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

Akitoshi Nakayama, PhD, Masataka Yokoyama, MD, PhD, Hidekazu Nagano, MD, PhD, Ikki Sakuma, MD, PhD, Naoko Hashimoto, MD, PhD, Seiichiro Higuchi, MD, PhD, Kazuyuki Yamagata, PhD, Tomoaki Tanaka, MD, PhD.
Chiba University Graduate School of Medicine, Chiba, Japan.

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

Andrea Sappl, non-degree[1], Christian Lottspeich, MD[1], Katharina Vill, MD[2], Monika Morak, PhD[1], Martin Bidlingmaier, MD[1], Nicole Reisch, MD[1].
[1]Medizinische Klinik und Poliklinik IV, Klinikum der Universität München, LMU - University of Munich, Munich, Germany, [2]Department of Pediatric Neurology and Developmental Medicine, Dr. v. Hauner Children's Hospital, LMU - University of Munich, Munich, Germany.

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).