proliferation and cell cycle are downregulated in SUR cells, while there is an increase in signatures related with cellular adhesion and DNA packaging (p<0.01, FDR<25%). We propose quiescent plasticity as a mechanism of resistance to BRAF and MEK inhibitors.

Keywords: melanoma, BRAF, PLX4032, GDC-0973, plastic resistance

(1686) **ONCOLYTIC ADENOVIRUS-LOADED MENSTRUAL MESENCHYMAL STEM CELLS OVERCOME THE BLOCKADE OF VIRAL ACTIVITY EXERTED BY OVARY CANCER PATIENTS' ASCITES**

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Ovary cancer patients present peritoneal ascites at recurrence as a marker of disseminated disease and dismal prognosis. Oncolytic immunotherapy is an emerging approach for the treatment of disseminated cancer. In the present work we show the construction of a novel oncolytic adenovirus, AR2011, to target malignant ovary tumors. The survival curves were made by infecting malignant cells with AR2011 at different MOIs and showed that AR2011 exhibited a clear lytic effect *in vitro* in human ovary cancer cell lines and malignant cells obtained from ovary cancer patients´ ascitic fluids (AFs). By mixed the oncolytics adenovirus and crescent dilutions of AFs we demonstrated that AR2011 activity was neutralized by antibodies present in 31 samples of patients´-derived AFs. However, this blockade was overridden by preloading menstrual blood stem cells (MenSC) with AR2011 (MenSC-AR) since under these conditions AFs exerted no *in vitro* inhibitory effect on viral lytic activity. We performed cytokines and chemokines arrays of AF to study the composition of the factors present in the patient samples. Moreover, we perfomormed migration assays and observed that soluble factors present in AFs act as MenSC chemoattractants. MenSC-AR treatment of nude mice carrying established peritoneal carcinomatosis following administration of human ovarian cancer cells was able to inhibit tumor growth at levels similar to those observed with AR2011 alone. This study demonstrates that MenSC can be used to override the blockade that ascitic fluids exert on viral oncolytic effect.

(970) **STUDY OF THE BROWNING PROCESS OF BREAST CANCER ADIPOSE TISSUE**

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Abstract: Adipose microenvironment is involved in signaling pathways that influence breast cancer progression. Although adipocytes have been shown to promote breast cancer development, adipocyte characteristics involved in this process remain poorly understood. The aim of this work was to investigate the effects of factors derived from conditioned media (CMs) from human breast cancer adipose tissue explants (hATT) or normal breast adipose tissue explants (hATN) on induction of white adipocyte cell line browning. Morphology changes and brown adipose tissue (BAT)-related markers (UCP1, PRDM16, PGC1α and TBX1 among others) expression were evaluated following exposure of 3T3-L1 adipocytes to hATT or hATN CM. Increased expression of UCP1, PRDM16 and PGC1α was observed in adipocytes 3T3-L1 exposed to hATT CM in comparison to hATN CM. Interestingly, adipocytes exposed to hATT CM displayed characteristics that morphologically resembled brown adipocytes. In contrast, adipocytes exposed to hATN CM increased lipid droplet size, characteristic features of white adipocytes. In summary, these findings suggest that hATT secrete a different set of factors compared to hATN, which may induce browning of white adipocytes. This simple experimental approach suggests that hATT attached to the tumor could induce white adipocyte browning present in its microenvironment, for paracrine signaling.

Keywords: Adipose tissue, Browning, Breast cancer

(720) **A NOVEL ROLE OF KLF6 ACTIVITY IN THE INDUCTION OF CELLULAR SENESCENCE AND GENOME INTEGRITY MAINTENANCE**

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Krüppel-like factor 6 (KLF6) is a transcription factor involved in the regulation of relevant biological processes as cell proliferation, differentiation and apoptosis. In addition, KLF6 have a tumor suppressor activity and, accordingly, loss-of-functions mutations of *klf6* gene have been found in many human malignancies. We have demonstrated that KLF6 knockdown leads to spontaneous transformation of fibroblast cells whereas forced KLF6 expression provokes a marked cell cycle arrest. In this regard, we hypothesized whether KLF6-mediated cell cycle arrest could be associated with induction of cellular senescence. In fact, this process limits proliferation of potentially detrimental cells, preventing tumorigenesis and restraining tissue damaging helping to avoiding neoplastic transformation. In this study, we observed that increased expression levels of KLF6 in HeLa cervical carcinoma cells was able to promote cellular senescence (Fisher Test, p<0,05), as determined by higher levels of senescence associated β-galactosidase activity. Then, cellular senescence induced by H_2O_2 treatment of NIH3T3 fibroblast cells was markedly reduced upon KLF6 downregulation by stable shRNA transduction (p<0,05). In addition to cellular senescence bypass, these cells also shown signs of genome instability as micronuclei and chromosome rings formation, suggesting that KLF6 may be involved in genome integrity maintenance. These surprising findings, along with the cytostatic function of KLF6 upon oncogenic activation is suggesting that its tumor suppressor activity could be mediated by cellular senescence as an alarm signal in response to certain stimuli producing exacerbated proliferation or cell transformation.

Palabras clave: Krüppel-like factor 6, Tumorigenesis, Cellular Senescence, Genome integrity.

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(557) **ANALYSIS OF THE INTERACTION BETWEEN THE GLUCOCORTICOID AND THE PROGESTERONE RECEPTORS**

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Glucocorticoid (GR) and progesterone (PR) receptors are members of the steroid receptors family. The active PR is associated with cell proliferation and mammary tumors progression. GR activation promotes cell differentiation. Thus, the relative abundance of both receptors may modulate the proliferative response of the mammary epithelium. In view of these precedents, the aim of this work was to test the ability of both receptors to be part of the same complex and to study if both receptors are able to be recruited at the same binding regions in the genome. To assess if PR and GR have the potential to form complexes in vivo, T47D cells were transfected with expression vectors encoding for both receptors fused to fluorescent proteins (eGFPPR and mCherryGR) and incubated with their ligands R5020 and/or Dex, respectively. Then, fluorescence correlation spectroscopy (FCS), which allows obtaining quantitative parameters related to the mobility of fluorescent molecules and their interaction with fixed targets in living cells was used. From these analyzes it was observed that when both receptors are activated, they move in the nucleus, simultaneously. Upon activation with their respective ligands, both receptors are also recruited to a large fraction of specific binding regions. This result led us to inquire whether receptor co-bin-