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INTRODUCTION

- Prostate cancer is among the most common cancers globally (1 in 8 men in the UK will be diagnosed in their lifetime).
- Major risk factors include age, ethnicity, and family history.
- Microbial infections contribute to many cancers, and the prostate microbiome influences prostate cancer.
- We have found a set of bacteria associated with poor prognosis in patients diagnosed with prostate cancer called the Anaerobic Bacterial Biomarker Set – *Fenollaria*, *Ezakiella*, *Peptoniphilus*, *Anaerococcus*, *Porphyromonas*, and *Fusobacterium*.<sup>(1)</sup>
- Identifying the ABBS bacteria may help predict aggressive prostate cancer at diagnosis.

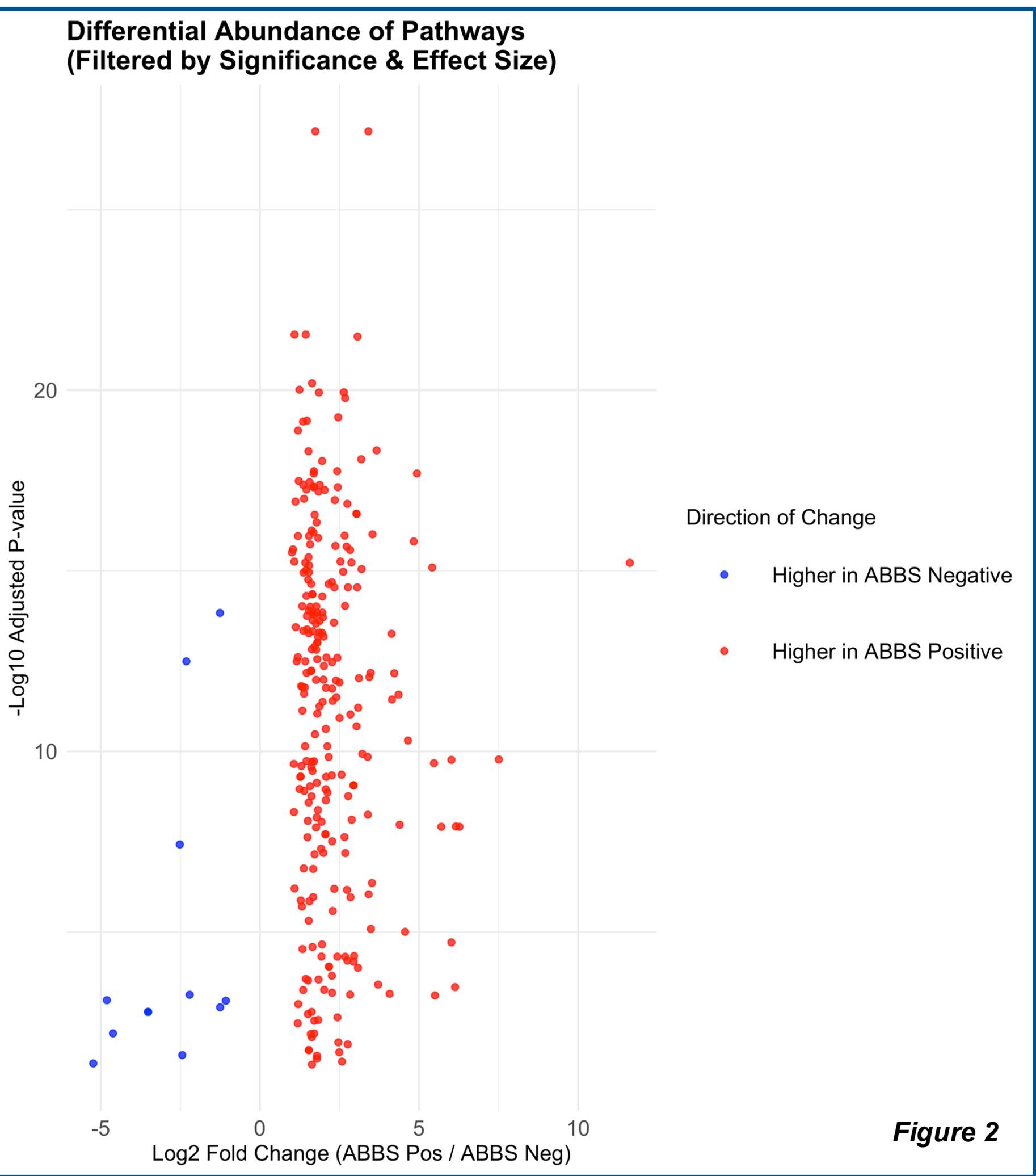
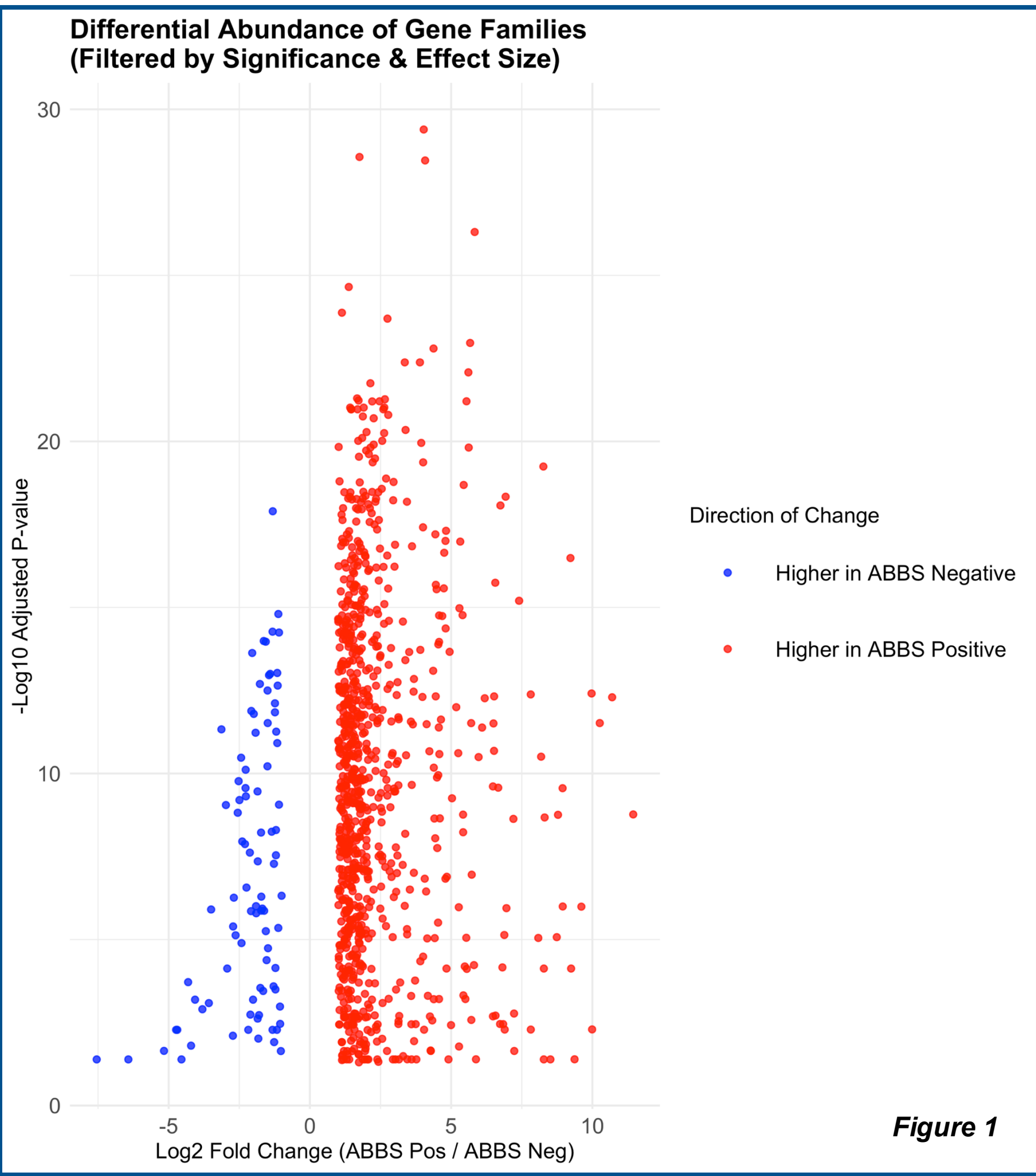
AIMS

- To investigate, through bioinformatics approaches, the potential mechanisms of action of ABBS bacteria in whole genome sequencing data from prostate tumours
- To determine the gene families and pathways whos presence is associated with ABBS-positive prostate cancers versus ABBS-negative prostate cancers.

METHODS

- Whole genome sequencing data from 678 tumour samples in the Pan-Prostate Cancer Group (PPCG) were analysed for microbial content.
- Unmapped reads were quality-trimmed, human-depleted, and classified using Kraken.
- The metabolic profiles of ABBS-positive and negative samples (also determined by Kraken classification) were assessed using HUMAnN (v3.7).
- Differential presence of gene families and pathways between ABBS positive and negative samples were determined using Maaslin2 (v1.12.0) in R (v4.2.0).

RESULTS

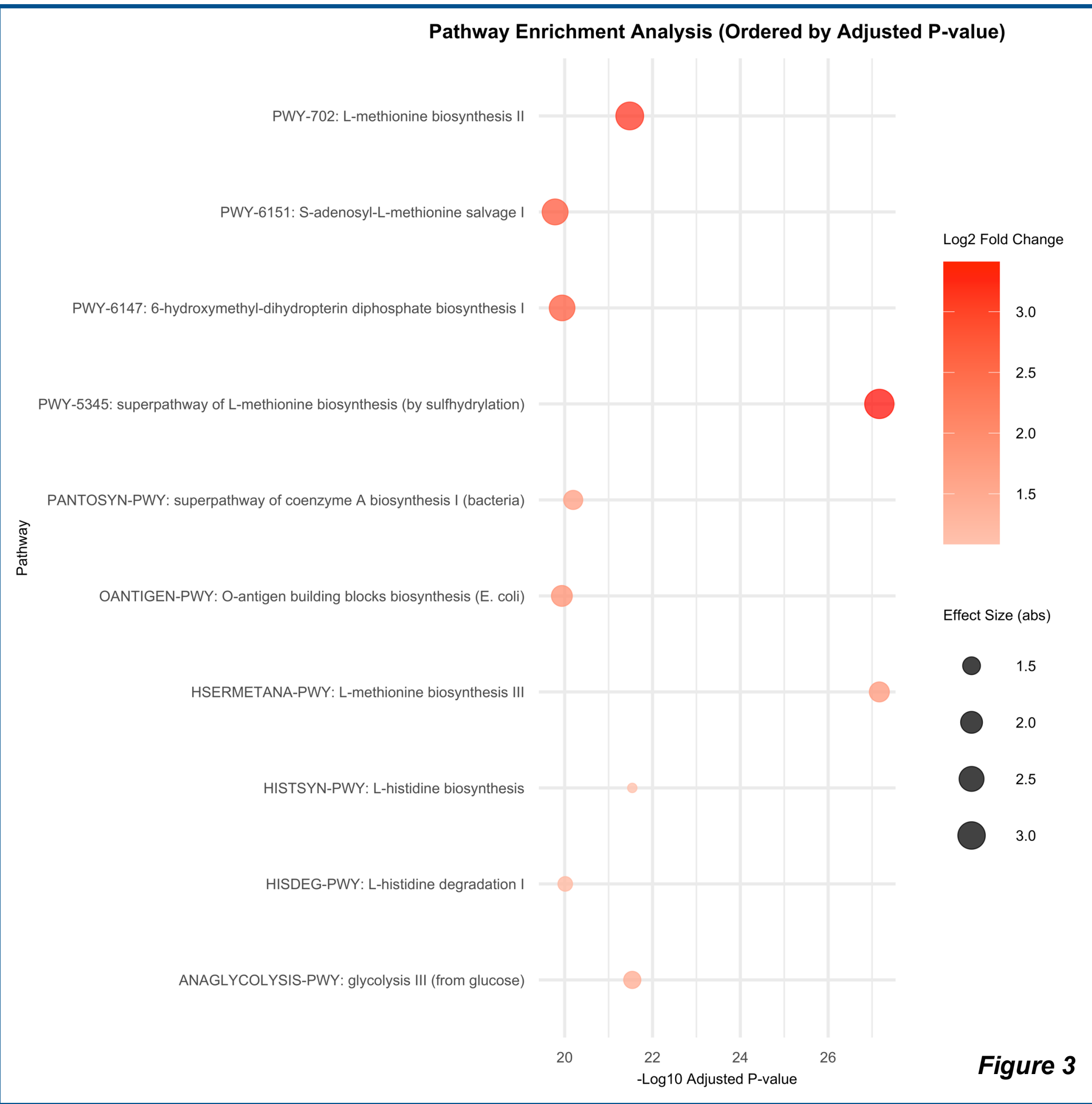


	ABBS Positive	ABBS Negative
Gene families enriched	899	90
Pathways enriched	263	12

Table 1

EC number	Top Gene families enriched in ABBS positive tumours
EC 4.3.3.6	Pyridoxal 5'-phosphate synthase (glutamine hydrolysing)
EC 6.3.5.7	Glutaminyl-tRNA synthase (glutamine hyrolysing)
EC 6.3.4.3	Formate—tetrahydrofolate ligase
EC 5.1.99.1	Methylmalonyl-CoA epimerase
EC 4.1.3.4	Hydroxymethylglutaryl-CoA lyase
EC 3.5.2.7	Imidazolonepropionase
EC 5.2.1.2	Maleylacetoacetate isomerase
EC 2.5.1.1	Dimethylallyltranstransferase
EC 4.1.3.36	1,4-dihydroxy-2-naphthoyl-CoA synthase
EC 1.2.7.4	Anaerobic carbon monoxide dehydrogenase

Table 2



DISCUSSION

- Significantly higher number of gene families and pathways are enriched in ABBS positive tumours (Figures 1 and 2)
- Key ABBS positive-associated pathways include methionine synthesis/salvage which ensure methioning production (Figure 3)
- Amino-acyl tRNA synthases are also among the top upregulated gene families (Glutaminyl-tRNA synthase is shown in Table 2 but all amino acyl-tRNA synthases are in the full list of 899 gene families) (Table 2)
- Cancer cells rely heavily on exogenous methionine (Hoffman effect) and can have an effect on aberrant cancer cell growth
- tRNA charging could be important in transformation from benign to malignant cells
- ABBS bacteria could be involved in the upregulation of these pathways and gene families, thus fulfilling a crucial role in cancer progression

REFERENCES

- Hurst R, Meader E, Gihawi A, Rallapalli G, Clark J, Kay GL, et al. Microbiomes of Urine and the Prostate Are Linked to Human Prostate Cancer Risk Groups. Eur Urol Oncol. 2022 Aug;5(4):412–9.
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- Hoffman RM, Jacobsen SJ. Reversible growth arrest in simian virus 40-transformed human fibroblasts. Proc Natl Acad Sci U S A. 1980 Dec;77(12):7306–10.
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ACKNOWLEDGEMENT

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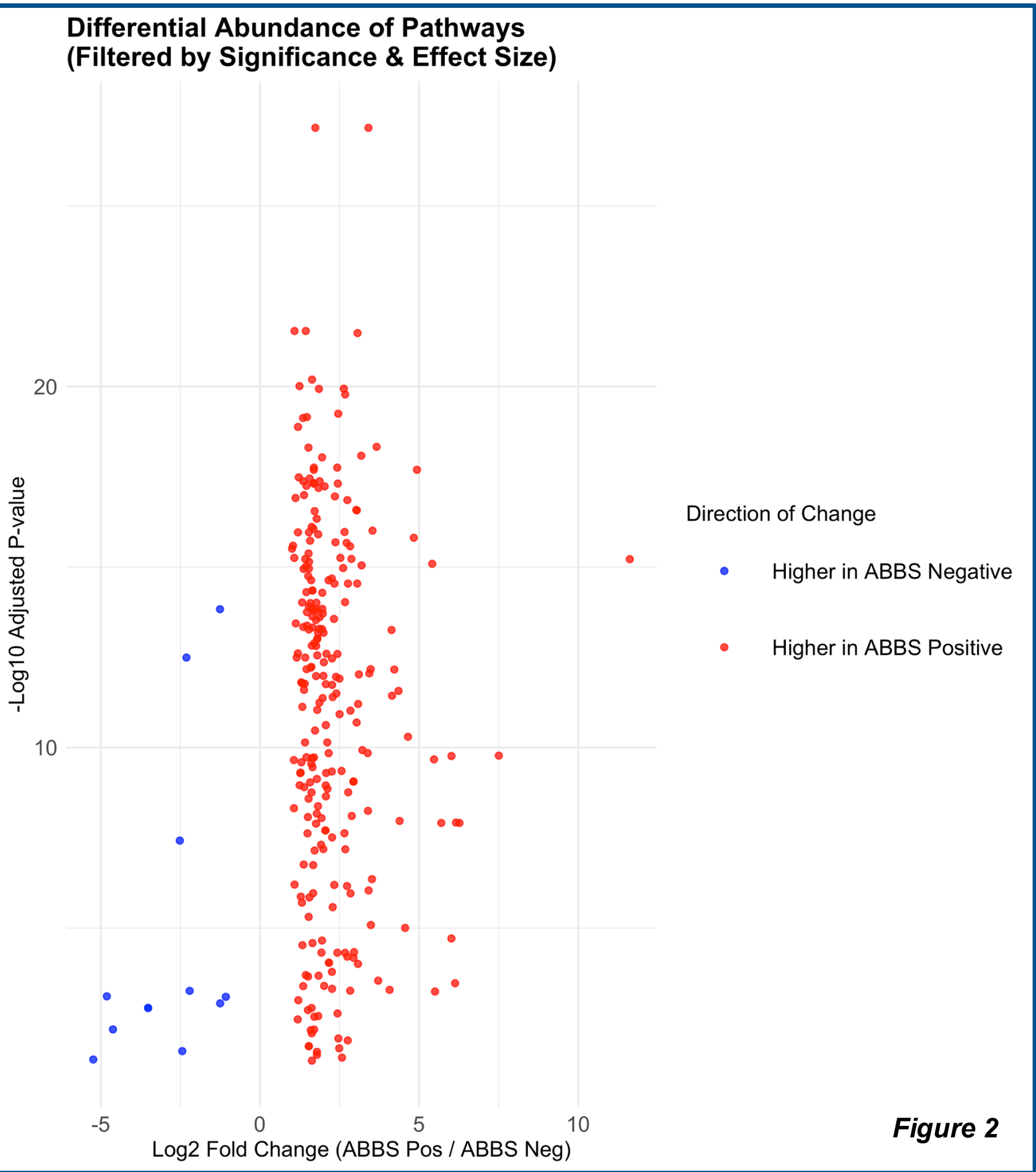
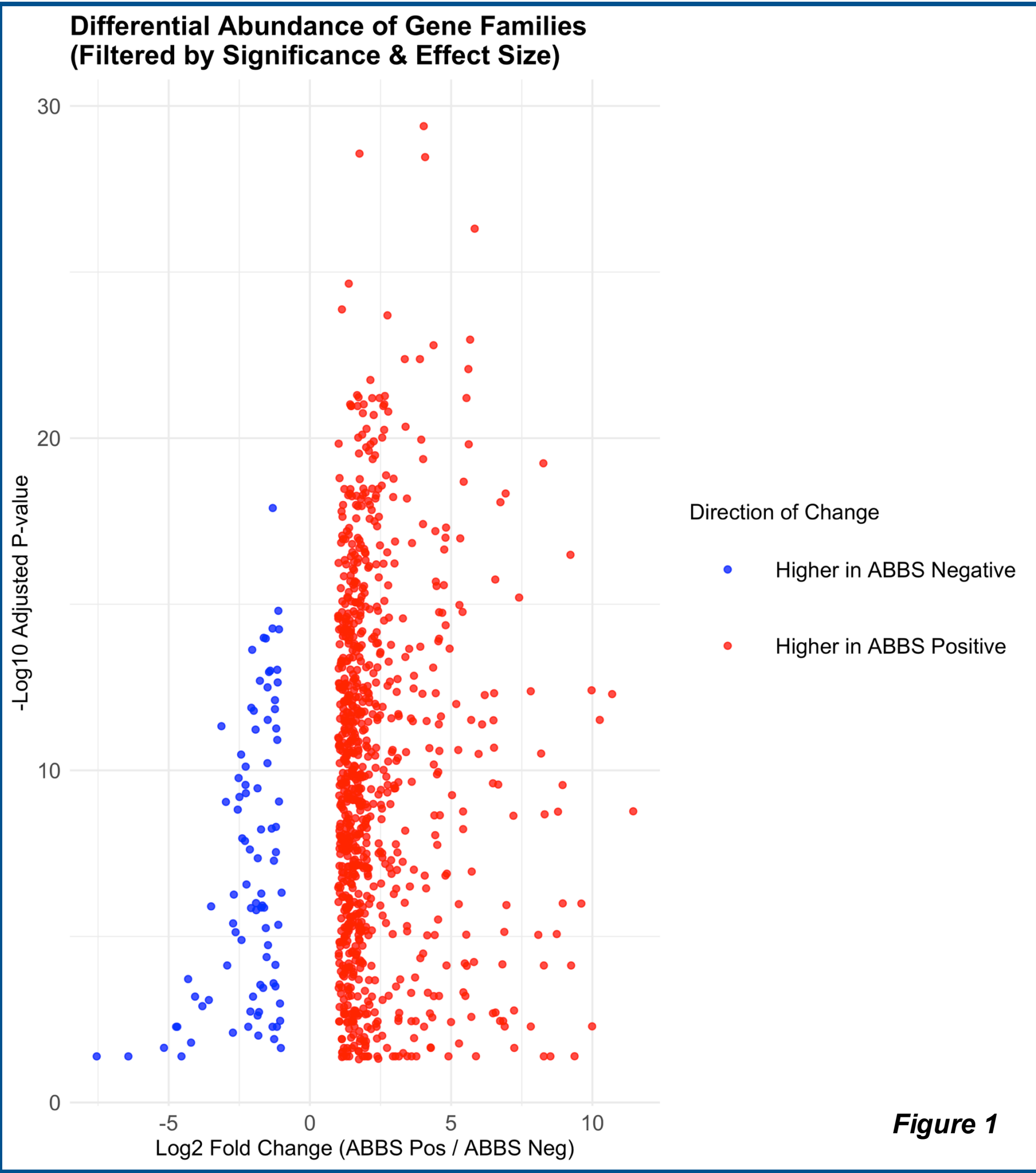
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Table 2

BioCyc ID	Top Pathways Enriched in ABBS Positive Tumours
HSERMATANA-PWY	L-methionine biosynthesis III
PWY - 5345	Superpathway of l-methionine biosynthesis
ANAGLYCOLYSIS-PWY	Anaerobic Glycolysis-III
HISTSYN-PWY	L-histidine biosynthesis II
PWY-702	L-methionine biosynthesis II
PANTOSYN-PWY	Superpathway of coenzyme A biosynthesis (bacteria)
HISDEG-PWY	L-histidine degradation I
PWY-6147	6-hydroxymethyl-dihydropterin diphosphate biosynthesis
OANTIGEN-PWY	O-antigen building blocks synthesis ( <i>E.coli</i> )
PWY-6151	S-adenosyl-L-methionine-salvage I

Table 3

DISCUSSION

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