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Lung cancer, like many other solid tumor types, presents deregulation of gene expression involved in cellular plasticity. Even though the molecular mechanism involved is not fully characterized, it is considered that the acquisition of stem-like properties would contribute to the maintenance of the heterogeneous cell population seen in tumors. Previously, AHCYL1 was identified by using a bioinformatic tool INSECT as a potential regulator of stem properties of cancer cells. In AHCYL1-depleted cells (i.e. AHCYL1 shRNA) genes associated with pluripotency such as OCT4/POU5F1 were increased, with a decrease of Mucin 5B expression linked to pulmonary differentiation. Also, these cells showed a higher spheres formation capacity in vitro and tumorigenic capacity in vivo (Nod/Scid mice). In AHCYL1-overexpressing cells, the expression of OCT4 was reduced. When OCT4 was overexpressed, AHCYL1 expression was decreased suggesting a mutual regulation. Statistical significance was obtained with a cut-off p-value of 0.05. We propose a better understanding of AHCYL1 roles would contribute to new strategies for both diagnosis and therapy of cancer.

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0367 - METABOLIC SYNDROME INDUCES EPIGENETIC CHANGES IN PROSTATE TUMORS

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DNA methylation and histone modifications are important epigenetic mechanisms of gene regulation that can be detected before prostate cancer (PCa) becomes invasive, suggesting they are pivotal events in tumor initiation and progression. Metabolic syndrome (MeS) increases PCa's risk and aggressiveness. Our hypothesis is that MeS induces aberrant epigenetic changes in PCa favoring tumor development and progression. To address this hypothesis, MeS was induced in NSG or C57BL/6J male mice by chronically feeding them with high fat diet (HFD). After 12 weeks of diet, PC3 (NSG) or TRAMP-C1 (C57BL/6J) PCa cells were injected s.c. on MeS and control diet fed mice. After tumor growth, mice were sacrificed and tumors were collected. DNMT1 and SUV39H1 expression levels were repressed while RIZ1 and GADD45A were increased in MeS mice. Also, mRNA levels of CHD1 and ZEB1, two DNMT1 targets, were repressed and induced, respectively, in these tumors. Additionally, we evaluated multiple microarray datasets from patients using Oncomine. We found that DNMT1 expression was significantly downregulated, whereas RIZ1 was upregulated, in prostate tumors compared to normal prostate gland. Although SUV39H1 expression showed no changes comparing prostate tumors vs normal tissue, we found a deep deletion in its expression compared to other tumor types, such as breast or lung cancer. We also analyzed whole exome data for these genes (cBioportal) revealing amplification or deletion as the most frequent genetic alterations in PCa. Finally, PCa patients with DNMT1 and SUV39H1 alterations showed a decreased in overall survival while no differences in disease/progression were observed. In summary, MeS induces epigenetic modifications that result in global alterations in chromatin packaging, regulating the access of the transcriptional machinery to target genes and thereby modulating gene expression profiles.

0372 - EPIGENETIC LATERALITY DIFFERENCES IN BREAST CANCER

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Breast Cancer is a heterogeneous disease. By previous studies we determined that mammary tumors of left-right sides (L-R) differ in their behavior as inferred from their methylation profiles. Normal breast L-R tissues have not identical environments; they differ in size, irrigation and fat composition. It is also known that epigenetics functions as a bridge between environment and gene expression. Our hypothesis sustains that L-R tumors differ in epigenetically regulated pathways, provoked by the diverse L-R microenvironment. To study this, we performed in-silico and in-vivo analyses. From database c-BioPortal Provisional Breast Cancer, 708 tumors with information for 16.000 genes were included and L-R methylation medias were compared for each gene. The top 169 genes with significant L-R difference above 3% were selected (T test, $p<0.0001$) and filtered by cancer related search terms in Metascape. Fifty three genes were associated with the terms "inflammation", "proliferation negative regulation", "immune response", "DNA damage response", "P53 pathway", "angiogenesis", "migration", "cell death regulation", "survival" and "apoptosis". Then, the methylation profiles were converted into the 7 cancer terms. Interestingly, the cancer term profiles clustered into 2 groups associated with L-R laterality (Hierarchical cluster analysis, bootstrap 90-100 %), suggesting the existence of different L-R methylation profiles associated with functional terms. In the in-vivo studies, the methylome of 6 L-R xenografts generated by inoculation of MDA-MB231 cells in NSG mice were analyzed by RRBS. Preliminary analyses reveal 197 gene promoters, with significant L-R difference (FDR corrected $p<0.01$). Further functional and expression studies will allow to evaluate the impact of these methylation differences on the tumor behavior. So far, our studies support an interesting epigenetic related laterality hypothesis for breast cancer, which could serve as proof of principle for other bilateral tumors.

0377 - CYTOSTATIC AND ANTIMIGRATORY ACTIVITY OF REPURPOSED HEMOSTATIC DRUG DESMOPRESSIN AGAINST AVPR2-EXPRESSING HUMAN OSTEOSARCOMA CELLS

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Osteosarcoma (OS) is the most common malignant primary bone tumor in children and young adults, with alarmingly elevated mortality rates. OS patients bear highly invasive and vascularized tumors, and are in urgent need of novel therapeutic strategies. Desmopressin (dDAVP) is a repurposed hemostatic drug in oncology that acts as a selective agonist for the AVPR2 receptor present in blood microvessels and several tumor types. dDAVP displayed cytostatic effects through canonical adenylate cyclase-cAMP-PKA axis activation in a wide variety of preclinical cancer models including breast and colorectal cancer, as well as a potent antiangiogenic and antimetastatic activity. The aim of this work was to evaluate in vitro dDAVP antitumor activity in OS cells. The human OS cell lines MG-63 and U2-OS were used. AVPR2 expression was assessed by qPCR, and sensitivity to dDAVP was evaluated by in vitro proliferation and Transwell chemotaxis assays. AVPR2 expression was detected in MG-63 cells but not in U2-OS. The presence of AVPR2 in MG-63 cells was confirmed by Western blot using MCF-7 breast cancer cells as a positive control. dDAVP showed significant cytostatic effects against exponentially growing MG-63 cell cultures after a 72-h exposure to the compound at 1 μM or higher (~30 % inhibition; $p<0.01$), while no direct cytotoxic effects were detected in semiconfluent, quiescent cell monolayers at the same concentrations (24-h incubation). A potent inhibitory effect on MG-63 cell chemotaxis was observed at concentrations of 100 nM or higher, reducing migratory capacity by up to 57% in comparison to vehicle-treated cells ($p<0.01$). dDAVP exerted cytostatic and antimigratory activity on AVPR2-expressing human OS cells. The compound could represent an interesting repurposing