next-generation, data independent acquisition based proteomics (96 patients) and immunohistochemistry (621 patients).

Results and discussions A quantitative cell surface proteomics identified the membrane-bound isoform of COMT as a cell surface protein overexpressed in a more migrating clone of MDA-MB-231 cells, indicating the association of COMT with cell motility in triple negative breast cancer. On the other hand, overexpression of COMT in MCF-7 cells decreased cell migration and invasiveness, supporting tumour suppressor role in oestrogen receptor dependent breast cancer. Analysis of 96 primary breast cancer tumours using next generation proteomics showed increased COMT protein levels in more aggressive tumours: in grade 3 vs. grade 1, in luminal B vs. luminal A, in triple negative vs. luminal A, and in triple negative lymph node positive vs. triple negative lymph node negative tumours.

Conclusion Based on our results, we hypothesise a dual role of COMT in breast cancer: while tumour suppressor role is further supported by our data in ER +breast cancer cells, in tissues COMT seems to be associated with more aggressive phenotype, namely in ER independent, triple negative breast cancer. It is thus evident that the dominance of catecholoestrogen methylation activity may be limited to ER dependent breast cancer. This may alter the perspective how COMT is considered as a potential diagnostic or therapeutic target.

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PO-245 FRUCTOSE SUPPORTS TUMOUR GROWTH AND AGGRESSIVENESS THROUGH A METABOLIC REPROGRAMMING IN PROSTATE CANCER

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Introduction PET-scanning can detect primary tumours relaying on their high glucose uptake ability through overexpression of the glucose transporter Glut-1. However, this method has shown limited clinical applicability for prostate cancer (PCa) diagnosis, suggesting that PCa cells do not use glucose as its primary source of energy. Preliminary data from our laboratory has shown overexpression of the fructose transporter Glut-5 in PCa cell lines and in clinical specimens of PCa, which suggest that fructose could play an important role in PCa biology.

Material and methods We analysed the effect of fructose on aggressiveness and metabolic reprogramming in benign prostate epithelial and PCa cell lines. Cells were incubated with glucose or fructose in the media for 24, 48, and 72 hour and then we evaluated: 1) the proliferative rate of benign and PCa cells, 2) the invasion and migration capacity of PCa cells, and 3) the mRNA levels of the enzymes involved in glycolysis, pentose phosphate and *de novo* lipogenesis pathways using real-time PCR in PCa cells. The effect of fructose on tumour growth was analysed by a PC3 cell line xenograft in immunosuppressed NSG mice. 15% fructose was added to the drinking water for 8 weeks. Tumour weight and the expression of glycolytic enzymes by qPCR was evaluated with respect to the control (water without additives).

Results and discussions PCa cells incubated with fructose or glucose, showed similar proliferative rate, invasion and migration capacities. However, fructose evokes a different expression profile of the enzymes involve in glycolysis, pentose phosphate and *de novo* lipogenesis pathways. Fructose promotes tumour growth of PC3 cells in the NSG mice.

Conclusion Our data suggest that fructose could play an important role in PCa pathophysiology, promoting proliferation and migration of PCa cells *in vitro*, and increasing tumour growth *in vivo* thanks to a reprogram in their metabolism that allows PCa cells to use fructose as effectively as glucose.

PO-246 NANDROLONE AFFECTS CELL GROWTH AND DIFFERENTIATION IN HEPATOMA CELLS

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Introduction Hepatocellular carcinoma (HCC) represents the sixth leading cancer and the third most common cause of death from cancer. Many different aetiological factors are involved in the development of HCC, which may be modulated by both estrogens and androgens hormones during its initiation, progression and metastasis. The misuse of anabolic androgenic steroids (AAS) is associated with serious adverse effects to the liver, including cellular adenomas and adenocarcinomas, and is considered a factor risk of developing hepatic sex hormone related tumours. The purpose of this study was to investigate the role of Nandrolone, one of the most commonly used AAS, in regulating proliferation and differentiation of HCC.

Material and methods Human HCC cell line HepG2 was treated with Nandrolone, a synthetic androgen ligand, for 48 hs and its viability and proliferation was assessed by MTS and cell cycle analysis, respectively. The expression of protein involved in cell cycle regulation and differentiation markers were analysed by western blot and real time PCR. Measurement of oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) were performed using Seahorse XF96 extracellular flux analyzer. Respiratory chain complex activities were assayed spectrophotometrically. Stemness surface markers expression was detected by FACSCalibur flow cytometer.

Results and discussions Nandrolone treatment caused cell growth inhibition associated to a downregulation of cyclin D1 and an upregulation of the cyclin-dependent kinase inhibitors p21Waf1/Cip1 leading to cell cycle arrest in the G2 phase. Moreover, a significant overall impairment of mitochondrial functions, resulting in a reduced OCR and impairment of OXPHOS complexes activities were also observed, thus suggesting a role in the control of the metabolic reprogramming. Finally, a significant increase of the stemness markers was detected following Nandrolone treatment, also confirmed in additional human stem cell types and in an *in vivo* mouse model.

Conclusion Nandrolone shows a strong anti-proliferative effect in differentiated tumour cells, promoting cancer cells stemness through cellular metabolic reprogramming. These results could have important public health implications in order to improve the primary prevention such as revising altered lifestyles, like AAS abuse.