

Title

Glycolysis and oxidative stress related redox pathway upregulation along the gut-liver axis by gut microbial perturbation and host response during giardiasis in C57BL/6J mouse model

Authors

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Infection analysis and mouse strain selection

The mouse strain with optimal for infection and *Giardia* colonisation among the tested strains, was selected by conducting the pilot study. During the study period of 14 days, the mice did not show visual diarrheic effects. Also, visual inspections and weight measurements (Figure 1A) indicated that the health of the mice was not drastically affected. Swiss mice showed considerable weight gains, with an average increase of 3.02 g during study period. Body weights of C57BL/6J and BALB/C mice, although fluctuate up to 8 dpi, did not increase considerably, with an average increase on 0.45 g and 0.11 g, respectively. C57BL/6J however, showed the highest response to *Giardia* infection, with the faecal *Giardia* cyst number peaking at 6 – 7 dpi (Figure 1B).

On 10 – 11 dpi, the *G. lamblia* cyst count showed a second peak before stabilising. Based on the outputs of both mice weights, *G. lamblia* cyst count and response to the infection, C57BL/6J strain was selected, with the follow-up main study shortened to 10 dpi.

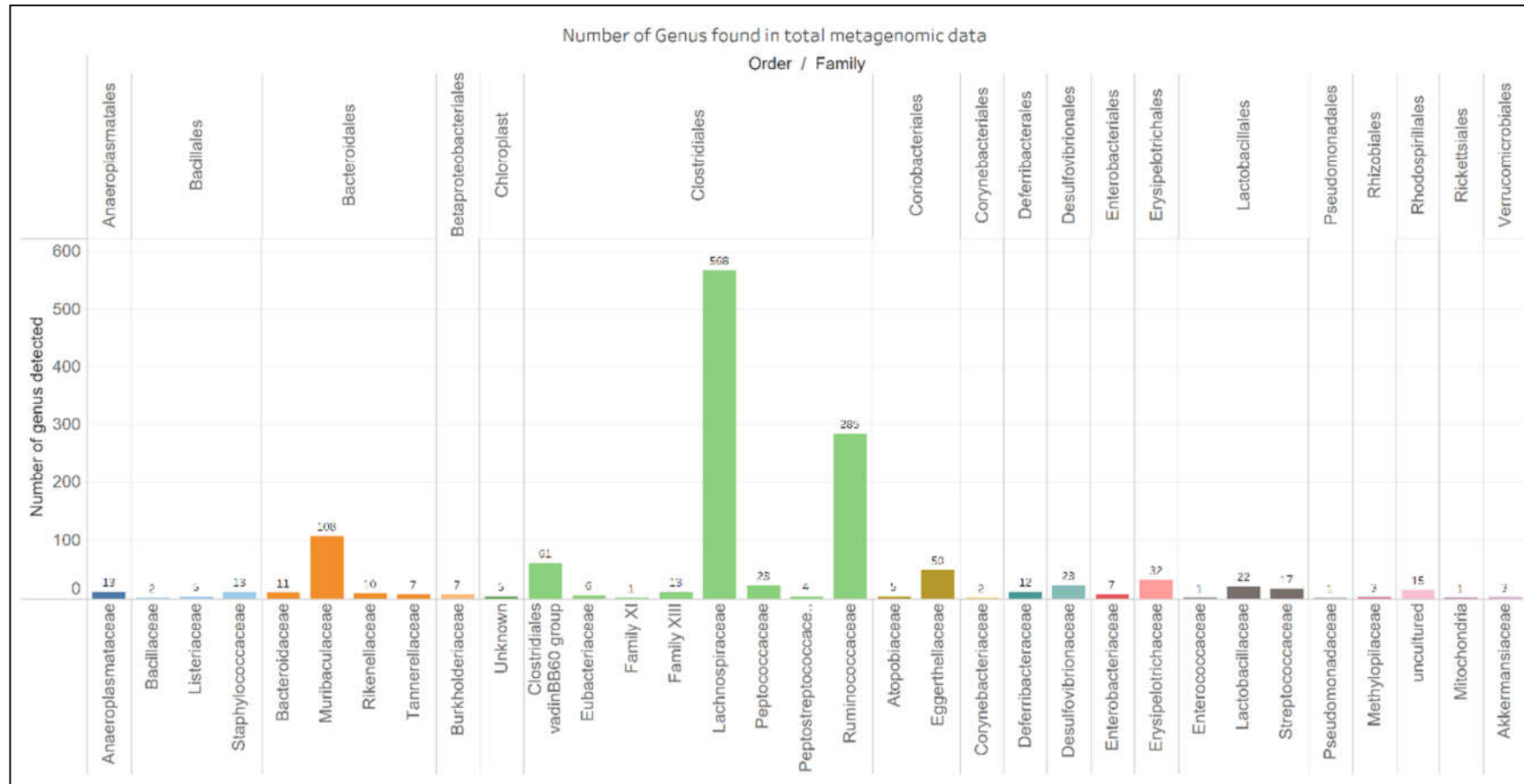


Figure S1. – Number of genera detected for each bacterial family. *Clostridiales* showed highest number of genera, followed by *Bacteroidales*. *Lachnospiraceae*, *Ruminococcaceae* and *Muribaculaceae*, in the mouse gut system during giardiasis

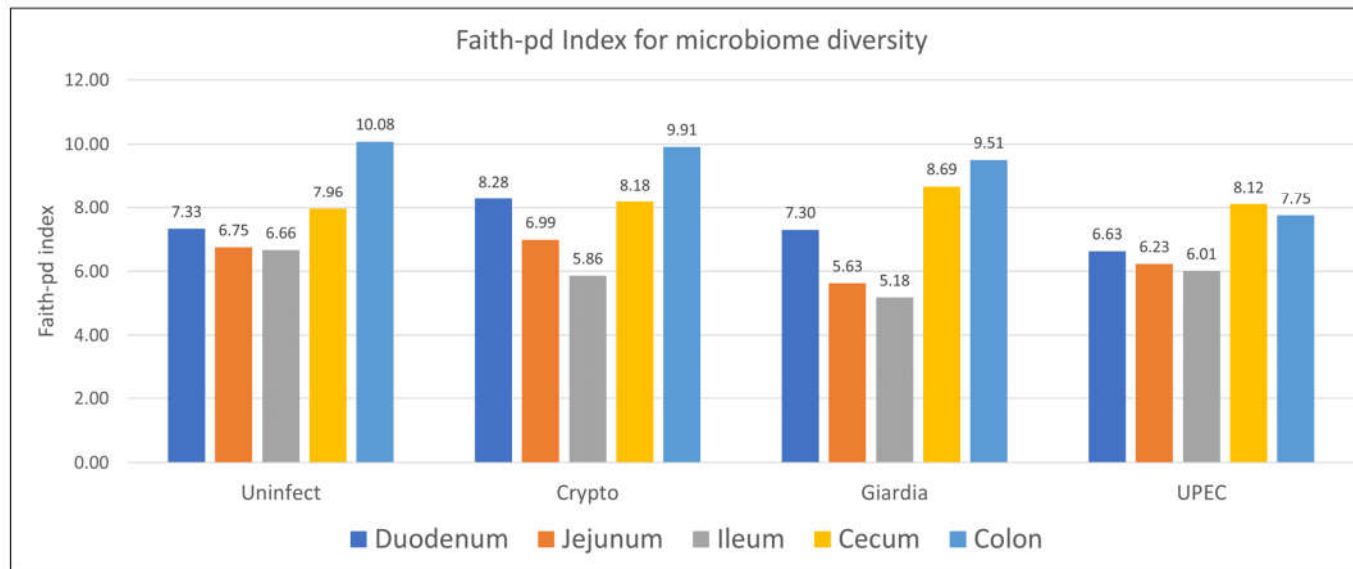


Figure S2. – Faith-pd index indicating overall microbial index detected in parts of the gut after specific diet treatment. Ileum was found most affected part of the gut showing decrease in the overall diversity during cryptosporidiosis and giardiasis.

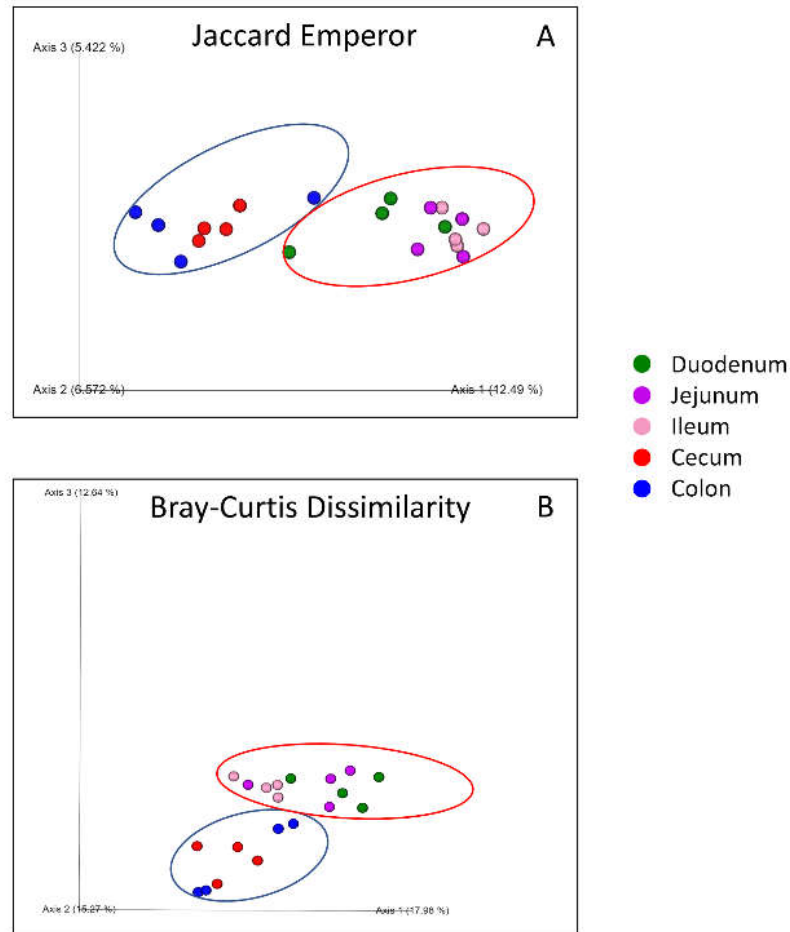
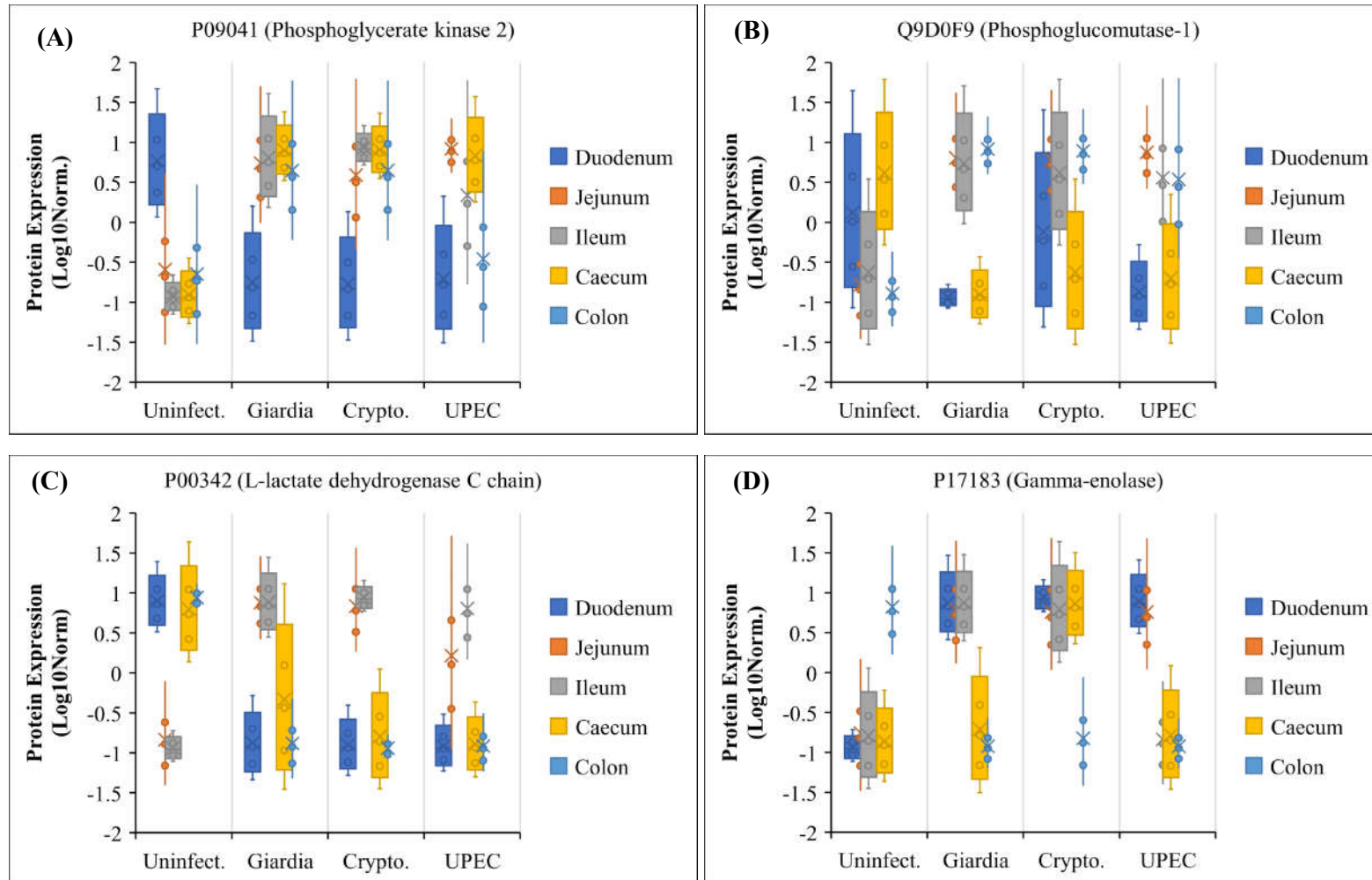


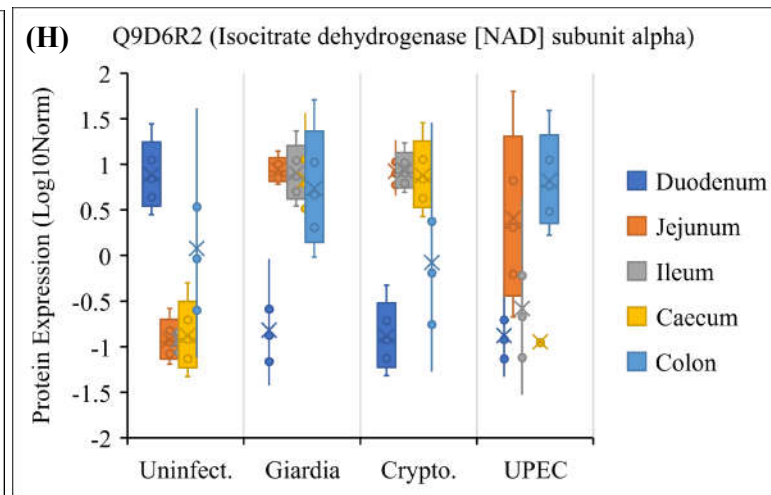
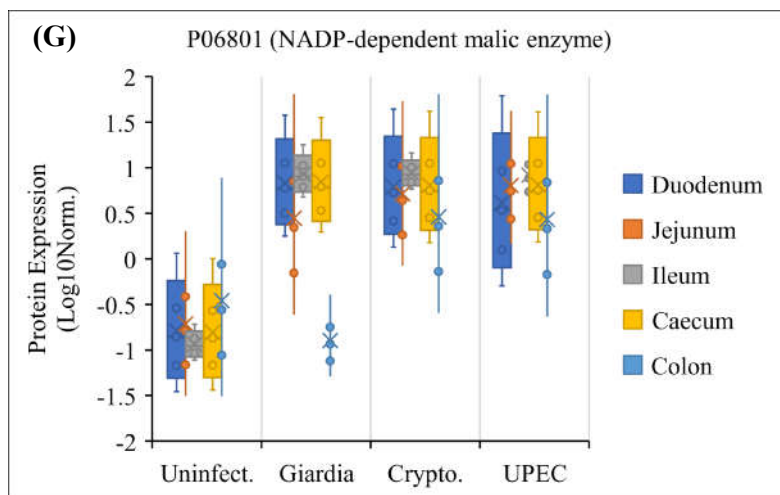
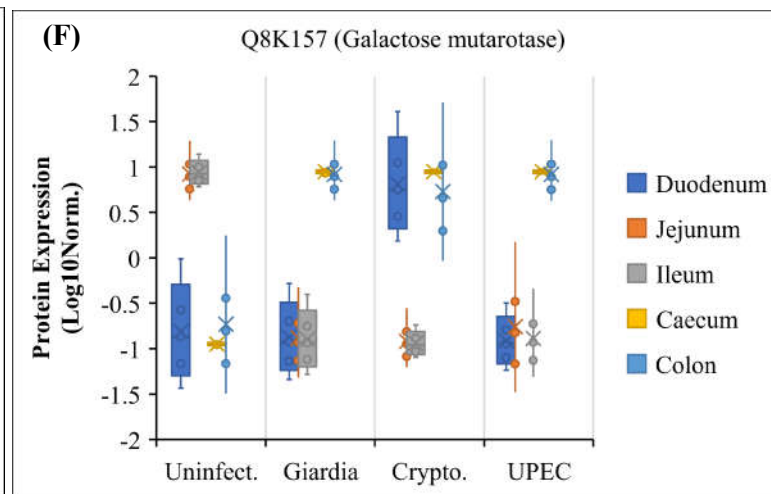
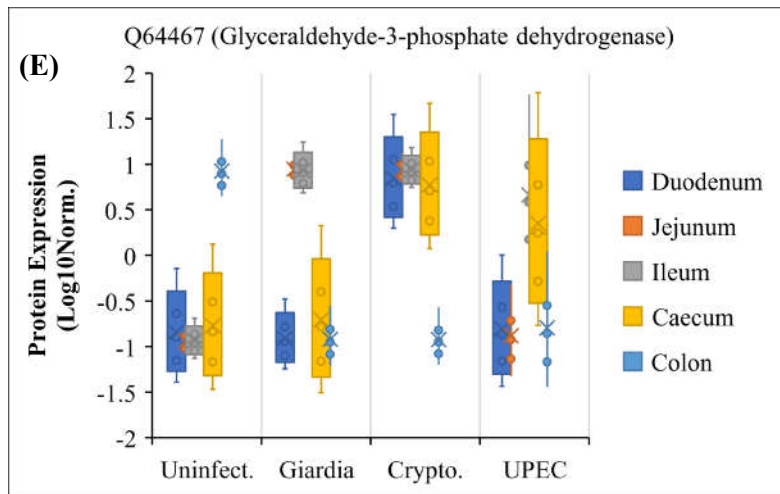
Figure S3. Jaccard Emperor (A) and Bray-Curtis Dissimilarity PCoA plots showing dissimilarity between small intestine (Duodenum, Jejunum and Ileum) and large intestine (Cecum and Colon). Axis 1 represents maximum dissimilarity followed by axis 2 and axis 3 between samples

Table S1. PLS-DA model fit (R^2) and predictability (Q^2) for metabolite profiles of all samples analysed for *Giardia* infection.

| Sample | R^2X | R^2Y | Q^2 |
|---------------|--------|--------|-------|
| Faeces | 0.802 | 0.997 | 0.985 |
| Duodenum wash | 0.682 | 0.999 | 0.954 |
| Jejunum wash | 0.65 | 0.994 | 0.865 |
| Ileum wash | 0.611 | 0.996 | 0.915 |
| Caecum wash | 0.702 | 0.999 | 0.975 |
| Colon wash | 0.603 | 0.996 | 0.972 |
| Serum | 0.691 | 0.996 | 0.980 |
| Lung | 0.659 | 0.989 | 0.929 |
| Liver | 0.574 | 0.999 | 0.955 |

Host protein expression during energy pathways (Glycolysis, Citrate cycle and Glyoxylate and gluconate pathway)





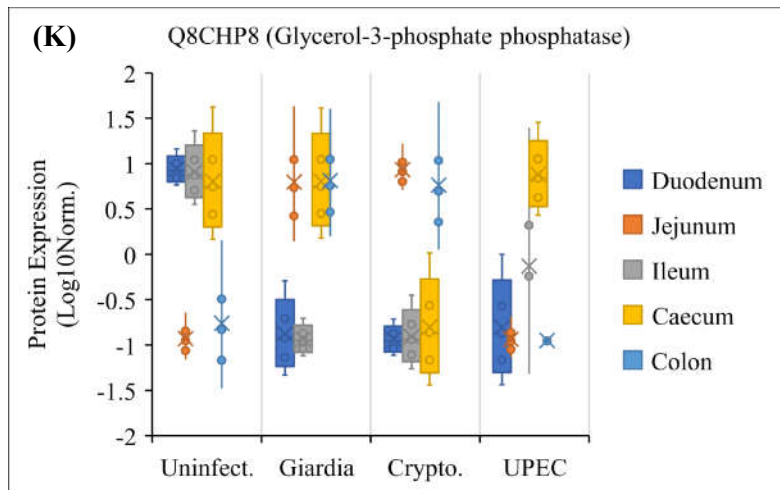
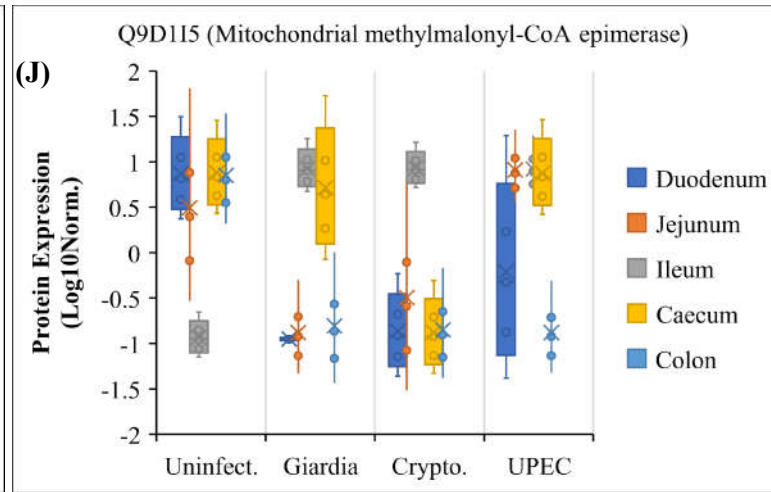
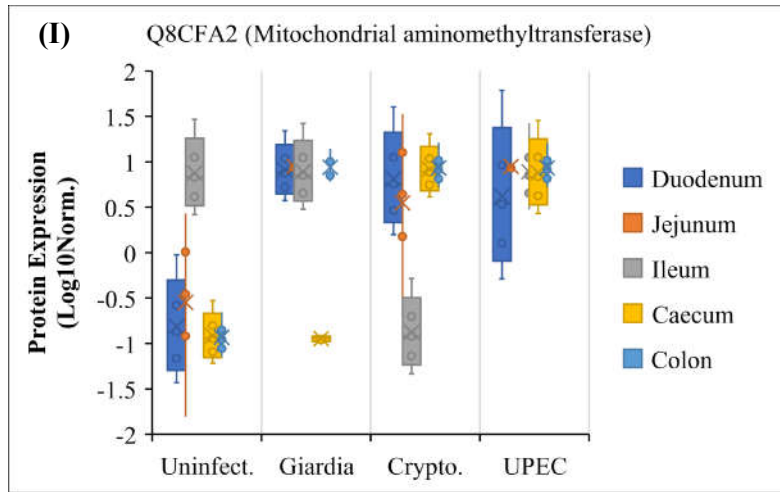
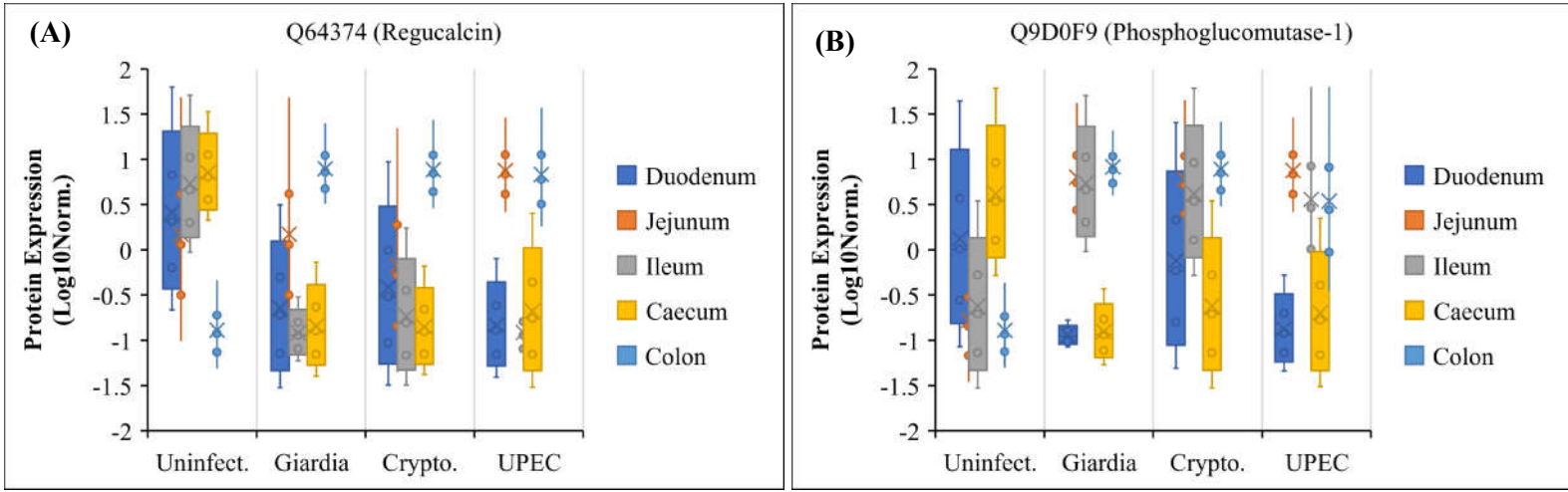
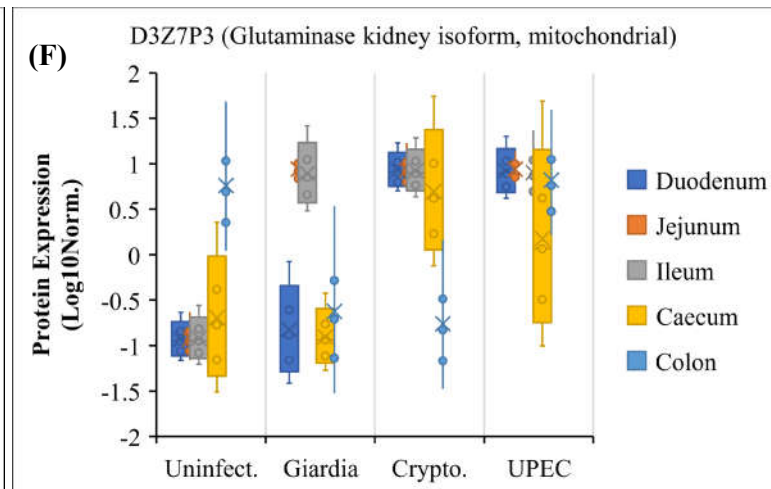
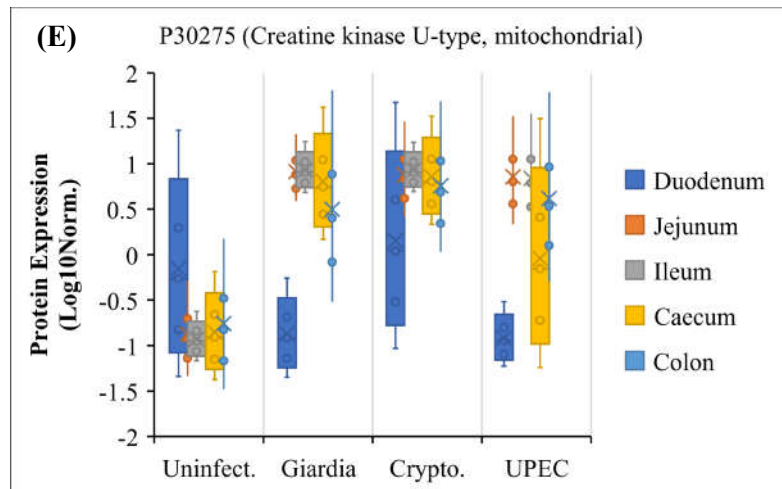
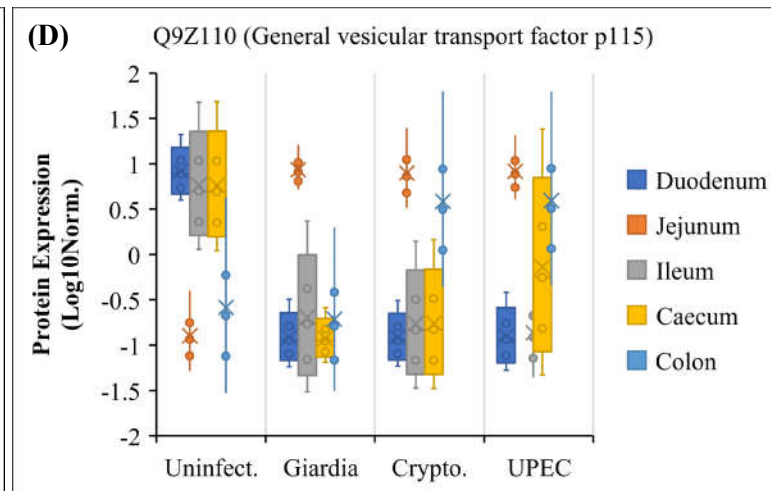
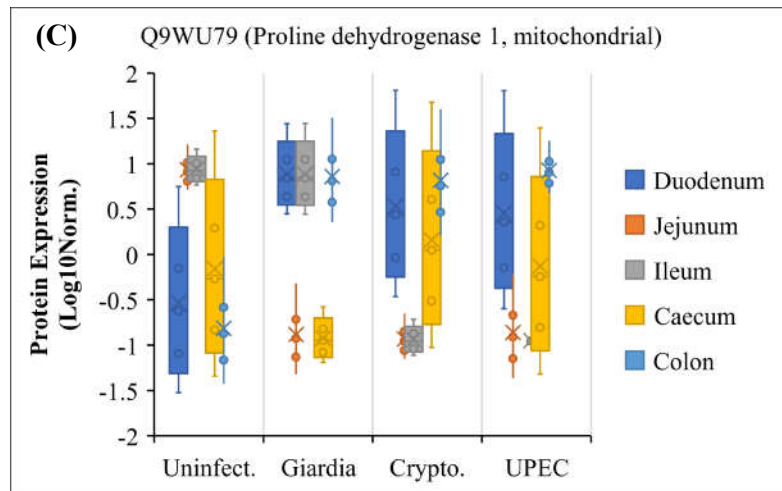


Figure S4. Log₁₀ normalised expression of major mouse proteins driving the energy metabolism pathways in the intestinal system during giardiasis, with respect to uninfected, cryptosporidiosis (positive control) and UPEC (negative control).

Pentose phosphate pathways and amino acid-sugar interconversions





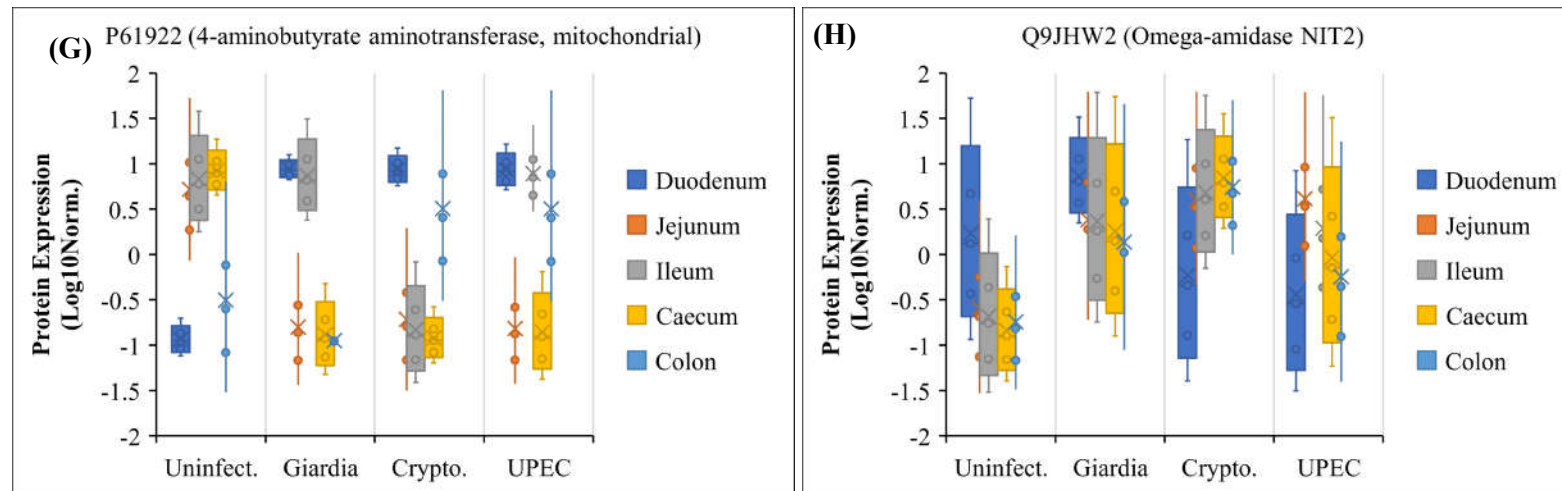
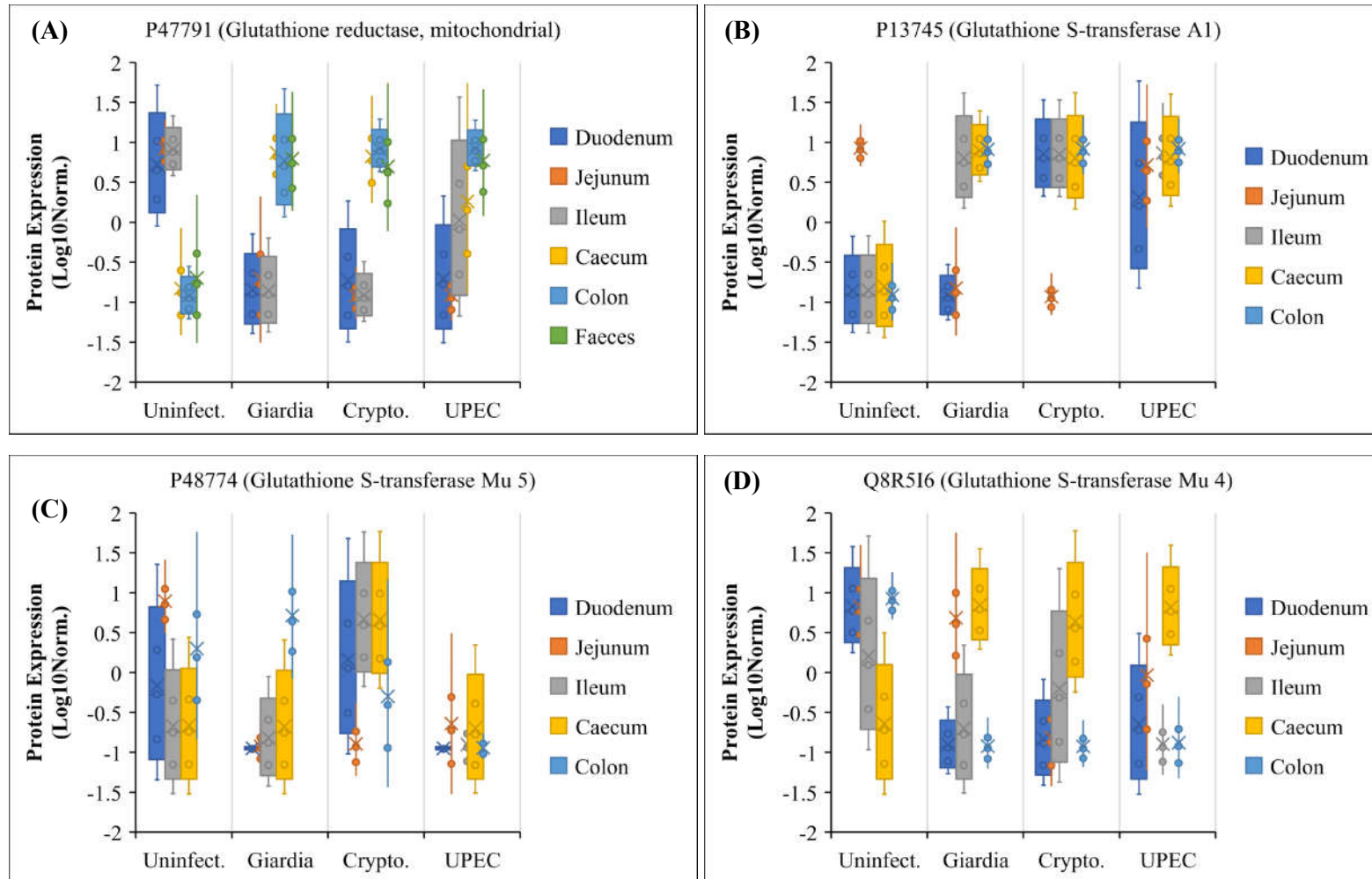
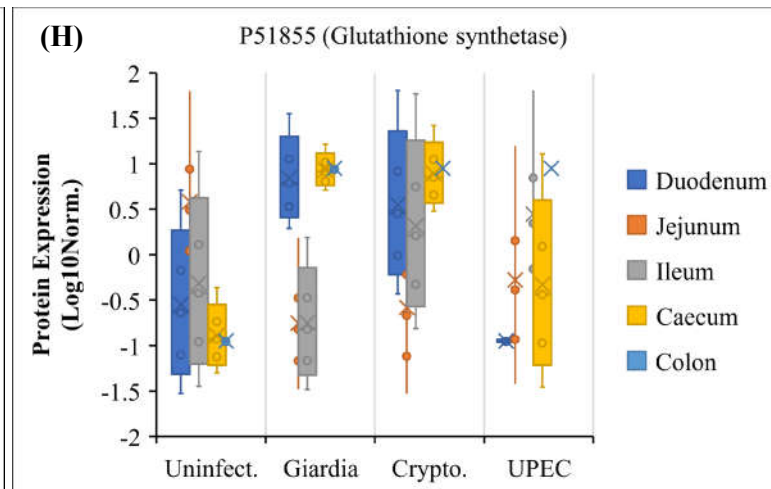
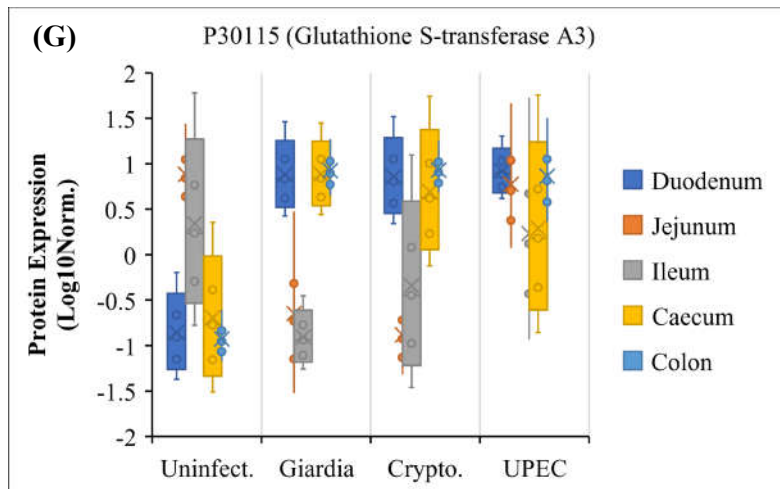
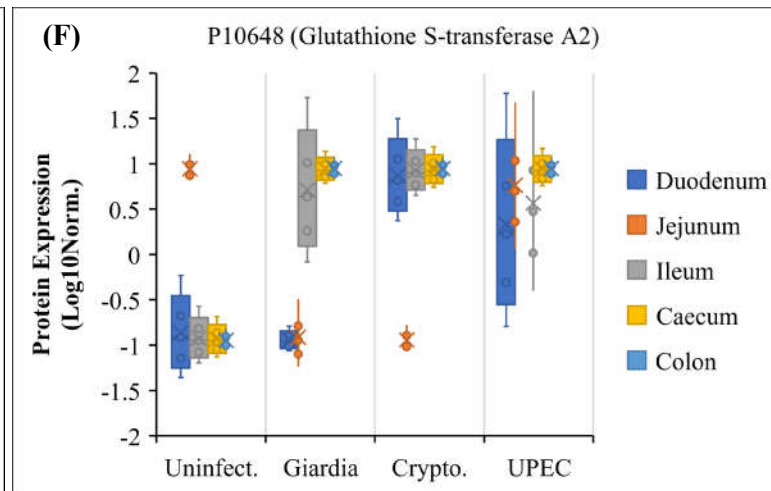
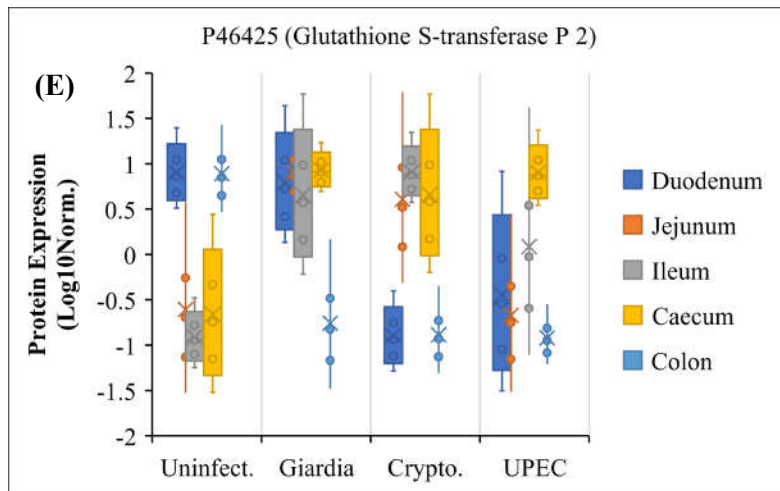


Figure S5. Log₁₀ normalised expression of major mouse proteins driving the pentose phosphate pathways and amino acid-sugar interconversions in the intestinal system during giardiasis, with respect to uninfected, cryptosporidiosis (positive control) and UPEC (negative control).

Sulphur pathways (Glutathione metabolism, Cysteine and methionine metabolism)





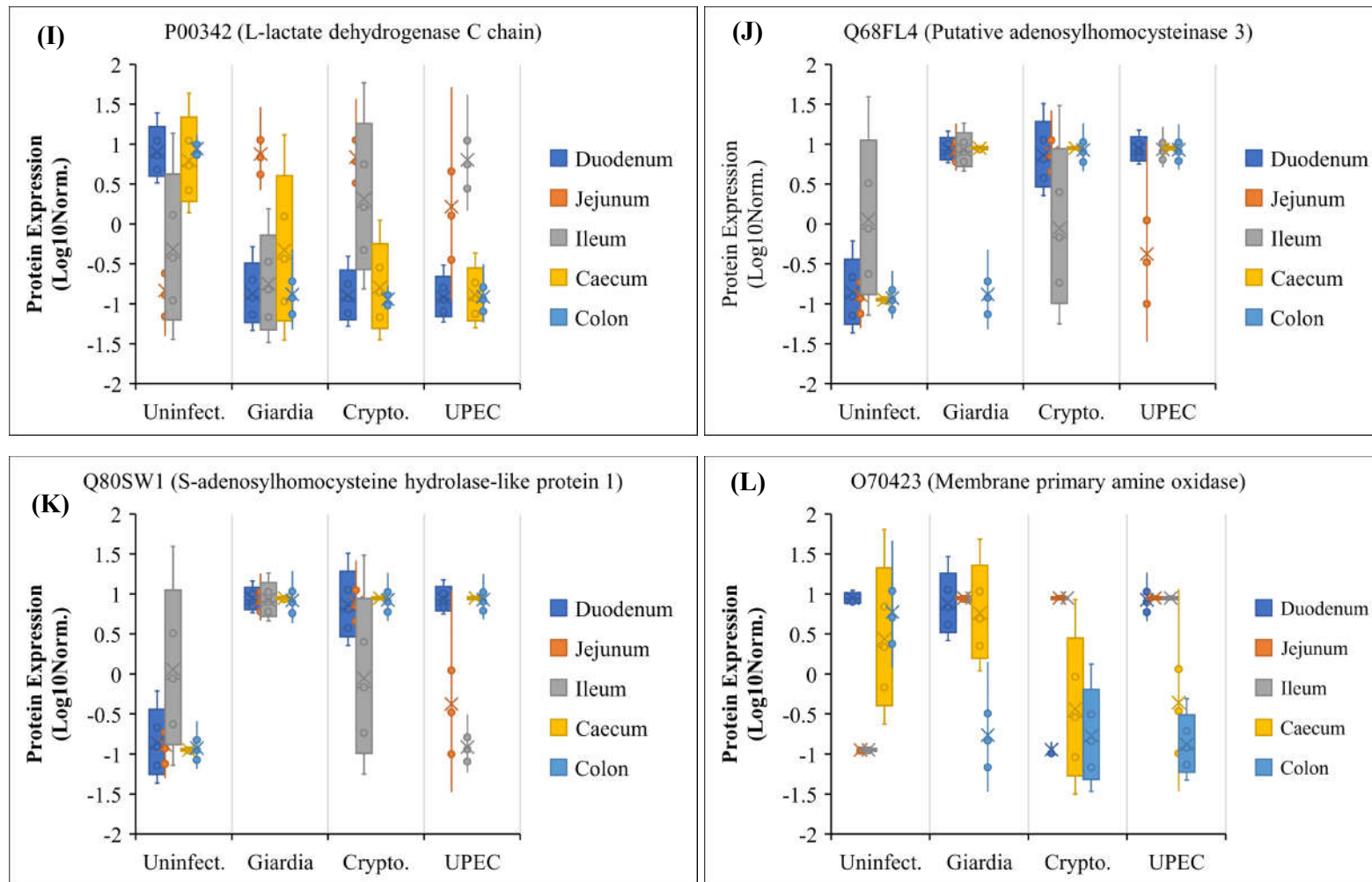
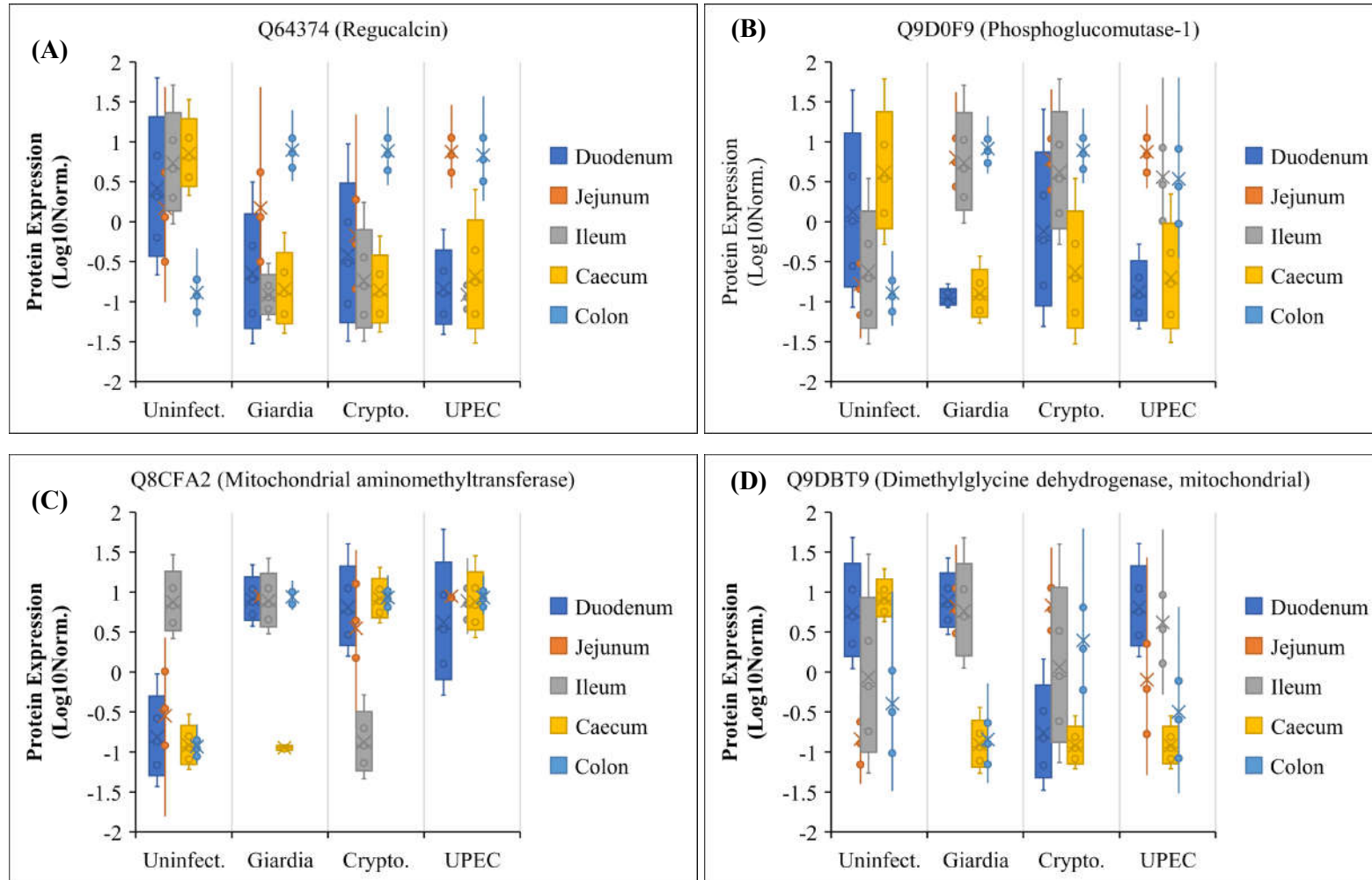
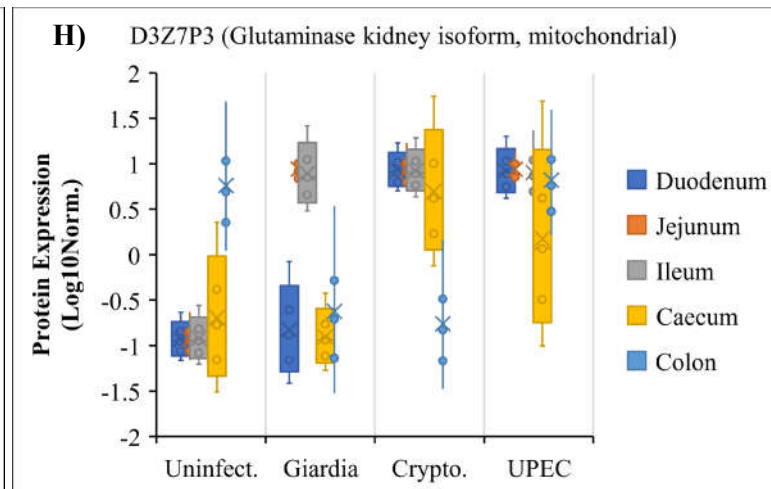
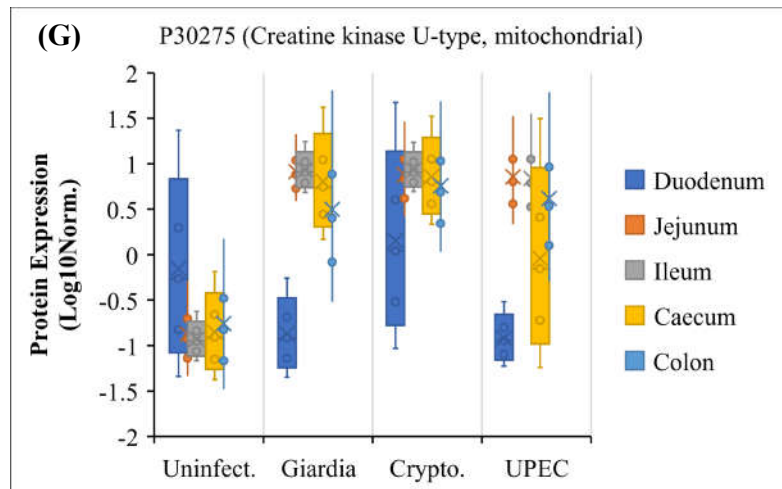
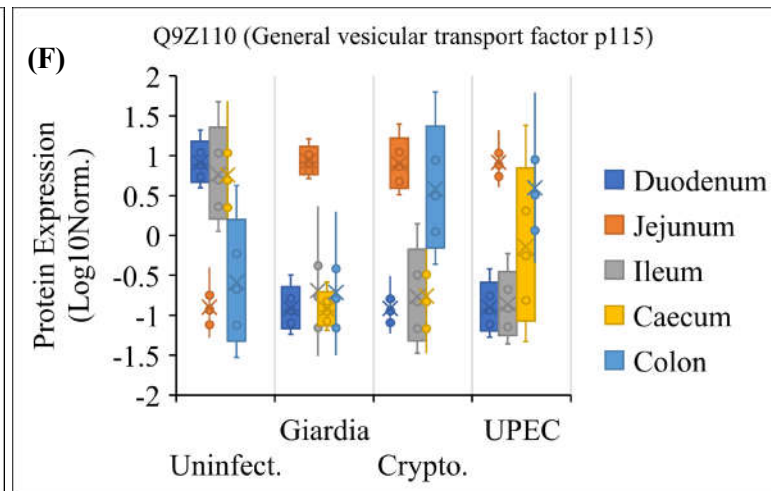
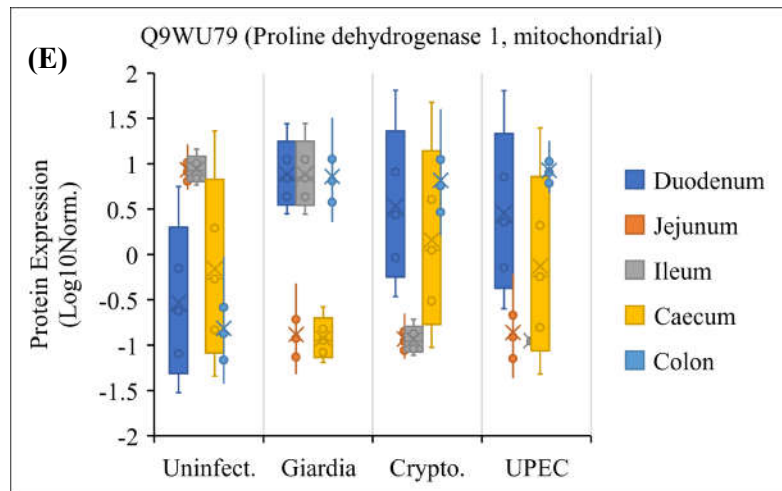


Figure S6. Log₁₀ normalised expression of major mouse proteins driving the sulphur metabolism pathways in the intestinal system during giardiasis, with respect to uninfected, cryptosporidiosis (positive control) and UPEC (negative control).

Nitrogen metabolism pathways





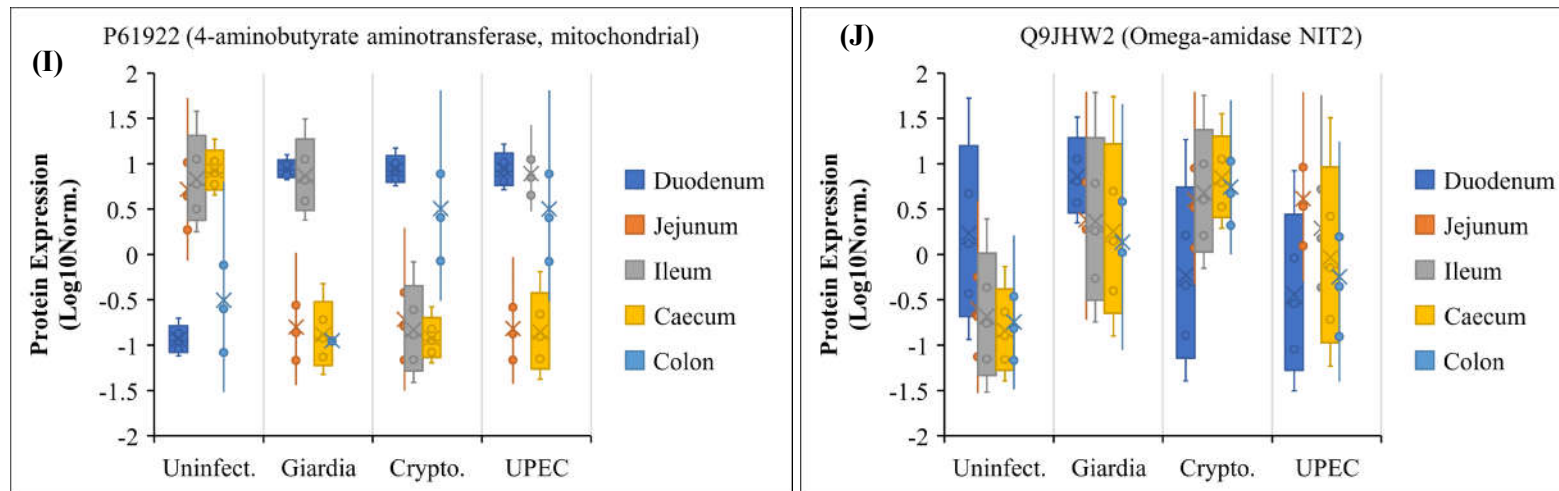


Figure S7. Log₁₀ normalised expression of major mouse proteins driving the nitrogen metabolism pathways in the intestinal system during giardiasis, with respect to uninfected, cryptosporidiosis (positive control) and UPEC (negative control).

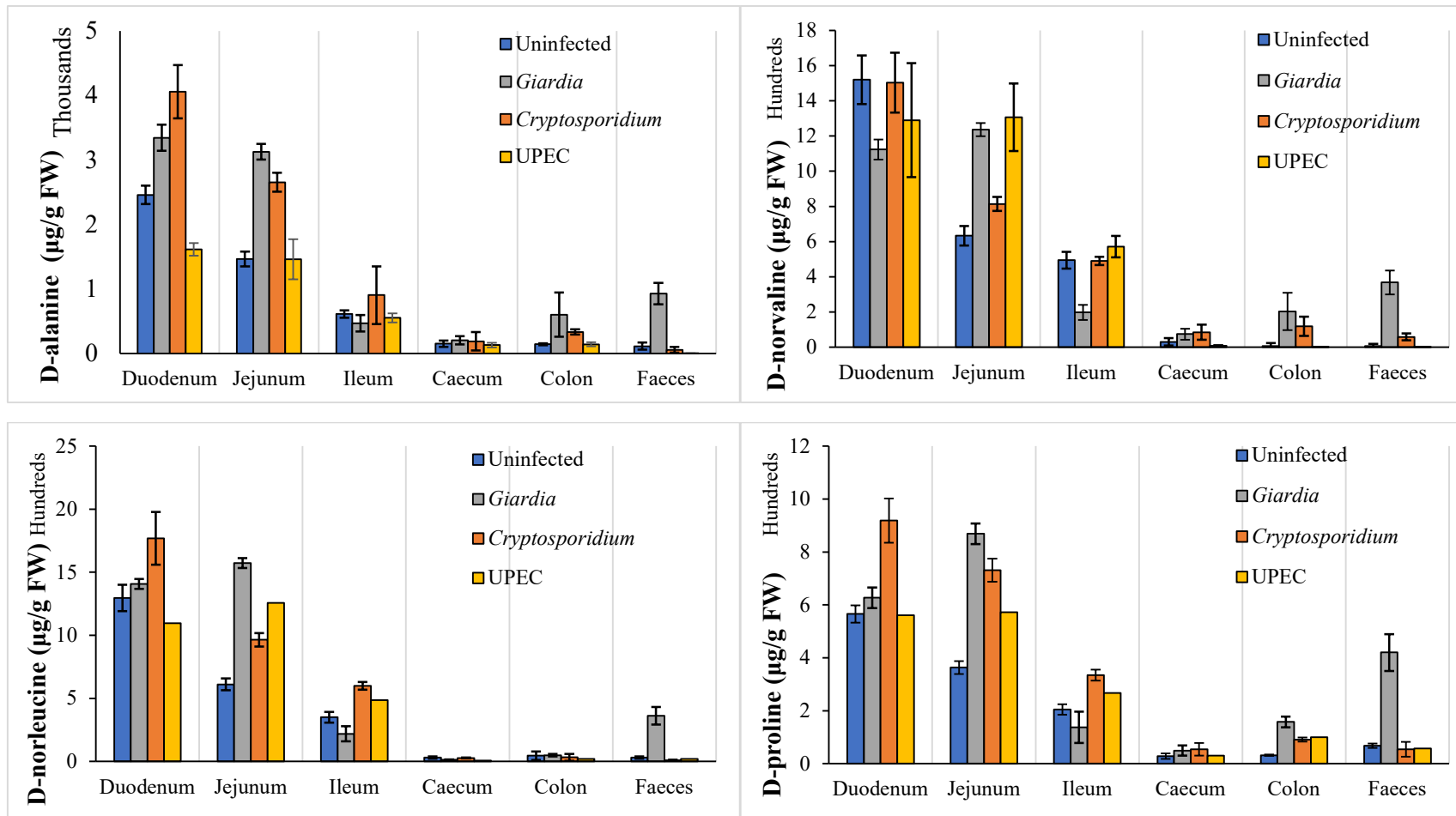


Figure S8. Accumulation of major D-amino acids throughout the mice gut during various infections. Error bars represent the standard deviation across experimental replicates (n = 5).

Table S2. Differential expression of major metabolic pathways in the mouse gut during cryptosporidiosis, giardiasis and UPEC infection in infected mice with respect to the uninfected mice. The values are represented as the normalised Log₂Fold changes, subjected to pareto scaling (n = 5). The terms refer to as C = *Cryptosporidium*, G = *Giardia*, U = UPEC.

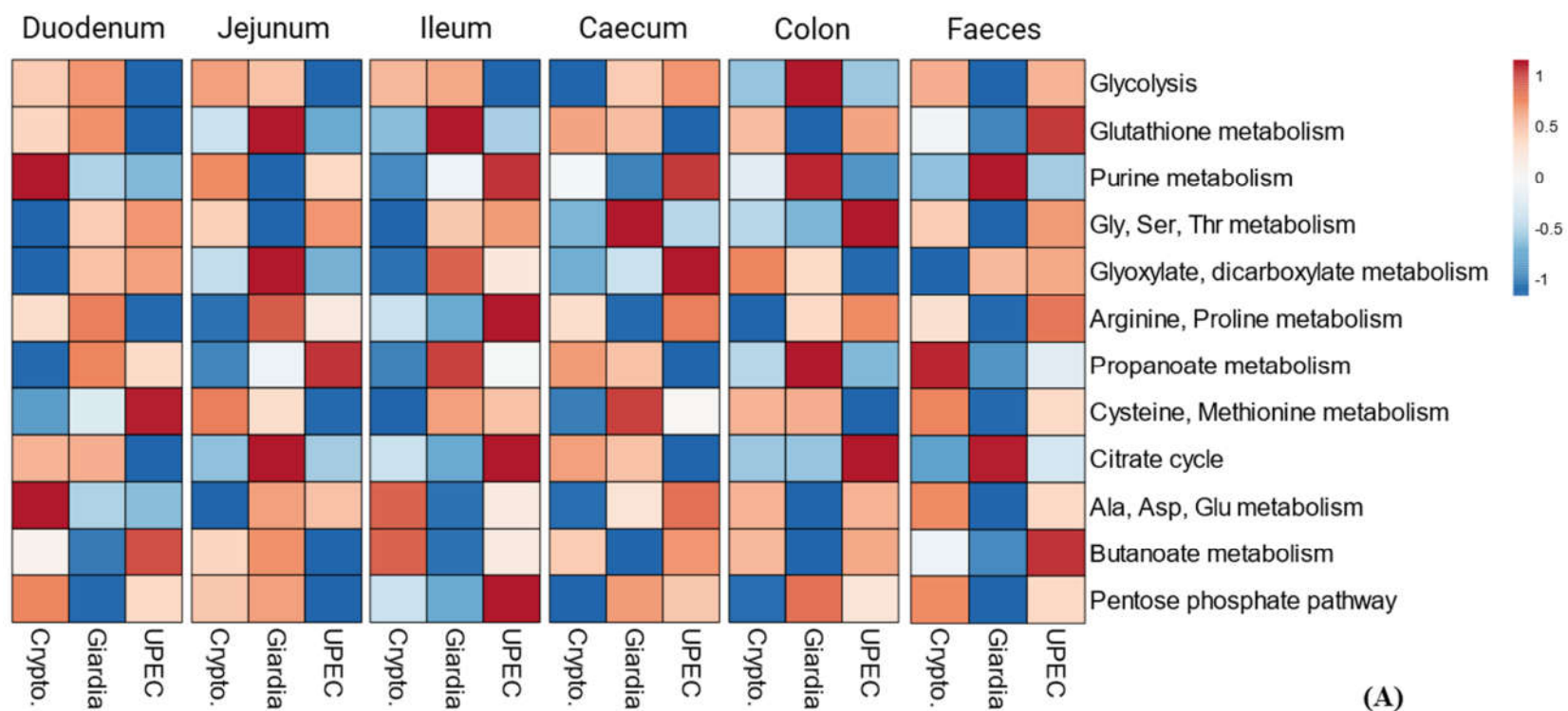
| Pathway | Metabolites↓ | Duodenum | | | Jejunum | | | Ileum | | | Caecum | | | Colon | | |
|---------------------------|-------------------|----------|-------|-------|---------|-------|-------|-------|-------|-------|--------|--------|-------|-------|-------|-------|
| | Infections → | C | G | U | C | G | U | C | G | U | C | G | U | C | G | U |
| Glutathione metabolism | Putrescine | -1.35 | -0.29 | -2.33 | 0.25 | 0.31 | -0.53 | 2.01 | 1.87 | 0.67 | -1.63 | 6.77 | 1.10 | -0.91 | 0.67 | -1.48 |
| | Glycine | 0.25 | -0.34 | 0.11 | 0.74 | 1.45 | 1.53 | 3.21 | 3.10 | 2.06 | 1.06 | -2.61 | 1.87 | -3.22 | -0.58 | -1.26 |
| | Dehydro-ascorbate | -1.13 | -0.07 | -1.10 | 0.44 | -0.04 | -0.49 | -0.14 | -0.14 | 0.33 | 11.11 | 10.41 | 1.06 | 0.16 | 1.20 | -0.45 |
| | Ascorbate | 0.05 | -0.76 | -1.12 | 0.41 | 1.15 | 0.50 | -2.18 | 0.83 | -3.18 | -1.34 | 0.29 | -4.38 | 10.67 | 9.68 | 9.34 |
| | Cysteine | -0.84 | -0.36 | -2.23 | 1.05 | 2.01 | 0.96 | -0.29 | 1.25 | 3.80 | -9.80 | 3.13 | -7.09 | 0.63 | 1.27 | 1.16 |
| | Glutathione | 0.30 | -0.24 | -0.01 | -0.08 | -0.14 | -0.55 | 2.89 | 2.35 | 1.77 | -10.00 | -10.19 | 1.52 | 0.40 | 2.40 | 1.46 |
| | Glutamate | 0.38 | 0.07 | 0.08 | -1.24 | -0.07 | -1.40 | 0.46 | 0.49 | 0.23 | 0.06 | -0.29 | -0.45 | 0.31 | -0.02 | 0.23 |
| Glycolysis | Glucose | -0.05 | -0.35 | -0.56 | 0.29 | 0.34 | -0.68 | -0.89 | -0.52 | -0.78 | 0.16 | -2.70 | -0.21 | 1.05 | 1.33 | 0.002 |
| | Lactate | 0.05 | -0.07 | -0.23 | 0.23 | 0.13 | 0.03 | 0.60 | 0.52 | -0.80 | -12.73 | -3.01 | -1.57 | -0.78 | 1.29 | 0.83 |
| | Glucose-6P | 0.59 | 0.40 | 0.37 | -0.05 | -1.01 | -1.13 | 1.34 | 1.13 | 0.27 | 10.19 | 2.05 | 7.96 | -1.69 | -0.18 | -1.39 |
| | Glyceraldehyde-3P | -0.38 | -0.25 | -0.44 | 0.38 | 0.21 | -0.28 | 0.94 | -0.63 | 0.97 | 10.41 | 1.23 | 1.95 | -0.32 | 1.56 | 0.07 |
| | Pyruvate | -0.76 | -0.50 | -0.62 | -1.34 | -1.39 | -1.59 | 7.19 | 7.44 | 8.77 | 1.30 | 6.29 | 7.99 | -0.37 | -1.63 | -2.26 |
| Pentose phosphate pathway | Glucose | -0.05 | -0.35 | -0.56 | 0.29 | 0.34 | -0.68 | -0.89 | -0.52 | -0.78 | 0.16 | -2.70 | -0.21 | 1.05 | 1.33 | 0.002 |
| | Glucose-6P | 0.59 | 0.40 | 0.37 | -0.05 | -1.01 | -1.13 | 1.34 | 1.13 | 0.27 | 10.19 | 2.05 | 7.96 | -1.69 | -0.18 | -1.39 |
| | Glyceraldehyde-3P | -0.38 | -0.25 | -0.44 | 0.38 | 0.21 | -0.28 | 0.94 | -0.63 | 0.97 | 10.41 | 1.23 | 1.95 | -0.32 | 1.56 | 0.07 |
| | Pyruvate | -0.76 | -0.50 | -0.62 | -1.34 | -1.39 | -1.59 | 7.19 | 7.44 | 8.77 | 1.30 | 6.29 | 7.99 | -0.37 | -1.63 | -2.26 |
| | Gluconolactone | -0.23 | -0.56 | -0.80 | -0.30 | -0.89 | -1.47 | 2.07 | 1.86 | 0.64 | 11.70 | 0.69 | 7.70 | 1.82 | 1.32 | 1.01 |
| | Ribose-5P | 0.70 | 0.20 | -0.27 | 0.78 | 0.36 | 0.57 | 1.04 | 0.45 | 0.15 | -2.33 | -0.48 | -0.27 | -0.68 | 0.48 | -0.80 |
| | Erythrose-4P | 0.16 | -0.14 | -0.39 | 0.28 | 0.27 | -0.63 | 1.61 | 1.15 | -0.30 | 3.20 | -1.85 | 5.75 | 0.08 | 0.75 | 1.00 |
| | Glyceraldehyde | -0.38 | -0.25 | -0.44 | 0.38 | 0.21 | -0.28 | 0.94 | -0.63 | 0.97 | 10.41 | 1.23 | 1.95 | -0.32 | 1.56 | 0.07 |
| | Glycerate | 0.07 | -0.21 | 0.07 | 0.37 | 0.55 | -0.10 | 0.54 | 1.14 | 1.42 | -2.94 | -0.56 | 0.97 | -1.13 | 1.80 | 0.79 |
| | Gluconate | -0.23 | -0.56 | -0.80 | -0.30 | -0.89 | -1.47 | 2.07 | 1.86 | 0.64 | 11.70 | 0.69 | 7.70 | 1.82 | 1.32 | 1.01 |

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|---|--------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|--------|-------|--------|-------|-------|
| Arginine and proline metabolism | Putrescine | -1.35 | -0.29 | -2.33 | 0.25 | 0.31 | -0.53 | 2.01 | 1.87 | 0.67 | -1.63 | 6.77 | 1.10 | -0.91 | 0.67 | -1.48 |
| | 5-aminovalerate | 0.61 | 0.60 | 0.92 | -0.91 | -1.27 | -2.19 | 1.74 | 1.59 | 1.46 | 3.78 | 3.13 | 1.38 | 0.33 | 2.06 | 1.96 |
| | Urea | -0.38 | -0.20 | -0.35 | 0.92 | 0.52 | 0.43 | 1.03 | 0.66 | 0.33 | -0.45 | 0.96 | -9.27 | 0.54 | 1.61 | -1.39 |
| | Creatinine | 0.12 | -0.06 | -0.15 | -0.20 | -0.06 | -0.30 | 0.54 | -0.32 | 0.84 | -12.90 | -4.52 | 7.85 | -0.13 | -0.53 | -0.19 |
| | 5-Amino-pentanoate | -1.46 | -0.31 | -2.99 | 0.65 | 0.41 | -0.54 | 0.40 | 0.74 | -6.82 | 10.72 | -3.99 | -9.91 | -1.27 | -0.66 | -1.59 |
| | Pyruvate | -0.76 | -0.50 | -0.62 | -1.34 | -1.39 | -1.59 | 7.19 | 7.44 | 8.77 | 1.30 | 6.29 | 7.99 | -0.37 | -1.63 | -2.26 |
| | Proline | 0.20 | 0.58 | 1.11 | -0.69 | -1.09 | -0.52 | 0.64 | 2.07 | 1.43 | 11.04 | 10.63 | 8.04 | 1.19 | 1.71 | 0.84 |
| | Glutamate | 0.38 | 0.07 | 0.08 | -1.24 | -0.07 | -1.40 | 0.46 | 0.49 | 0.23 | 0.06 | -0.29 | -0.45 | 0.31 | -0.02 | 0.23 |
| Cysteine and methionine metabolism | Aspartate | 1.44 | 0.33 | 1.35 | 0.95 | 0.46 | -0.12 | 2.15 | 2.01 | 0.59 | 5.93 | -5.59 | 5.17 | -0.95 | -0.16 | -1.49 |
| | Alanine | 0.65 | -0.20 | -0.63 | 0.51 | 0.09 | -1.11 | -5.89 | -2.71 | 0.30 | 0.49 | 5.25 | 4.69 | 0.69 | 0.93 | -0.24 |
| | Serine | 0.35 | -0.02 | 0.41 | -0.27 | 0.02 | -0.40 | -4.38 | -8.76 | -0.42 | -11.82 | 2.80 | -6.96 | -11.37 | 0.57 | -0.80 |
| | Methionine | 0.48 | -0.18 | 0.92 | 0.22 | 0.22 | 0.01 | 0.58 | 0.85 | -0.60 | -0.39 | 10.34 | 1.27 | -0.66 | 1.29 | 0.50 |
| | Cysteine | -0.84 | -0.36 | -2.23 | 1.05 | 2.01 | 0.96 | -0.29 | 1.25 | 3.80 | -9.80 | 3.13 | -7.09 | 0.63 | 1.27 | 1.16 |
| | Glutathione | 0.30 | -0.24 | -0.01 | -0.08 | -0.14 | -0.55 | 2.89 | 2.35 | 1.77 | -10.00 | -10.19 | 1.52 | 0.40 | 2.40 | 1.46 |
| | Pyruvate | -0.76 | -0.50 | -0.62 | -1.34 | -1.39 | -1.59 | 7.19 | 7.44 | 8.77 | 1.30 | 6.29 | 7.99 | -0.37 | -1.63 | -2.26 |
| Citrate Cycle | Succinate | 0.19 | -0.35 | -0.31 | 0.48 | -1.35 | -0.67 | 0.91 | 1.74 | 1.42 | 10.93 | 0.66 | 1.05 | 0.37 | 2.09 | 1.80 |
| | Fumarate | 0.22 | 0.00 | -0.34 | 0.18 | 0.00 | -0.50 | 0.10 | -0.96 | -0.22 | -2.71 | -0.71 | 1.52 | -0.97 | 1.43 | 0.13 |
| | cis-Aconitate | 0.16 | 0.82 | 0.51 | -0.25 | -0.24 | -1.12 | 4.51 | 3.73 | 2.05 | 1.02 | 1.67 | -0.99 | 1.09 | 2.97 | 2.37 |
| | Citrate | -0.17 | -0.20 | -0.87 | -0.38 | 0.80 | 0.11 | 2.33 | 1.94 | 2.41 | -2.82 | -2.51 | -0.08 | 9.42 | 10.32 | 9.62 |
| | Pyruvate | -0.76 | -0.50 | -0.62 | -1.34 | -1.39 | -1.59 | 7.19 | 7.44 | 8.77 | 1.30 | 6.29 | 7.99 | -0.37 | -1.63 | -2.26 |
| | Oxoglutarate | 0.19 | 0.47 | -1.00 | 0.34 | 0.14 | -0.01 | 0.30 | 0.27 | 0.38 | -7.93 | 0.11 | 2.07 | -0.82 | 0.36 | -0.28 |
| Alanine, aspartate and glutamate metabolism | Aspartate | 1.44 | 0.33 | 1.35 | 0.95 | 0.46 | -0.12 | 2.15 | 2.01 | 0.59 | 5.93 | -5.59 | 5.17 | -0.95 | -0.16 | -1.49 |
| | Alanine | 0.65 | -0.20 | -0.63 | 0.51 | 0.09 | -1.11 | -5.89 | -2.71 | 0.30 | 0.49 | 5.25 | 4.69 | 0.69 | 0.93 | -0.24 |
| | Succinate | 0.19 | -0.35 | -0.31 | 0.48 | -1.35 | -0.67 | 0.91 | 1.74 | 1.42 | 10.93 | 0.66 | 1.05 | 0.37 | 2.09 | 1.80 |
| | Fumarate | 0.22 | 0.00 | -0.34 | 0.18 | 0.00 | -0.50 | 0.10 | -0.96 | -0.22 | -2.71 | -0.71 | 1.52 | -0.97 | 1.43 | 0.13 |
| | Glutamine | -0.32 | -1.47 | -0.28 | -1.14 | -0.67 | -1.44 | 0.90 | 2.02 | 0.43 | -0.50 | -0.68 | 8.56 | 6.34 | 6.95 | 7.55 |
| | Asparagine | -0.18 | -0.32 | -1.40 | -0.20 | 0.36 | 0.24 | 0.92 | 0.89 | 0.34 | -2.92 | -0.11 | 3.37 | 0.20 | 1.73 | 0.98 |
| | Citrate | -0.17 | -0.20 | -0.87 | -0.38 | 0.80 | 0.11 | 2.33 | 1.94 | 2.41 | -2.82 | -2.51 | -0.08 | 9.42 | 10.32 | 9.62 |
| | Pyruvate | -0.76 | -0.50 | -0.62 | -1.34 | -1.39 | -1.59 | 7.19 | 7.44 | 8.77 | 1.30 | 6.29 | 7.99 | -0.37 | -1.63 | -2.26 |

| | | | | | | | | | | | | | | | | |
|--|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|-------|-------|
| Propanoate and Butanoate metabolism | Oxoglutarate | 0.19 | 0.47 | -1.00 | 0.34 | 0.14 | -0.01 | 0.30 | 0.27 | 0.38 | -7.93 | 0.11 | 2.07 | -0.82 | 0.36 | -0.28 |
| | Glutamate | 0.38 | 0.07 | 0.08 | -1.24 | -0.07 | -1.40 | 0.46 | 0.49 | 0.23 | 0.06 | -0.29 | -0.45 | 0.31 | -0.02 | 0.23 |
| | Succinate | 0.19 | -0.35 | -0.31 | 0.48 | -1.35 | -0.67 | 0.91 | 1.74 | 1.42 | 10.93 | 0.66 | 1.05 | 0.37 | 2.09 | 1.80 |
| | Lactate | 0.05 | -0.07 | -0.23 | 0.23 | 0.13 | 0.03 | 0.60 | 0.52 | -0.80 | -12.73 | -3.01 | -1.57 | -0.78 | 1.29 | 0.83 |
| | Methylmalonate | 0.62 | 0.71 | 0.27 | -0.54 | -0.28 | -0.42 | 1.50 | 1.45 | 0.49 | -1.50 | 9.57 | -6.84 | -2.05 | 1.65 | -0.01 |
| | 2-hydroxy- butyrate | -1.25 | 0.78 | -0.26 | -1.80 | -0.16 | -0.31 | -0.42 | 0.06 | -1.58 | -0.68 | -1.23 | 1.24 | 1.46 | 1.54 | 0.45 |
| | Fumarate | 0.22 | 0.00 | -0.34 | 0.18 | 0.00 | -0.50 | 0.10 | -0.96 | -0.22 | -2.71 | -0.71 | 1.52 | -0.97 | 1.43 | 0.13 |
| | Pyruvate | -0.76 | -0.50 | -0.62 | -1.34 | -1.39 | -1.59 | 7.19 | 7.44 | 8.77 | 1.30 | 6.29 | 7.99 | -0.37 | -1.63 | -2.26 |
| | Oxoglutarate | 0.19 | 0.47 | -1.00 | 0.34 | 0.14 | -0.01 | 0.30 | 0.27 | 0.38 | -7.93 | 0.11 | 2.07 | -0.82 | 0.36 | -0.28 |
| | Glutamate | 0.38 | 0.07 | 0.08 | -1.24 | -0.07 | -1.40 | 0.46 | 0.49 | 0.23 | 0.06 | -0.29 | -0.45 | 0.31 | -0.02 | 0.23 |
| | D-malate | 0.32 | 0.12 | -0.26 | 0.37 | 0.39 | -0.50 | 1.34 | 1.24 | 0.21 | -6.09 | -6.86 | 0.00 | -0.21 | -1.27 | -0.85 |
| | Maleate | 0.32 | 0.12 | -0.26 | 0.29 | 0.39 | -0.57 | 1.47 | 1.15 | 0.08 | 1.71 | 1.58 | 0.87 | -1.10 | 0.01 | 0.43 |

Table S3. Differential expression of major metabolic pathways in the mouse extra-gut organs during cryptosporidiosis, giardiasis and UPEC infection in infected mice with respect to the uninfected mice. The values are represented as the normalised Log₂Fold changes, subjected to pareto scaling (n = 5).

| Pathway | Serum | | | Liver | | |
|---------------------------------------|---------|---------|-------|---------|---------|-------|
| | Crypto. | Giardia | UPEC | Crypto. | Giardia | UPEC |
| Glycolysis | -0.51 | 1.27 | -0.76 | 0.85 | 1.08 | -1.92 |
| Glutathione metabolism | -0.32 | 3.68 | -3.36 | 0.26 | -2.68 | 2.42 |
| Purine metabolism | 0.81 | -1.24 | 0.42 | 1.22 | 1.37 | -2.59 |
| Gly, Ser, Thr metabolism | 0.91 | -2.21 | 1.30 | 1.27 | -0.39 | -0.89 |
| Glyoxylate, dicarboxylate metabolism | 0.41 | -1.35 | 0.95 | 1.34 | 0.12 | -1.46 |
| Arginine, proline metabolism | -1.89 | 2.33 | -1.14 | 0.82 | 0.55 | -1.37 |
| Propanoate metabolism | 0.49 | 1.01 | -1.50 | 1.03 | -1.85 | 0.81 |
| Cysteine, methionine metabolism | 0.79 | 1.05 | 1.85 | 1.93 | -1.73 | -0.21 |
| Citrate cycle | -0.94 | 1.18 | -0.24 | -0.21 | 0.86 | -0.65 |
| Ala, Asp, Glu metabolism | -1.21 | 0.20 | 1.00 | 1.22 | -0.44 | -0.78 |
| Butanoate metabolism | 0.29 | -0.52 | 0.24 | 0.15 | -0.60 | 0.45 |
| Pentose phosphate pathway | -0.34 | 0.73 | -0.39 | 0.66 | -0.90 | 0.24 |
| Phenylalanine metabolism | 0.89 | -2.39 | 1.51 | -0.46 | 0.05 | 0.41 |
| Val, Leucine, Isoleucine biosynthesis | 0.42 | 1.22 | -1.64 | -0.07 | 1.09 | -1.02 |
| Pyruvate metabolism | 0.46 | -0.94 | 0.48 | 0.71 | 1.27 | -1.97 |



(A)

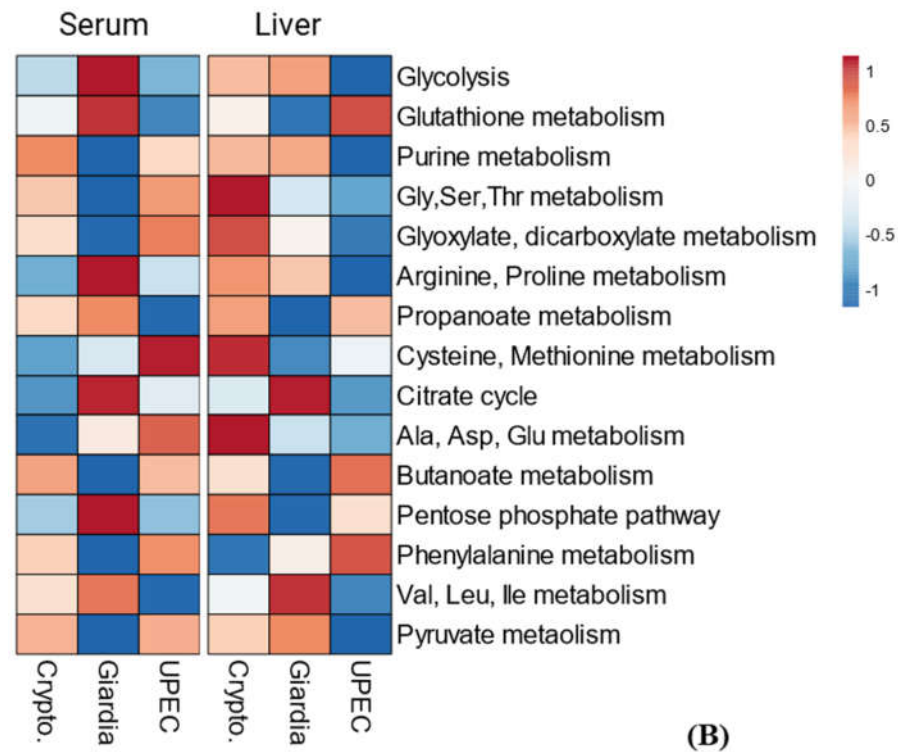


Figure S9. The heatmap represents relative upregulation (red) and downregulation (blue) of major metabolic pathways in (A) Intestine and faeces and, (B) Serum and liver, during cryptosporidiosis, giardiasis and UPEC infections in the infected mice with respect to the uninfected mice. The individual boxes indicate the relative impact as determined by the integrated proteomics-metabolomics analysis. The heatmaps were designed using Clustvis web tool.

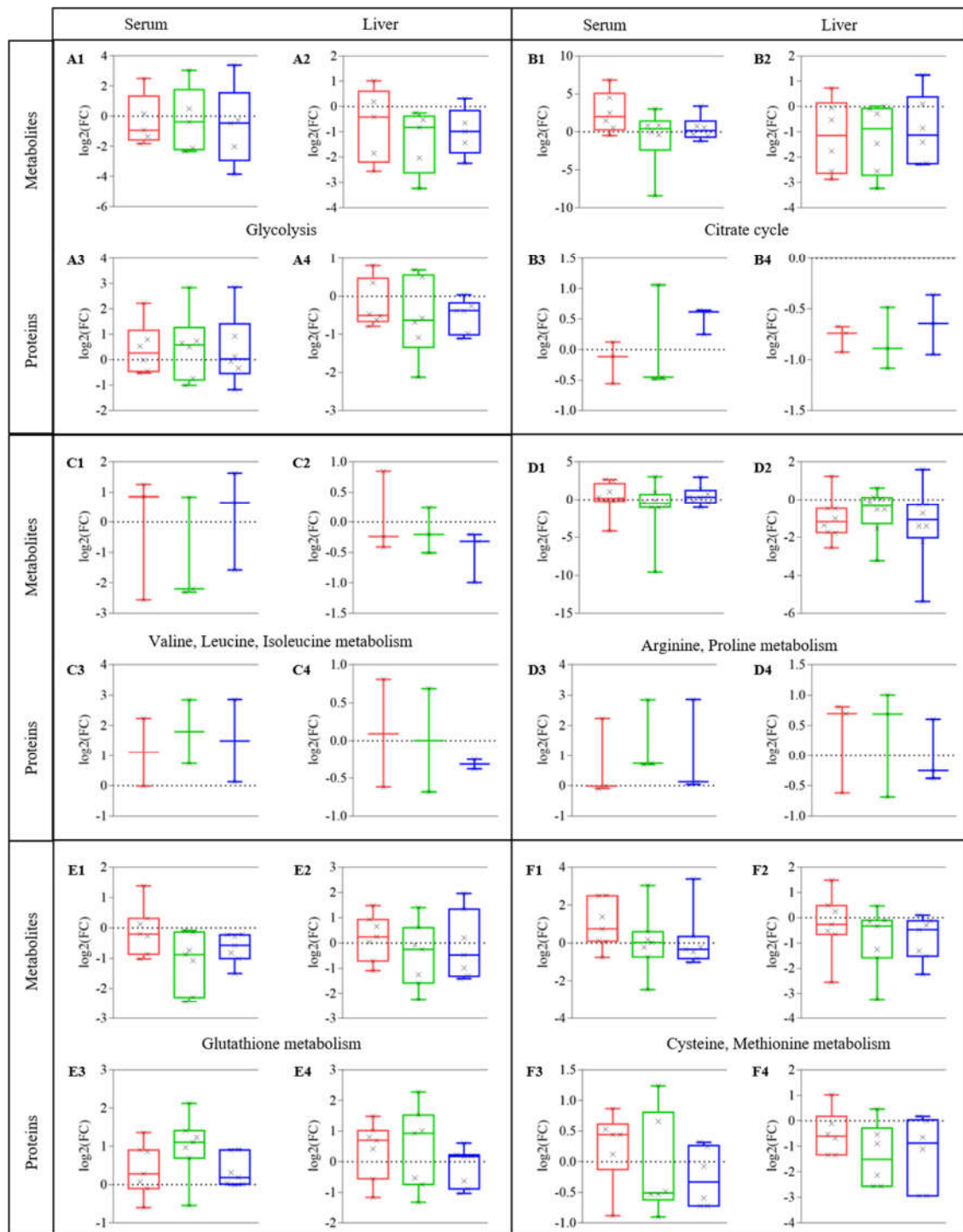


Figure S10. The comparative metabolite and protein expressions driving the key metabolic pathways in serum and liver during cryptosporidiosis (red), giardiasis (green) and UPEC (blue). The individual metabolites and proteins contributing to these expressions are presented in Table S4 and S5.

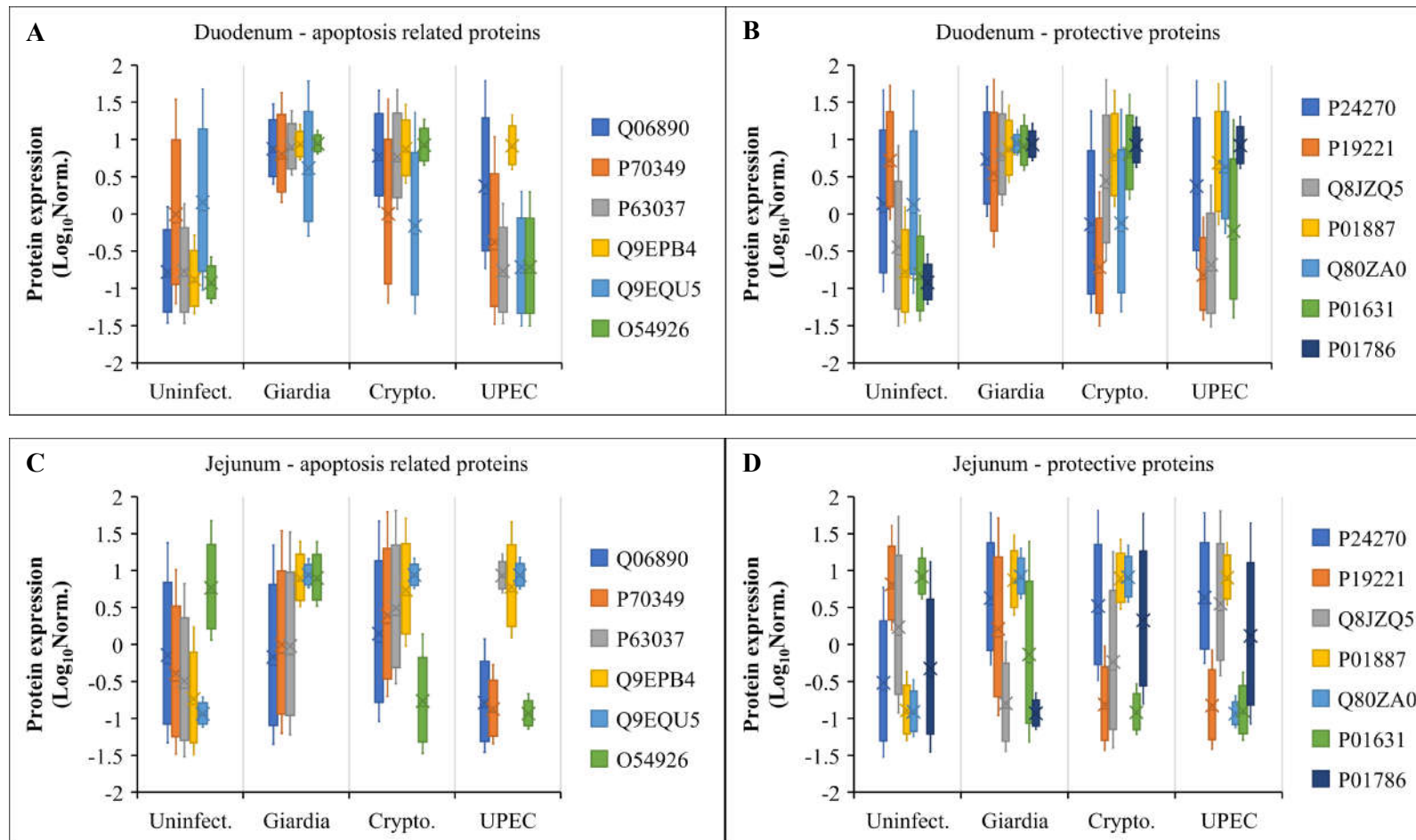
Table S4. Major metabolites contributing to the most significant metabolic pathways in serum and liver during various infections with respect to the uninfected mice.

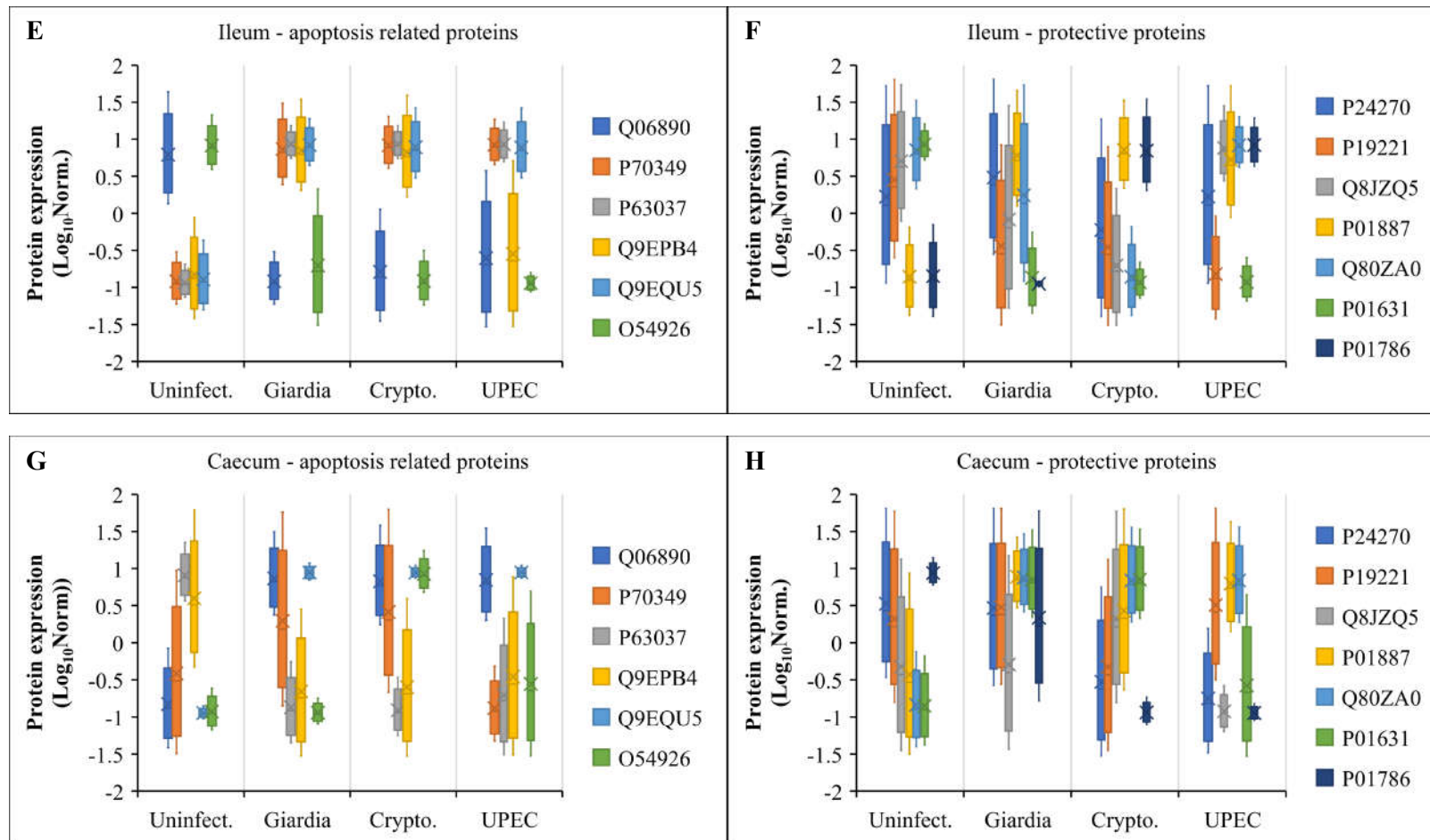
| Pathway | Metabolites | Serum (Log ₂ Fold change) | | | Liver (Log ₂ Fold change) | | |
|--|-------------------------------------|---|---------|-------|---|---------|-------|
| | | Crypto | Giardia | UPEC | Crypto | Giardia | UPEC |
| Glycolysis | Glucose | -0.93 | -0.39 | -0.47 | 1.02 | -0.26 | -1.42 |
| | Lactate | -1.35 | 0.49 | -0.27 | 0.19 | -0.52 | 0.33 |
| | Glucose-6P | -1.82 | -2.12 | -2.02 | -1.84 | -2.02 | -0.98 |
| | Glyceraldehyde-3P | 0.16 | -2.34 | -3.84 | -0.41 | -0.83 | -0.65 |
| | Pyruvate | 2.49 | 3.04 | 3.37 | -2.55 | -3.23 | -2.24 |
| Citrate cycle | Succinate | 4.51 | 0.88 | 0.57 | -0.04 | -0.28 | -0.85 |
| | Fumarate | 6.83 | 0.00 | -1.23 | 0.72 | 0.02 | 1.25 |
| | Cis-acotinate | 0.52 | -8.41 | -0.29 | -1.76 | -2.55 | -2.28 |
| | Citrate | 1.48 | 0.83 | 0.76 | -2.87 | -1.46 | -1.40 |
| | Pyruvate | 2.49 | 3.04 | 3.37 | -2.55 | -3.23 | -2.24 |
| | Oxoglutarate | -0.46 | -0.36 | -0.53 | -0.53 | -0.10 | 0.10 |
| Valine, leucine, isoleucine metabolism | Valine | -2.56 | -2.30 | 1.62 | 0.84 | 0.24 | -0.21 |
| | Methylmalonate | 0.85 | 0.83 | 0.64 | -0.24 | -0.51 | -0.99 |
| | Isoleucine | 1.25 | -2.20 | -1.58 | -0.41 | -0.20 | -0.32 |
| Arginine and proline metabolism | Putrescine | 0.31 | -1.08 | 0.28 | -1.01 | 0.61 | -1.41 |
| | 2-oxo-4-hydroxy-5- aminovalerate | -4.17 | -9.55 | -0.18 | -0.49 | -1.54 | -1.41 |
| | Urea | -0.19 | -1.06 | -1.08 | -1.36 | -0.52 | -0.72 |
| | Creatinine | 0.09 | -0.10 | 0.36 | 1.24 | 0.14 | 1.60 |
| | 5-aminopentanoate | -0.14 | -0.64 | -0.46 | -1.73 | -0.52 | -0.29 |
| | Pyruvate | 2.49 | 3.04 | 3.37 | -2.55 | -3.23 | -2.24 |
| | Proline | 2.68 | 0.95 | 0.76 | -1.77 | 0.03 | -5.38 |
| | Glutamate | 1.08 | -0.38 | 1.40 | -0.49 | -0.17 | -0.26 |
| Glutathione metabolism | Putrescine | 0.31 | -1.08 | -0.28 | -1.10 | 0.61 | -1.41 |
| | Glycine | -0.26 | -2.29 | -1.51 | 0.93 | -2.24 | 0.21 |
| | Dehydroascorbate | -1.02 | -0.09 | -0.22 | 0.04 | -0.08 | -0.99 |
| | Ascorbate | -0.86 | -0.88 | -0.58 | 0.66 | 1.41 | 1.96 |
| | Cysteine | 1.38 | -2.45 | -1.02 | 1.48 | -1.59 | -1.31 |
| | Glutathione | 0.13 | -0.74 | -0.82 | 0.25 | -1.26 | -0.48 |
| | Glutamate | 1.08 | -0.38 | 1.40 | -0.49 | -0.17 | -0.26 |
| Cysteine, Methionine metabolism | Aspartate | 2.51 | 0.60 | -0.46 | -0.52 | -0.10 | 0.10 |
| | Alanine | 0.09 | 0.18 | 0.35 | -0.26 | -0.16 | -0.12 |
| | Serine | -0.76 | 0.02 | -0.22 | 0.49 | 0.47 | -0.30 |
| | Methionine | 0.74 | -0.22 | -0.33 | -0.66 | -0.33 | -1.52 |
| | Cysteine | 1.38 | -2.45 | -1.02 | 1.48 | -1.59 | -1.31 |
| | Glutathione | 0.13 | -0.74 | -0.82 | 0.25 | -1.26 | -0.48 |
| | Pyruvate | 2.49 | 3.04 | 3.37 | -2.55 | -3.23 | -2.24 |

Table S5. Major protein expressions driving the metabolic pathways in serum and liver during various infections with respect to the uninfected mice.

| Pathway | Serum (Log ₂ Fold change) | | | | Liver (Log ₂ Fold change) | | | |
|--|--------------------------------------|---------|----------|-------|--------------------------------------|--------|----------|-------|
| | Protein (Uniprot ID) | Crypt o | Giardi a | UPEC | Protein (Uniprot ID) | Crypto | Giardi a | UPEC |
| Glycolysis | O70250 | 1.65 | 0.99 | 2.30 | P05064 | 0.35 | 0.51 | 0.04 |
| | P15327 | 0.76 | 0.76 | 1.38 | P47740 | 0.81 | 0.69 | -0.25 |
| | P05064 | -0.45 | -0.74 | -0.33 | Q9D0F9 | -0.41 | -0.96 | -1.03 |
| | P47740 | -0.01 | 0.74 | 0.12 | Q9DBJ1 | -0.47 | -0.57 | -0.38 |
| | Q9DBJ1 | 0.79 | 0.50 | 0.93 | P16125 | -0.52 | -2.13 | -1.11 |
| | P16125 | 0.53 | 0.66 | -0.07 | Q9DBF1 | -0.51 | -0.45 | -0.63 |
| | O08749 | -0.92 | -0.53 | -0.78 | P00329 | -0.72 | -0.55 | -0.94 |
| | P16858 | -0.64 | -0.65 | -0.74 | P17182 | -0.29 | -0.61 | -0.43 |
| | P09041 | 0.02 | -0.60 | 0.04 | P28474 | -0.79 | -1.08 | -0.98 |
| | Q9JII6 | -0.65 | 0.60 | 0.72 | | | | |
| | P28474 | -0.52 | -1.01 | -1.18 | | | | |
| | P06745 | -0.17 | 0.63 | -0.27 | | | | |
| | Q9JLJ2 | 2.23 | 2.85 | 2.86 | | | | |
| Citrate cycle | P14152 | 0.12 | -0.49 | 0.25 | P54071 | -0.77 | -0.88 | -0.93 |
| | Q60597 | 0.06 | -0.94 | -0.08 | P08249 | -0.41 | -0.58 | -0.25 |
| | Q9WUM5 | -0.11 | -0.45 | 0.62 | P14152 | -0.68 | -0.89 | -0.64 |
| | O08749 | -0.92 | -0.53 | -0.79 | Q9D6R2 | 0.62 | 1.25 | 0.29 |
| | Q8K2B3 | -0.52 | 0.59 | 0.19 | P28271 | 0.04 | -0.54 | -0.86 |
| | Q91V92 | -0.56 | 1.06 | 0.65 | Q9WUM5 | -0.74 | -1.09 | -0.36 |
| | O88844 | 0.04 | 0.57 | 0.08 | P97807 | -0.11 | -0.59 | -0.32 |
| | | | | | Q91V92 | -0.93 | -0.48 | -0.95 |
| Valine, Leucine, Isoleucine metabolism | | | | | Q9Z2I9 | -0.85 | -0.85 | -0.86 |
| | Q9JHI5 | -0.21 | 0.58 | -0.48 | Q91ZA3 | -0.26 | -0.76 | -0.35 |
| | P47740 | -0.01 | 0.74 | 0.12 | G3X982 | -1.24 | -1.22 | -1.05 |
| | P50136 | -2.52 | -1.77 | -1.31 | P47740 | 0.81 | 0.69 | -0.25 |
| | O08749 | -0.92 | -0.53 | -0.79 | P38060 | -0.22 | -0.68 | -0.01 |
| | Q8QZS1 | -0.97 | -0.47 | -2.46 | Q9DBF1 | -0.51 | -0.45 | -0.63 |
| | Q99MR8 | 1.71 | 1.72 | 0.87 | O08756 | 0.21 | 0.75 | -0.18 |
| | Q8QZT1 | 0.11 | -0.67 | 0.07 | Q8BMS1 | -0.60 | -0.75 | -0.76 |
| | Q8VCH0 | -0.28 | -0.58 | 0.59 | P61922 | -0.53 | -0.64 | -0.55 |
| | Q9JLJ2 | 2.23 | 2.85 | 2.86 | Q8BH95 | -0.37 | -0.52 | -0.13 |
| | | | | | P47738 | -0.38 | -0.59 | -0.67 |
| | | | | | Q61425 | -0.41 | -0.46 | -0.30 |
| | | | | | Q9JLJ2 | -0.62 | -0.68 | -0.38 |
| | | | | | Q921H8 | -0.83 | -0.75 | -0.52 |
| Arginine, proline metabolism | P47740 | -0.01 | 0.74 | 0.12 | P47740 | 0.81 | 0.69 | -0.25 |
| | A2AS89 | -0.16 | 2.57 | 0.22 | Q61176 | 1.37 | 1.76 | 1.07 |
| | O08691 | 0.89 | 1.05 | -0.26 | Q9Z110 | -1.13 | -0.46 | -0.69 |

| | | | | | | | | |
|---------------------------------|--------|-------|-------|-------|--------|-------|-------|-------|
| Glutathione metabolism | Q9D1A2 | 0.08 | -0.56 | 1.18 | Q9DBF1 | -0.51 | -0.45 | -0.63 |
| | P30275 | 0.16 | 1.57 | 0.32 | Q9DCU9 | 0.54 | 0.44 | -0.97 |
| | Q9CPY7 | -0.10 | 0.70 | 0.04 | P29758 | -0.32 | -0.63 | -0.39 |
| | P05201 | 0.28 | 1.62 | 0.99 | P07310 | 0.39 | 0.90 | 1.47 |
| | Q9JLJ2 | 2.23 | 2.85 | 2.86 | Q9CPY7 | 0.69 | 1.00 | 0.60 |
| | | | | | P05202 | -0.91 | -0.75 | -0.87 |
| | | | | | P47738 | -0.38 | -0.59 | -0.67 |
| | | | | | Q9JLJ2 | -0.62 | -0.68 | -0.38 |
| | Q64471 | 0.07 | 1.11 | 0.19 | P47791 | 0.42 | 0.93 | 0.18 |
| | O70325 | -0.73 | -0.83 | -0.08 | P54071 | -0.77 | -0.88 | -0.93 |
| | Q9CPY7 | 1.36 | 2.13 | 0.92 | P10649 | -0.60 | -0.91 | -0.91 |
| | P21765 | 0.28 | 1.41 | -0.01 | Q8R5I6 | -1.17 | -1.33 | -0.89 |
| | P97494 | -0.59 | -0.55 | 0.02 | P19639 | -1.46 | -2.21 | -0.76 |
| | P97449 | 0.21 | 0.78 | -0.76 | O35660 | -0.35 | -1.77 | 0.27 |
| | O88844 | -0.10 | 0.70 | 0.04 | Q9DCD0 | -0.14 | 0.71 | 0.32 |
| Cysteine, Methionine metabolism | P30115 | 0.91 | 0.97 | 0.90 | P46412 | 0.64 | 1.37 | 0.37 |
| | P51855 | 0.87 | 1.24 | 0.32 | P11352 | 0.80 | 1.52 | -1.04 |
| | P13745 | 1.04 | 0.71 | 0.84 | Q64471 | -0.56 | -0.75 | -0.63 |
| | Q64471 | 0.04 | 0.57 | 0.08 | Q91VS7 | 0.17 | -1.31 | -0.36 |
| | O70325 | 0.15 | 1.79 | -0.16 | Q9DCM2 | -0.77 | -0.54 | -1.23 |
| | Q9CPY7 | 1.72 | 1.40 | 0.14 | Q80W21 | -0.35 | -1.77 | 0.27 |
| | P21765 | 0.95 | 4.26 | -1.67 | P15626 | -0.29 | -0.65 | -0.88 |
| | | | | | Q9CPY7 | 0.69 | 1.00 | 0.60 |
| | | | | | Q8K010 | 0.74 | 0.73 | -0.07 |
| | | | | | P21765 | 1.48 | 2.28 | 0.23 |
| | | | | | P97494 | 1.02 | -0.53 | 0.17 |
| | | | | | Q60928 | 1.25 | 1.12 | 0.71 |
| | P47791 | 0.44 | -0.53 | -0.72 | Q91WT9 | -0.79 | -0.70 | -0.92 |
| | Q9CQU0 | -0.17 | -0.47 | -0.03 | P06151 | -0.35 | -0.69 | -0.91 |
| | Q8R5I6 | 0.53 | 0.66 | -0.07 | Q8VBT2 | -0.50 | -1.14 | -0.73 |
| | P11352 | 0.12 | -0.49 | 0.25 | P16125 | -0.52 | -2.13 | -1.11 |
| | Q80SW1 | 1.29 | 1.50 | -0.14 | P08249 | -0.41 | -0.58 | -0.25 |
| | Q91X83 | 0.44 | -0.65 | 0.92 | P14152 | -0.68 | -0.89 | -0.64 |
| | P16125 | 0.44 | -0.53 | -0.72 | Q80SW1 | -1.34 | -2.56 | -2.94 |
| | P14152 | 0.28 | 1.62 | 0.99 | Q68FL4 | -1.34 | -2.56 | -2.94 |
| | P52196 | -0.88 | -0.90 | -0.59 | P05202 | -0.91 | -0.75 | -0.87 |
| | Q3THS6 | 0.87 | 1.24 | 0.32 | Q99J99 | -0.10 | 0.46 | 0.00 |
| | Q68FL4 | 1.72 | 1.40 | 0.14 | P97494 | 1.02 | -0.53 | 0.17 |
| | | | | | P50247 | -0.60 | -0.88 | -0.68 |
| | | | | | Q8VCN5 | -0.67 | -0.68 | -0.42 |





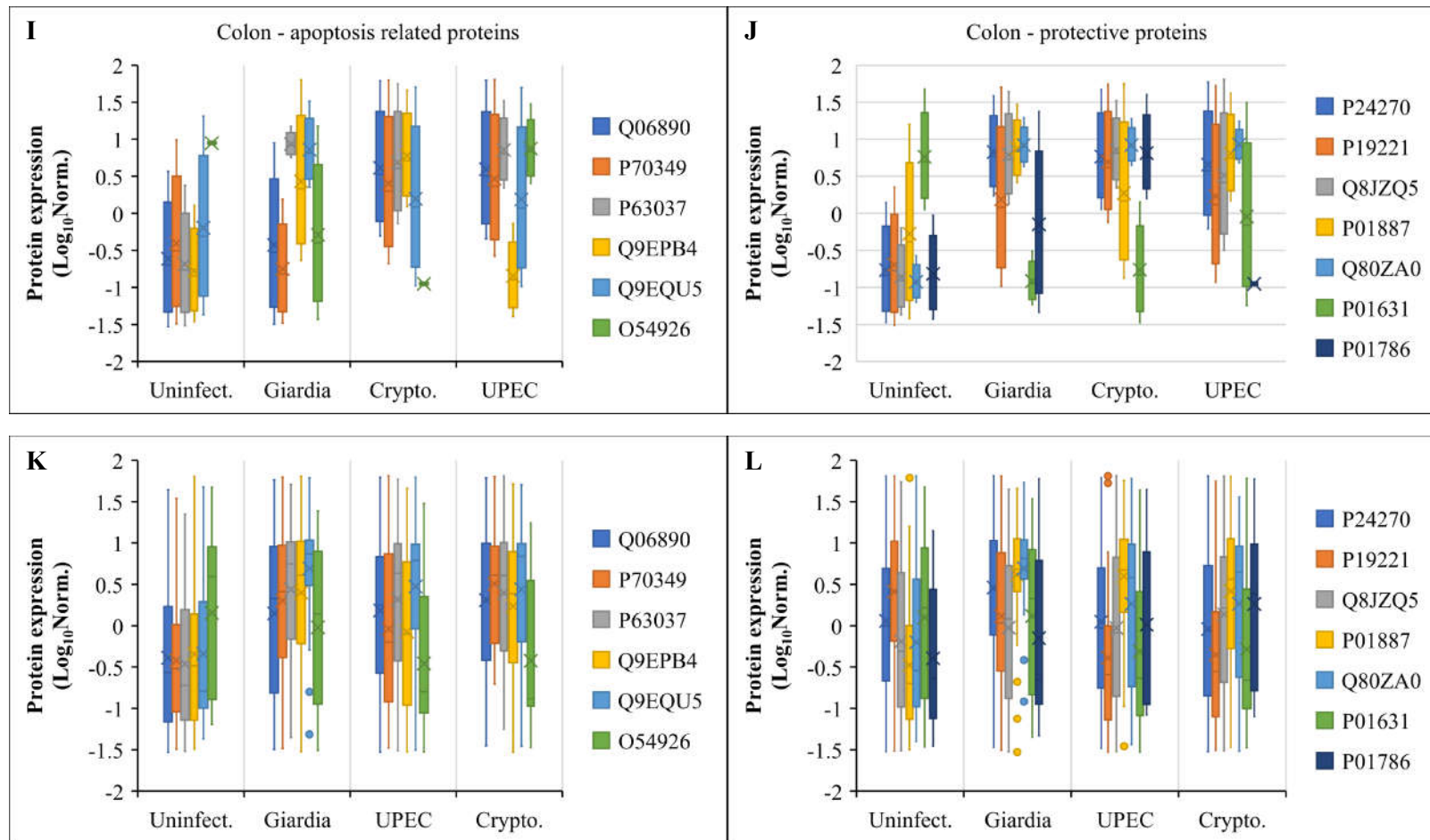
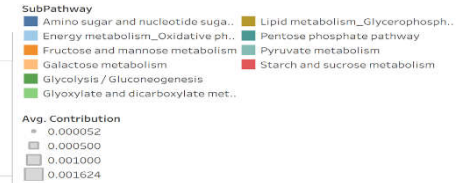


Figure S11. Log_{10} normalised expression of proteins involved in apoptosis process and cellular protection during various infections in the mouse gut sections of (A and B) Duodenum, (C and D) Jejunum, (E and F) Ileum, (G and H) Caecum and (I and J) Colon. Furthermore, an overall inter-species comparison is shown in (K) and (L).

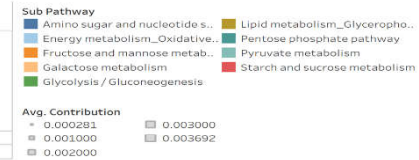
Duodenum

| Family | Category | Super Pathway | SubPathway | Uninfect | Crypto | Sample | Giardia | UPEC |
|-----------------|------------|-------------------------|---|----------|--------|--------|---------|------|
| F__Atopobiaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | ■ | ■ | | ■ | ■ |
| | | | Fructose and mannose metabolism | ■ | ■ | | ■ | ■ |
| | | | Galactose metabolism | ■ | ■ | | ■ | ■ |
| | | | Glycolysis / Gluconeogenesis | ■ | ■ | | ■ | ■ |
| | | | Glyoxylate and dicarboxylate metabolism | ■ | ■ | | ■ | ■ |
| | | | Pentose phosphate pathway | ■ | ■ | | ■ | ■ |
| | | | Pyruvate metabolism | ■ | ■ | | ■ | ■ |
| | | | Starch and sucrose metabolism | ■ | ■ | | ■ | ■ |
| | | | Energy metabolism | ■ | ■ | | ■ | ■ |
| | | | Lipid metabolism | ■ | ■ | | ■ | ■ |



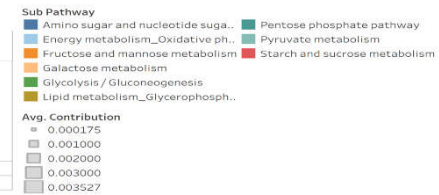
Jejunum

| Family | Category | Super Pathway | Sub Pathway | Uninfect | Crypto | Sample | Giardia | UPEC |
|-----------------|------------|-------------------------|---|----------|--------|--------|---------|------|
| F__Atopobiaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | ■ | ■ | | ■ | ■ |
| | | | Fructose and mannose metabolism | ■ | ■ | | ■ | ■ |
| | | | Galactose metabolism | ■ | ■ | | ■ | ■ |
| | | | Glycolysis / Gluconeogenesis | ■ | ■ | | ■ | ■ |
| | | | Pentose phosphate pathway | ■ | ■ | | ■ | ■ |
| | | | Pyruvate metabolism | ■ | ■ | | ■ | ■ |
| | | | Starch and sucrose metabolism | ■ | ■ | | ■ | ■ |
| | | | Energy metabolism | ■ | ■ | | ■ | ■ |
| | | | Lipid metabolism | ■ | ■ | | ■ | ■ |
| | | | Glycerophospholipid metabolism | ■ | ■ | | ■ | ■ |



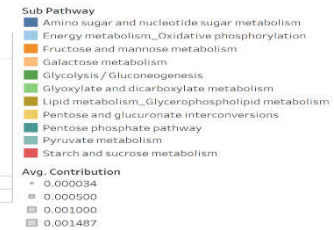
Ileum

| Family | Category | Super Pathway | Sub Pathway | Uninfect | Crypto | Sample | Giardia | UPEC |
|-----------------|------------|-------------------------|---|----------|--------|--------|---------|------|
| F__Atopobiaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | ■ | ■ | | ■ | ■ |
| | | | Fructose and mannose metabolism | ■ | ■ | | ■ | ■ |
| | | | Galactose metabolism | ■ | ■ | | ■ | ■ |
| | | | Glycolysis / Gluconeogenesis | ■ | ■ | | ■ | ■ |
| | | | Pentose phosphate pathway | ■ | ■ | | ■ | ■ |
| | | | Pyruvate metabolism | ■ | ■ | | ■ | ■ |
| | | | Starch and sucrose metabolism | ■ | ■ | | ■ | ■ |
| | | | Energy metabolism | ■ | ■ | | ■ | ■ |
| | | | Lipid metabolism | ■ | ■ | | ■ | ■ |
| | | | Glycerophospholipid metabolism | ■ | ■ | | ■ | ■ |



Cecum

| Family | Category | Super Pathway | Sub Pathway | Uninfect | Crypto | Sample | Giardia | UPEC |
|-----------------|------------|-------------------------|---|----------|--------|--------|---------|------|
| F__Atopobiaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | ■ | ■ | | ■ | ■ |
| | | | Fructose and mannose metabolism | ■ | ■ | | ■ | ■ |
| | | | Galactose metabolism | ■ | ■ | | ■ | ■ |
| | | | Glycolysis / Gluconeogenesis | ■ | ■ | | ■ | ■ |
| | | | Glyoxylate and dicarboxylate metabolism | ■ | ■ | | ■ | ■ |
| | | | Pentose and glucuronate interconversions | ■ | ■ | | ■ | ■ |
| | | | Pentose phosphate pathway | ■ | ■ | | ■ | ■ |
| | | | Pyruvate metabolism | ■ | ■ | | ■ | ■ |
| | | | Starch and sucrose metabolism | ■ | ■ | | ■ | ■ |
| | | | Energy metabolism | ■ | ■ | | ■ | ■ |



Colon

| Family | Category | Super Pathway | Sub Pathway | Uninfect | Crypto | Sample | Giardia | UPEC |
|-----------------|------------|-------------------------|---|----------|--------|--------|---------|------|
| F__Atopobiaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | ■ | ■ | | ■ | ■ |
| | | | Fructose and mannose metabolism | ■ | ■ | | ■ | ■ |
| | | | Galactose metabolism | ■ | ■ | | ■ | ■ |
| | | | Glycolysis / Gluconeogenesis | ■ | ■ | | ■ | ■ |
| | | | Glyoxylate and dicarboxylate metabolism | ■ | ■ | | ■ | ■ |
| | | | Pentose and glucuronate interconversions | ■ | ■ | | ■ | ■ |
| | | | Pentose phosphate pathway | ■ | ■ | | ■ | ■ |
| | | | Pyruvate metabolism | ■ | ■ | | ■ | ■ |
| | | | Starch and sucrose metabolism | ■ | ■ | | ■ | ■ |
| | | | Energy metabolism | ■ | ■ | | ■ | ■ |

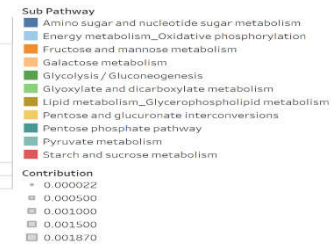
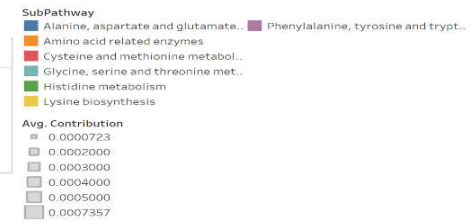
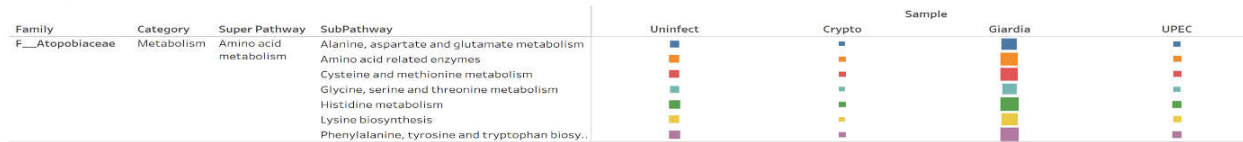
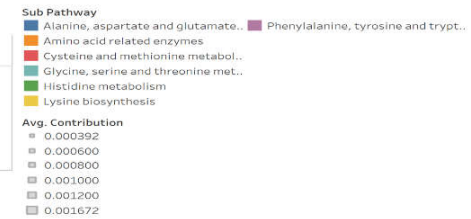
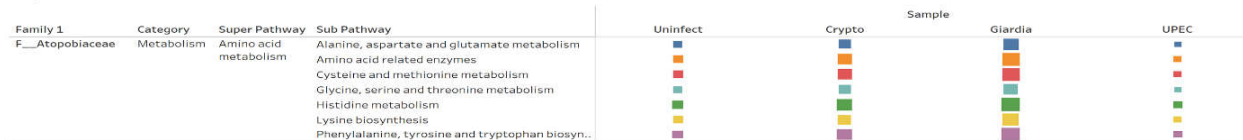


Figure S12. Functional analysis for *Atopobiaceae* family to predict its effect on **carbohydrate metabolism, energy metabolism and lipid metabolism** during cryptosporidiosis and giardiasis.

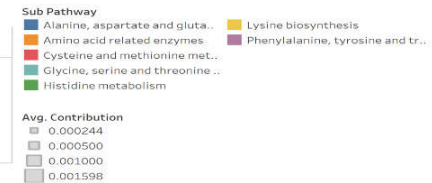
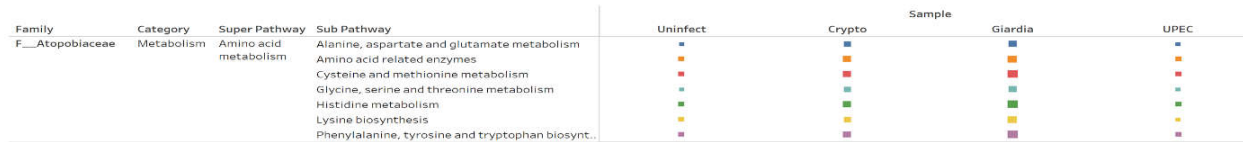
Duodenum



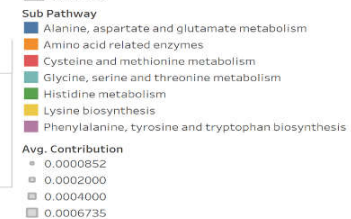
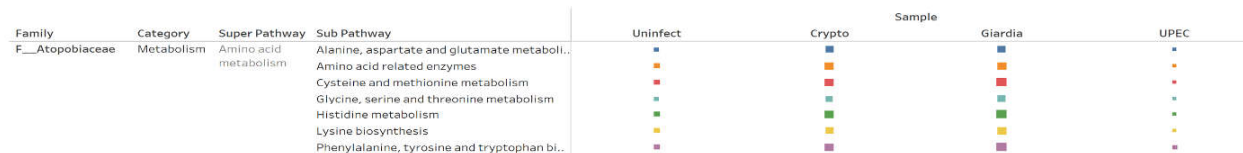
Jejunum



Ileum



Cecum



Colon

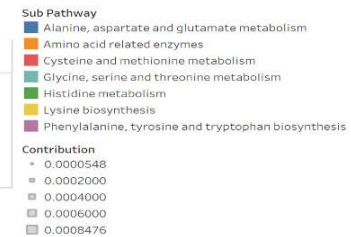
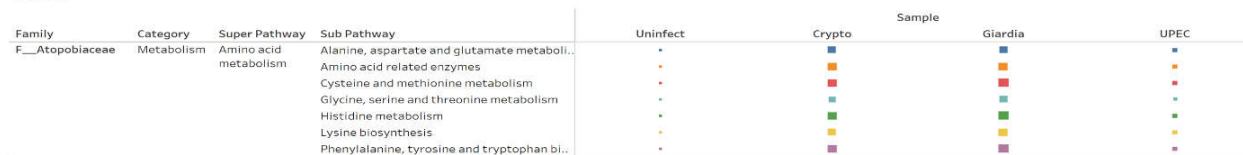


Figure S13. – Functional analysis for *Atopobiaceae* family to predict its effect on **amino acid metabolism** during cryptosporidiosis and giardiasis.

Duodenum

| Family | Category | Super Pathway | SubPathway | Sample | | | |
|------------------------|------------|-------------------------|---|----------|--------|---------|------|
| F__Desulfovibrionaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | Uninfect | Crypto | Giardia | UPEC |
| | | | Fructose and mannose metabolism | | | | |
| | | | Galactose metabolism | | | | |
| | | | Glycolysis / Gluconeogenesis | | | | |
| | | | Glyoxylate and dicarboxylate metabolism | | | | |
| | | | Pentose phosphate pathway | | | | |
| | | | Pyruvate metabolism | | | | |
| | | | Starch and sucrose metabolism | | | | |
| | | Energy metabolism | Oxidative phosphorylation | | | | |
| | | Lipid metabolism | Glycerophospholipid metabolism | | | | |

SubPathway

- Amino sugar and nucleotide sugar metabolism
- Energy metabolism_Oxidative phosphorylation
- Fructose and mannose metabolism
- Galactose metabolism
- Glycolysis / Gluconeogenesis
- Glyoxylate and dicarboxylate metabolism
- Lipid metabolism_Glycerophospholipid metabolism
- Pentose phosphate pathway
- Pyruvate metabolism
- Starch and sucrose metabolism

Avg. Contribution

- 0.0000264
- 0.0001000
- 0.0002000
- 0.0003000
- 0.0003919

Jejunum

| Family | Category | Super Pathway | Sub Pathway | Sample | | | |
|------------------------|------------|-------------------------|---|----------|--------|---------|------|
| F__Desulfovibrionaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | Uninfect | Crypto | Giardia | UPEC |
| | | | Fructose and mannose metabolism | | | | |
| | | | Galactose metabolism | | | | |
| | | | Glycolysis / Gluconeogenesis | | | | |
| | | | Pentose phosphate pathway | | | | |
| | | | Pyruvate metabolism | | | | |
| | | | Starch and sucrose metabolism | | | | |
| | | Energy metabolism | Oxidative phosphorylation | | | | |
| | | Lipid metabolism | Glycerophospholipid metabolism | | | | |

Sub Pathway

- Amino sugar and nucleotide sugar metabolism
- Energy metabolism_Oxidative phosphorylation
- Fructose and mannose metabolism
- Galactose metabolism
- Glycolysis / Gluconeogenesis
- Lipid metabolism_Glycerophospholipid metabolism
- Pentose phosphate pathway
- Pyruvate metabolism
- Starch and sucrose metabolism

Avg. Contribution

- 0.000091
- 0.000200
- 0.000400
- 0.000600
- 0.000800
- 0.001181

Ileum

| Family | Category | Super Pathway | Sub Pathway | Sample | | | |
|------------------------|------------|-------------------------|---|----------|--------|---------|------|
| F__Desulfovibrionaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | Uninfect | Crypto | Giardia | UPEC |
| | | | Fructose and mannose metabolism | | | | |
| | | | Galactose metabolism | | | | |
| | | | Glycolysis / Gluconeogenesis | | | | |
| | | | Pentose phosphate pathway | | | | |
| | | | Pyruvate metabolism | | | | |
| | | | Starch and sucrose metabolism | | | | |
| | | Energy metabolism | Oxidative phosphorylation | | | | |
| | | Lipid metabolism | Glycerophospholipid metabolism | | | | |

Sub Pathway

- Amino sugar and nucleotide sugar metabolism
- Energy metabolism_Oxidative phosphorylation
- Fructose and mannose metabolism
- Galactose metabolism
- Glycolysis / Gluconeogenesis
- Lipid metabolism_Glycerophospholipid metabolism
- Pentose phosphate pathway
- Pyruvate metabolism
- Starch and sucrose metabolism

Avg. Contribution

- 0.000078
- 0.000200
- 0.000400
- 0.000600
- 0.000800
- 0.001000
- 0.001168

Cecum

| Family | Category | Super Pathway | Sub Pathway | Sample | | | |
|------------------------|------------|-------------------------|---|----------|--------|---------|------|
| F__Desulfovibrionaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | Uninfect | Crypto | Giardia | UPEC |
| | | | Fructose and mannose metabolism | | | | |
| | | | Galactose metabolism | | | | |
| | | | Glycolysis / Gluconeogenesis | | | | |
| | | | Glyoxylate and dicarboxylate metabolism | | | | |
| | | | Pentose and glucuronate interconversions | | | | |
| | | | Pentose phosphate pathway | | | | |
| | | | Pyruvate metabolism | | | | |
| | | | Starch and sucrose metabolism | | | | |
| | | Energy metabolism | Oxidative phosphorylation | | | | |
| | | Lipid metabolism | Glycerophospholipid metabolism | | | | |

Sub Pathway

- Amino sugar and nucleotide sugar metabolism
- Energy metabolism_Oxidative phosphorylation
- Fructose and mannose metabolism
- Galactose metabolism
- Glycolysis / Gluconeogenesis
- Glyoxylate and dicarboxylate metabolism
- Lipid metabolism_Glycerophospholipid metabolism
- Pentose and glucuronate interconversions
- Pentose phosphate pathway
- Pyruvate metabolism
- Starch and sucrose metabolism

Avg. Contribution

- 0.0000163
- 0.0002000
- 0.0004000
- 0.0006000
- 0.0007926

Colon

| Family | Category | Super Pathway | Sub Pathway | Sample | | | |
|------------------------|------------|-------------------------|---|----------|--------|---------|------|
| F__Desulfovibrionaceae | Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | Uninfect | Crypto | Giardia | UPEC |
| | | | Fructose and mannose metabolism | | | | |
| | | | Galactose metabolism | | | | |
| | | | Glycolysis / Gluconeogenesis | | | | |
| | | | Glyoxylate and dicarboxylate metabolism | | | | |
| | | | Pentose and glucuronate interconversions | | | | |
| | | | Pentose phosphate pathway | | | | |
| | | | Pyruvate metabolism | | | | |
| | | | Starch and sucrose metabolism | | | | |
| | | Energy metabolism | Oxidative phosphorylation | | | | |
| | | Lipid metabolism | Glycerophospholipid metabolism | | | | |

Sub Pathway

- Amino sugar and nucleotide sugar metabolism
- Energy metabolism_Oxidative phosphorylation
- Fructose and mannose metabolism
- Galactose metabolism
- Glycolysis / Gluconeogenesis
- Glyoxylate and dicarboxylate metabolism
- Lipid metabolism_Glycerophospholipid metabolism
- Pentose and glucuronate interconversions
- Pentose phosphate pathway
- Pyruvate metabolism
- Starch and sucrose metabolism

Contribution

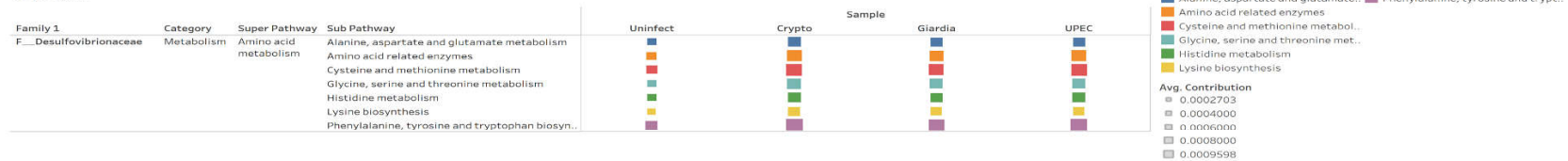
- 0.0000130
- 0.0002000
- 0.0004000
- 0.0006761

Figure S14. Functional analysis for *Desulfovibrionaceae* family to predict its effect on **carbohydrate metabolism, energy metabolism and lipid metabolism** during cryptosporidiosis and giardiasis.

Duodenum



Jejunum



Ileum



Cecum



Colon

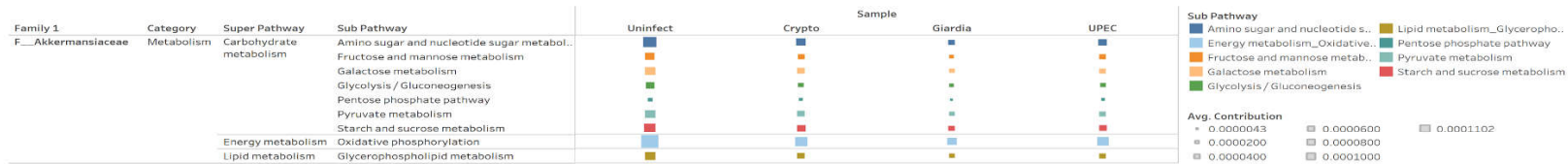


Figure S15. Functional analysis for *Desulfovibrionaceae* family to predict its effect on **amino acid metabolism** during cryptosporidiosis and giardiasis.

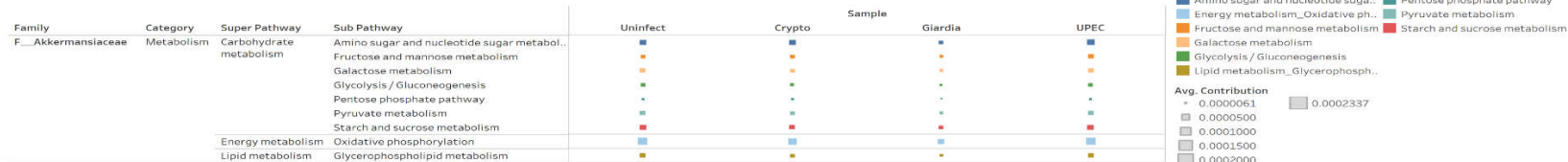
Duodenum



Jejunum



Ileum



Cecum

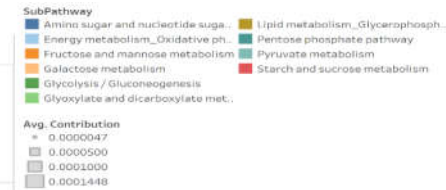
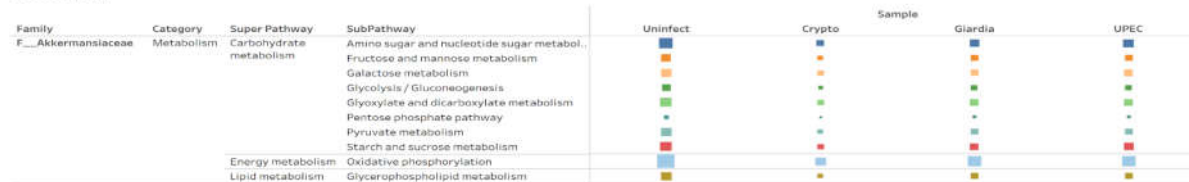


Colon

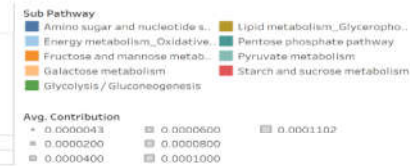
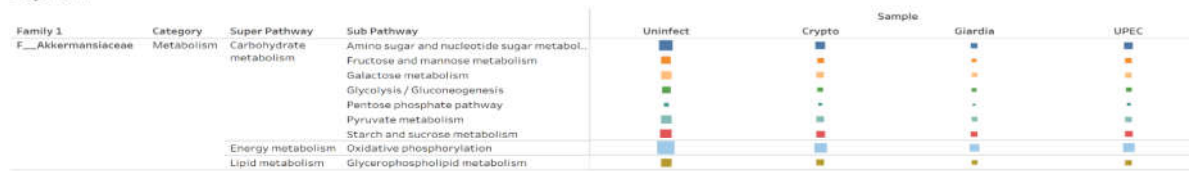


Figure S16. Functional analysis for *Akkermansiaceae* family to predict its effect on **carbohydrate metabolism, energy metabolism and lipid metabolism** during cryptosporidiosis and giardiasis.

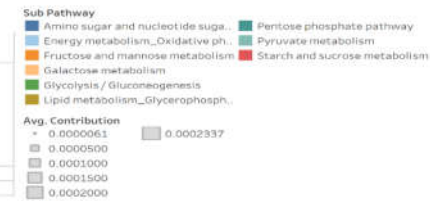
Duodenum



Jejunum



Ileum



Cecum



Colon



Figure S 17. Functional analysis for *Akkermansiaceae* family to predict its effect on **amino acid metabolism** during cryptosporidiosis and giardiasis.