factor-α (TNF-α) and nuclear factor kappa B (NF-kB). Whereas, levels of progesterone are reported to be decreased in the patients with endometriosis. Less production of progesterone activity of 17β-hydroxysteroid dehydrogenase-II (17β-HSD-II) decreases that converts estradiol to less potent estrone. Intake of excess trans-fats and deficiency of vitamin D raises level of arachidonic acid and converts PGE-2 by the action cyclooxygenase (COX-2). PGE2 in theca cells of ovaries increases cAMP and activity of liver receptor homologue-1/steroidogenic factor-1(LRH-1/SF-1) thus leading to the stimulation of aromatase enzyme. **MATERIALS AND METHODS:** Two hundred eighty-eight (n=288) females with endometriosis and hundred (n=100) controls were enrolled. Informed consent was obtained before the collection of samples. Levels of estradiol, progesterone, aromatase enzymes, 17β-HSD-II, COX-2, PGE-2, MMPs (2, 7, 9), vitamin D and lipopolysaccharides (LPO) were estimated by respective protocols. **RESULTS:** Findings suggests significant increase in the levels of estradiol, aromatase enzymes, COX-2, PGE-2, MMPs (2,7,9) and LPO (67.08±5.55 pg/ml, 7.16±1.28 ng/ml, 1.56±0.144 ng/ml, 4.89±0.61 pg/ml, 995.2±8.15 ng/ml, 105.2±7.19 ng/ml, 109.2±12.25 ng/ml and 125.25±11.26 pg/ml) in patients as compared to (21.08±3.65 pg/ml, 2.08±0.15 ng/ml, 0.61±0.056 ng/ml, 1.158±0.18 pg/ml, 388.26±14.26 ng/ml, 66.29±5.26 ng/ml, 38.29±15.2 ng/ml and 17.25±1.26 pg/ml) controls respectively. Whereas, levels of progesterone, 17β-HSD-II and vitamin D remained significantly low in the endometrial patients (3.07±1.08 ng/ml, 0.183±0.024 ng/ml and 17.17±2.3 ng/ml) as compared to healthy females (29.22±3.29 ng/ml, 1.43±0.153 ng/ml and 36.26±3.09 ng/ml). **CONCLUSION:** Current study suggests the role of estradiol in triggering ECM degradation and initiating signalling cascades that following a feedback loop enhances the levels of estradiol and contributes in the development and progression of endometriosis. Hence, therapies with supplementation of vitamin D and progesterone may help in regressing the role estradiol and other contributing factors that are involved in the development and progression of endometriosis in the patients. **Keyword:** Endometrial glands, Stromal tissues, Estrogen, Progesterone, Endometriosis, Vitamin D