

## Correlation of Serum and Tissue Biomarkers with Hyperpolarized <sup>13</sup>C Lactate Production in the Monitoring of Neuroendocrine Prostate Cancer

### Introduction

Neuroendocrine prostate cancer (NEPC) is a subtype that arises as the tumor develops resistance to androgen deprivation therapy (ADT). Preliminary data has displayed the ability of hyperpolarized (HP) <sup>13</sup>C pyruvate MRI to detect high-grade PC and provide early evidence of metabolic response to therapy<sup>1,2</sup>. The goal of this study was to develop a serum marker to measure the development of NEPC during ADT in the transgenic adenocarcinoma of the mouse prostate (TRAMP) model and use immunohistochemical staining (IHC) to quantify the NEPC % of the tumor to correlate with HP <sup>13</sup>C MRI findings.

### Methods

TRAMP mice that developed 0.5-1cc MRI detectable tumors at ~12 weeks received ADT. Mice with a  $\geq 20\%$  increase in tumor volume two weeks post-treatment were labeled non-responders, containing varying amounts of androgen-insensitive adenocarcinoma (CRPC) and NEPC. Single time-point, frequency-specific <sup>13</sup>C 3D imaging was performed 35s after an injection of polarized [<sup>1-<sup>13</sup>C</sup>] pyruvate using a gradient spin-echo (GRASE) sequence<sup>2</sup>.  $\approx 100\mu\text{L}$  of blood was drawn and an enolase activity assay was performed to determine serum neuron specific enolase (sNSE) activity. Tumor sections were stained for NEPC using NSE and synaptophysin stains and was quantified by pixel HSV values.

### Results

sNSE activity increased significantly in ADT resistant mice as compared to mice with androgen-sensitive adenocarcinoma and mice without tumors. sNSE activity was linearly correlated to the amount of NEPC. HP lactate/pyruvate (Lac/Pyr) ratio significantly increased with increasing amounts of neuroendocrine dedifferentiation.

### Conclusion

This study demonstrated that sNSE activity correlates to NEPC dedifferentiation as measured by quantitative IHC of the resected tumor, thereby providing a means for selecting tumors for correlation with HP <sup>13</sup>C MRI findings and further treatment. Preliminary HP <sup>13</sup>C pyruvate studies suggest that the HP Lac/Pyr ratio can differentiate between CRPC and NEPC based on the degree of increased HP <sup>13</sup>C lactate production.

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