Assessing the predominant metabolic immunophenotype would help to predict prostate cancer aggressiveness

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Despite its implication in virtually all malignant cells, the role of altered cellular metabolism as an essential factor in prostate malignancy has been largely ignored.

This work aims to study and identify metabolic changes associated with malignant transformation, identifying key metabolic proteins overexpressed in prostate cancer and linked to cancer progression and poor prognosis in order to infer about the most important metabolic alterations in prostate cancer, giving a special focus on the role of monocarboxylate transporters (MCTs) in this malignancy.

Expression of MCTs as well as key metabolic markers involved in lipidic β-oxidation and glycolytic metabolism was assessed by immunohistochemistry in 480 prostate samples and different prostate cell lines models. Also, the levels of glycolytic metabolism were assessed in the cell lines using commercial colorimetric assays and inhibition studies using the classical MCT inhibitor were performed. Immunofluorescence techniques were done in order to localize MCTs in prostate cells. Finally, ultra-structural studies were performed by classical EM techniques in order to better understand the morphology of human prostatic cancer and perhaps provide an insight into the structure-function relationship.

This study revealed that prostate cancer cells overexpress a variety of key metabolic proteins and the assessment of a “metabolic signature” appears to be indicative of prostate cancer initiation since we observed that many alterations are already evident in PIN lesions. Also studies in cell lines support a switch from low glycolytic metabolism in the localized and less aggressive *in situ* tumor to high levels of glycolytic metabolism in the highly aggressive and metastatic prostate tumor. All together, these results suggest that localized prostate cancer is not as glycolytic as the majority of the cancers and increased glycolysis is found mainly in the advanced stages of the disease correlating with poor prognosis. In contrast an increase in lipidic β-oxidation seems to be early event in prostate cancer tumorigenesis and is correlated with the initiation and progression of the disease.