

Metabolic Modulation of Dual Therapy Resistance of Prostate Cancer

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Therapeutic resistance remains a major challenge in cancer treatments. Metabolic modulation has recently emerged as a strategy to enhance cancer therapy and overcome therapy resistance. For metastatic castration-resistant prostate cancer, Enzalutamide and PARP-inhibitor are concurrently being used for treatment. Using the cell line and PDX models our team developed, we have identified transcription and super-enhancer drivers for dual resistance and the consequent upregulation of DNA repair and ferroptosis suppressors are contributing factors to the resistance. Importantly, we have also identified metabolic/nutritional modulation which targets these transcription/super-enhancer pathways, thereby overcoming the dual resistance. The detailed mechanisms and tumor biology of our findings will be described.