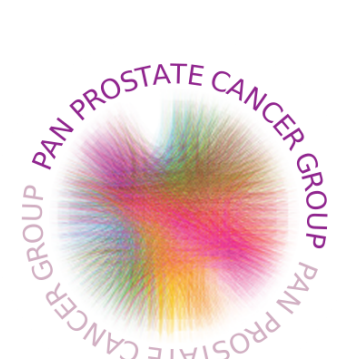


# tRNA Charging and Methionine: Exploring bacterial metabolic mechanisms in Prostate Cancer



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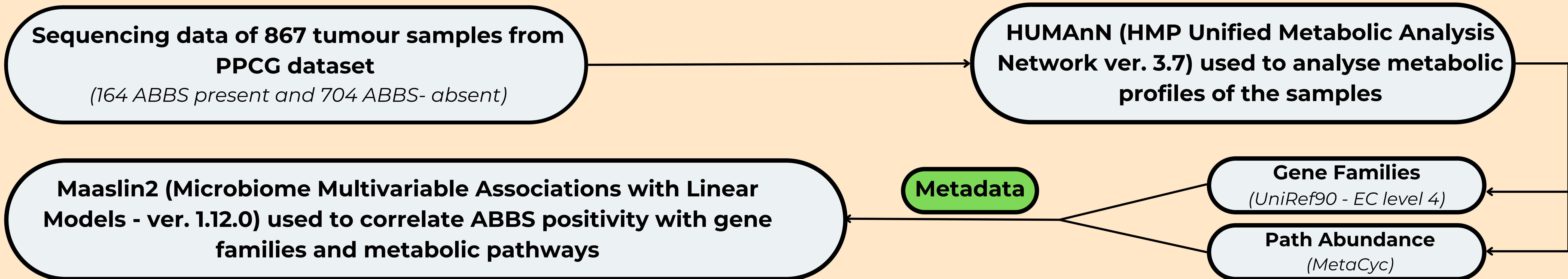
## INTRODUCTION

- Prostate cancer is one of the most common cancers in the UK (**1 in 8 men** will be diagnosed with it in their lifetime)
- Prostate cancer is heterogeous - challenging to predict aggressiveness accurately
- Bacterial involvement in other cancers is well known - e.g. *H. pylori* in gastric carcinoma. Bacteria also have a role in prostate cancer
- Some bacteria (known as the **Anaerobic Bacterial Biomarker Set - ABBS** - bacteria) tend to be associated with more aggressive cancers and lower overall survival - *Fenollaria*, *Peptoniphilus*, *Anaerococcus*, *Porphyromonas* and *Fusobacterium* (Hurst et al., 2022)

## OBJECTIVES

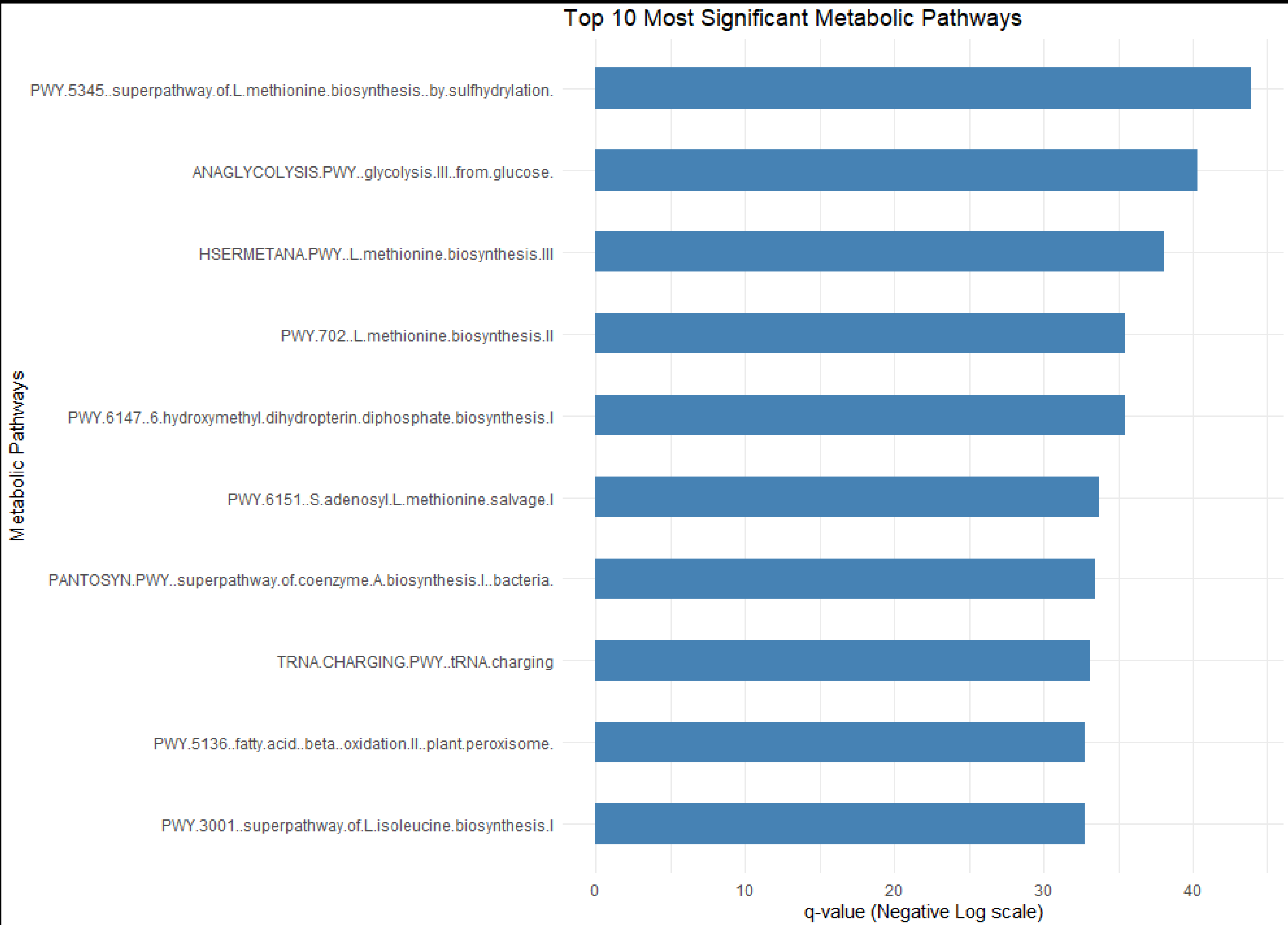
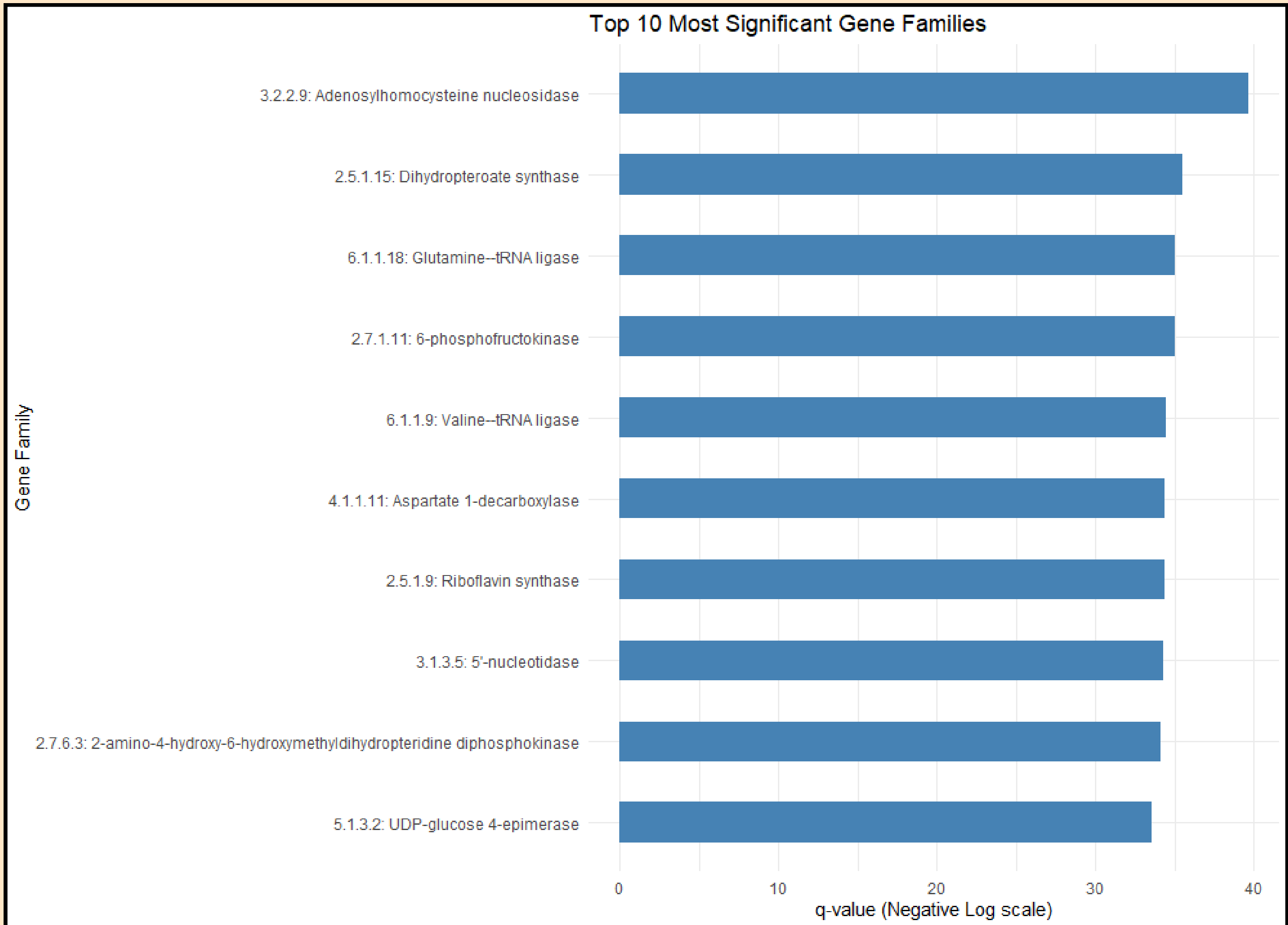
To use bioinformatics packages on the Pan Prostate Cancer Group dataset (a dataset with whole genome sequencing data of tumour tissue) to determine the bacterial genes and metabolic pathways which are associated with the presence of ABBS bacteria in prostate cancer patients

## METHODS



## RESULTS

- 667 bacterial gene families and 207 metabolic pathways were deemed to be significantly associated with ABBS presence from the 867 tumour samples of PPCG**
- tRNA synthetase enzymes and methionine synthesis/salvage pathways and enzymes** were found to be significantly associated with ABBS presence in tumours including PWY 6151: S-adenosyl-L-methionine salvage I;PWY5345: superpathway of L-methionine biosynthesis and PWY702: L-methionine biosynthesis II



## DISCUSSION

- Transfer RNA (tRNA)** - The **physical link between the genetic code in messenger RNA (mRNA) and the amino acid sequence that makes up proteins**
- tRNA charging - Aminoacylation of tRNA through aminoacyl-tRNA synthetases (ARSs)** to form an amino-acyl tRNA which can then allow for peptide bond formation
- tRNA charging is **promotes tumour growth** in various human cancers (Hyeon et al., 2019; Park et al., 2008) and could play a role in prostate cancer patients who have the presence of ABBS bacteria in their tumours
- Hoffman Effect** - Regardless of cancer type, tumours demonstrate a general condition of dependence on methionine (Hoffman, 2017, 2015).
- Increased methionine synthesis/salvage is **associated with increased cell division (a hallmark of cancer cells)** and methionine restriction can arrest the cell cycle in the S/G2 phases of the cell cycle (Hoffman & Jacobsen, 1980; Yano et al., 2014).
- The pathways mentioned above could also be part of the mechanisms of action by human cell invasive intracellular pathogenic bacterial species (Hurst et al., 2024)
- Methionine synthesis/salvage thus could be significantly associated with cancer aggressiveness in patients with tumours in which ABBS bacteria are present.**

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