INVESTIGATION INTO THE MECHANISMS OF PROSTATE CANCER ANDROGEN INDEPENDENCE USING LABEL-FREE DATA-INDEPENDENT QUANTITATIVE LC-IM-DA-MS AND PATHWAY ANALYSIS

INTRODUCTION

Prostate cancer (PCa) is the most common male cancer and third leading cause of cancer deaths among men in the Western world. Primary treatment of localized prostate cancer (PCa) fails in up to 35% of patients resulting in disease recurrence. These patients are of course often given androgen deprivation treatment (ADT) as a curative regime. However, over a period of several years, patients again show recurrence of the disease with the development of castrate resistant tumours that frequently progress to uncontrolled metastatic disease. The ‘onset of castrate resistance, which marks aggressive disease, is difficult to predict’ and biomarkers to monitor progression to this state are required to assess the effectiveness of ADT. LNCaP cells, an immortalized cell line derived from androgen-dependent human PCa, has been previously maintained in steroid deprived conditions to produce LNCaP cells. The ‘progression’ from androgen-dependent to androgen-independent LNCaP cells provides an excellent model of the development of castrate resistant PCas that occurs in vivo following ADT. An in-depth analysis of the molecular events underlying castrate resistant prostate cancer has been performed using a label free LC-MS.

METHODS

Protein expression analysis was performed using a nanoACQUITY system and a HSS T3 1.7 µm gradient from 5 to 40% acetonitrile (0.1% formic acid) at 300 nL/min using a nanoACQUITY system and a HSS T3 1.7 µm gradient from 5 to 40% acetonitrile (0.1% formic acid) at 300

RESULTS

Quantitative and statistical analysis of LC-MS data was undertaken with ProteinLynx Global SERVER and TransComp software. ProteinLynx Global SERVER was used to acquire and analyse the acquired data. The raw files were converted and processed using Cambridge Mass Spectrometry software (CAMS). Pathway analysis was conducted with Panther Classification System.

CONCLUSIONS

A label-free proteomic approach has been applied for the analysis of prostate cancer cell models by implementing a data-independent HDMS approach to provide both qualitative and quantitative information in a single experiment. Employing the label-free methodology into the workflow provides greater specificity and confidence of identified proteins that are regulated. Identified proteins were subsequently cross-validated using the Panther Classification System. Unique or significantly regulated proteins from ABL and LNCaP cells were further analysed using the Panther Classification System. This analysis revealed the presence of numerous dominant pathways in each cell type (Figure 6), which may have a critical role in prostate cancer androgen independence.

REFERENCES

4. LNCaP cells. Normalized abundance at this level is shown with associated upper and lower error limits.

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