METASTATIC PROSTATE CANCER CELL MECHANIC PHENOTYPE ASSOCIATED WITH OXPHOS INCREASE VIA MITOCHONDRIAL NETWORK REMODELLING

Gumulec J.

Department of Pathological Physiology, Faculty of Medicine, Masaryk University, Brno, Czech republic

Cancer cell invasion is energetically highly demanding process. The increase of cancer cell mobility during metastasis formation is, above others, accompanied by cytoskeletal remodelling. Literature indicates that that more deformable cells are favoured for higher invasion. However, our data on prostate tumors suggest softening in primary tumours followed by stiffening in higher-stage prostate metastatic cells. Accordingly, the metabolism of prostate cancer cells is highly specific compared to most other tumors. Due to zinc accumulation, benign cells exhibit a decrease in OXHPOS. In contrast, malignant cells show a decrease in zinc accumulation and thus increased OXPHOS and no Warburg effect in primary tumours. In this study we focused on consequences of an interplay between cell biomechanics and metabolic reprogramming in prostate tumors. Metastatic cell lines (PC-3 and LNCaP) characteristic of increased aggressiveness in vitro and in vivo were significantly stiffer than cells derived from the primary tumour not expressing CAV1, (22Rv1). We further developed zinc-resistant metastatic prostate tumour cells, which demonstrated to be more invasive in vitro. An increase of OXPHOS occurred upon induction of zinc resistance, as determined by OCR. To explain the unexpected increase of OXPHOS-related ATP production in zinc-resistant PC-3 cells, coupling efficiency was measured and mitochondrial network was analysed. Our data suggest that prostate cancer cells' mitochondria are highly interconnected and differ in coupling efficiency. Although this might be beneficial regarding ATP production, the resulting cellular stiffening, on the contrary, might prevent migration and aggressiveness.