

**Studying mutualism and pathogenesis using UPLC-HRMS based
metabolomics**

**A Thesis Presented for the
Master of Science
Degree
The University of Tennessee, Knoxville**

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DEDICATION

I dedicate this thesis to my husband, Wes, and to my family for your continuous love and support.

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Thank you to my advisor, Shawn Campagna, for your insight and guidance. Thank you to my committee members, Dr. Ampofo Darko and Dr. Bhavya Sharma for your positive influences. Thank you to my lab members Allen Bourdon, Abigail Farmer, Brandon Kennedy, Alex Fisch, Eric Tague, Caleb Gibson, Josh Powers, Katha Höland, Katarina Jones, Ashley Lato, and Haley Bruer along with Dr. Hector Castro and Sara Howard for your assistance, encouragement, and company.

ABSTRACT

In this thesis, mutualistic and pathogenic relationships between *Galleria mellonella*, *Steinernema carpocapsae*, and *Xenorhabdus nematophila* were studied. Using Ultra Performance Liquid Chromatography in tandem with High Resolution Mass Spectrometry (UPLC-HRMS), metabolite intensities were measured. In the first experiment, *Galleria mellonella* was infected with entomopathogenic *Steinernema carpocapsae* nematodes and the progress of infection was analyzed using metabolomics. In a mutualistic relationship, *Steinernema carpocapsae* nematodes transport *Xenorhabdus nematophila* bacteria into the host and kill the insect for nematode development. Metabolomics analysis of *Galleria mellonella* showed statistical significant differences in metabolite intensities as infection progressed in both known and unknown spectral features.

In the second experiment, the metabolic profile of two strains of *Xenorhabdus nematophila* were studied for differences in colonization abilities induced by the nematode intestinal location (*nil*) locus. The *nil* locus was deleted in both strains, but the control strain was complemented for the deletion. Metabolomics analysis using UPLC-HRMS was performed on both whole cell samples and supernatant samples with an interest in known and unknown spectral features. Of metabolites detected, 18 more were detected in the whole cell samples versus the supernatant samples. Unknown spectral features were analyzed with 1301 more spectral features being detected in the whole cell samples. After reduction by statistical significance, unknown spectral features were analyzed for database matches by exact mass.

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INTRODUCTION TO METABOLOMICS AND MASS SPECTROMETRY TECHNIQUES

Metabolomics

Metabolomics is the comprehensive analysis of small molecules, referred to as metabolites, in a biological system with a mass of less than 1 kDa.^{1,2} By studying metabolites in a biological system, the biochemistry of cellular responses can be related to phenotype.³ Metabolomics is a vital tool for studying the cause of biological effects in a system by providing a snapshot of cellular regulation and control.⁴ By gaining an understanding of cellular phenotype, we can begin to understand how a system interacts with its surrounding environment.⁵

The amount and type of metabolites synthesized represent the metabolome of an organism.⁴ The metabolome consists of a wide variety of compound classes such as organic acids, amino acids, nucleotides, and amino acids, which all have diverse properties and occur in a wide range of concentrations.³ These small molecules participate in general metabolic reactions and are required for maintenance, growth, and normal functions of a cell.⁶ Metabolomics is at the bottom of the omics cascade (Figure 1) below gene expression and amplifies changes in the transcriptome and proteome. This type of analysis reflects the activities of the cell at a functional level.^{6,7}

The two main types of metabolomics analysis are targeted and untargeted metabolomics. Targeted metabolomics is known as a hypothesis-driven technique. Targeted metabolomics focuses on quantifying and identifying specific metabolites within the biological system.¹ The metabolites analyzed are usually part of a specific group related to a pathway or class of compounds.⁸ In this technique, the chemical properties of compounds are known meaning sample preparation can be changed to reduce interference from other compounds or reduce matrix effects.¹

Untargeted metabolomics aims to detect as many mass spectral features from a sample as possible.⁹ An untargeted approach allows for the potential to provide an understanding of biological processes from a global perspective in response to disease or environmental changes.⁸ Results from an untargeted experiment are used to generate new

hypotheses for future experiments.¹ The disadvantage to this type of analysis is a large number of metabolites change as a result of changing conditions and many of these changing metabolites remain uncharacterized by structure and function.⁹ Output from an untargeted metabolomics analysis results in a large number of unidentified spectral features, which must be searched in a database such as Human Metabolome Database¹⁰ (HMDB) or METLIN (The Scripps Research Institute) for punitive matches based on exact mass. Most searches do not return any matches or return multiple matches for each exact mass making identification difficult.^{1,11} Any possible matches may not be accurate but can be confirmed by comparing retention times of standards and performing subsequent experiments to compare fragmentation patterns from MS/MS spectra.⁸

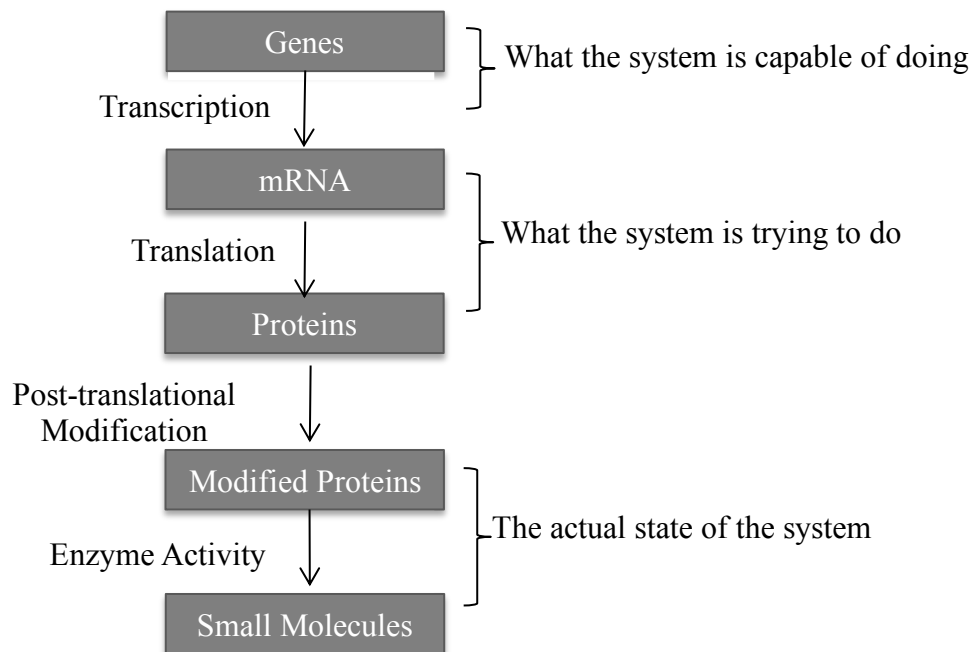


Figure 1. The omics cascade.

Analytical Instrumentation

Liquid Chromatography

Separation techniques prior to analysis by mass spectrometry are used to reduce the complexity of a mass spectrum and aid in metabolite identification by providing information on physiochemical properties of a metabolite. Mainly, separations reduce the number of ions entering a mass spectrometry ion source at one time which reduces ion suppression leading to a reduction in background noise and an improvement in detection thus improving quality of the mass spectra. Liquid chromatography (LC) is commonly coupled with mass spectrometry because of its ability to separate a wide range of polar, water-soluble molecules such as metabolites.¹²

In LC, mixtures are separated based on their retention time, or the amount of time spent in the column, which is influenced by their interaction with the mobile phase and stationary phase. As the name suggests, the stationary phase is stationary in the column and is passed over by the mobile phase. Analytes migrate through the column at different rates due to chemical interactions with the stationary phase. An analyte that has a greater affinity for the mobile phase means the analyte will spend more time in the mobile phase and will travel faster and elute off the column before an analyte with a greater affinity for the stationary phase. An LC separation reduces ion suppression so ion pairing agents can be added to the mobile phase to decrease detectability of unwanted analytes.¹³

Isocratic or gradient elutions can be used to facilitate LC separations. Isocratic conditions consist of a constant solvent composition throughout analysis. In gradient conditions, the composition of the mobile phase changes as analysis progresses. In reverse-phase high performance liquid chromatography (RP-HPLC), the stationary phase is nonpolar and the starting mobile phase is very polar. As analysis progresses, the mobile phase is changed by increasing the proportion of the less polar component. Gradients are chosen to separate complex samples and shorten analysis times.¹³

High performance liquid chromatography (HPLC) is a type of liquid chromatography that has led to the development of ultra-high performance liquid chromatography (UPLC).¹⁴ HPLC offers higher resolution, more reproducible responses,

and an increased speed of analysis than other LC techniques. HPLC utilizes particle sizes of 3-5 μm while UPLC can use particle sizes of less than 2 μm . The use of smaller particle size increases resolution, efficiency, and sensitivity, but also increases backpressure due to an increase in flow rate. HPLC columns can withstand a maximum pressure of around 600 bar where as UPLC columns can withstand pressures of over 1200 bar.¹⁴ The improved chromatographic efficiency of UPLC systems over other LC techniques allows for the detection of more metabolites.¹²

Mass Spectrometry

The purpose of mass spectrometry is to generate ions, separate those ions by their mass to charge ratio (m/z), and detect those ions by their respective m/z and abundance using an ion source, a mass analyzer, and a detector.¹⁵ A schematic of a basic mass spectrometer is shown in Figure 2. Mass spectrometry is an important analytical tool in the area of metabolomics because when coupled with LC, it offers high selectivity and low detection limits for trace compounds in complex mixtures, such as the detection of metabolites in biological samples, allowing for rapid measurements from minimal amounts of sample.^{9,15} When coupled with LC, mass spectrometry reduces the complexity of the mass spectra by separating co-eluting compounds.³

Once a sample has been introduced through a sample inlet, the ion source is responsible for transferring ions from the sample into the gas phase. Ion sources can be tailored to each experiment based on the type of sample and the ions being produced. For metabolomics experiments, electrospray ionization (ESI) is chosen because it is considered a soft ionization technique that forms intact molecular ions and is capable of producing a large number of ions.¹

ESI sources are often referred to as ESI interfaces because they do not actively produce ions. ESI requires ions to be present in the sample and will transfer them to the gas phase through a three-step process: Taylor cone formation, reduction of droplet size, and ion liberation. The Taylor cone is formed from increasing field strength surrounding the spray capillary. Once a critical electric field strength is reached, a fine jet of liquid is ejected from the apex towards the counter electrode. The jet carries a large surplus of ions

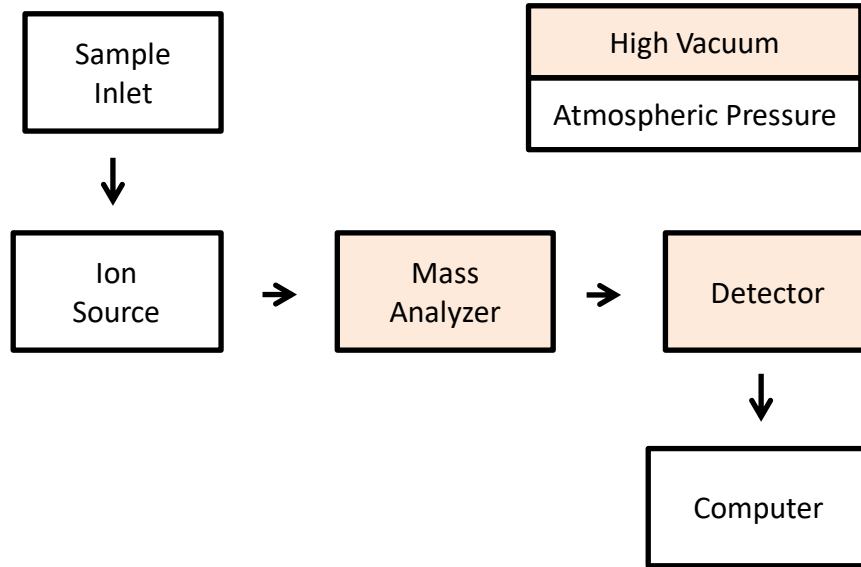


Figure 2. Schematic of mass spectrometer.

of one particular charge sign determined by ionization mode that break up into smaller droplets and are driven apart by Columbic repulsion. The charge density of the droplet increases as solvent evaporates until the *Rayleigh* limit is reached and the droplet breaks into smaller droplets. Two theories currently exist for ion liberation. The charge-residue model (CRM) suggests the droplet size is reduced until the droplet contains one ion and the remaining solvent is then evaporated. The ion-evaporation model (IEM) suggests an increasing charge density of a small droplet causes the ejection of an ion out of solution. Evidence shows that both theories are correct with CRM being the mostly likely model for large mass ions while IEM is the most likely model for small mass ions.¹⁵

An orbitrap is a mass analyzer that uses an electrostatic field to trap ions in a stable trajectory. An orbitrap has a spindle-like center electrode and barrel-like outer electrode.¹⁵ Ions orbit around the central electrode while simultaneously oscillating in the z-direction.¹⁶ All ions have the same amplitude but the axial motion is determined by m/z ratio. The m/z of an ion can be determined from the frequency of oscillation after Fourier

transform. A C-trap is used to accumulate and store ions before being injected into the orbitrap by a high voltage electric pulse.¹⁵ An orbitrap mass analyzer has a high mass resolution, which is necessary to resolve two peaks with small mass differences. High mass resolution is important for experiments with complex mixtures because they contain a large number of background ions.¹⁷

The performance of a mass spectrometer is determined by its sensitivity, limit of detection (LOD), and signal to noise ratio (S/N). Sensitivity is electric charge of a specified ion reaching the detector per mass of analyte used and can be affected by the ionization method, mass range, and transmission of the mass analyzer. The LOD is the smallest amount of analyte necessary to obtain a signal that can be distinguished from the background noise. The S/N describes the uncertainty of the intensity of a measured ion.

Orbitrap mass spectrometers are known to have high resolution and low mass accuracy. Resolution refers to the smallest difference in m/z that can be separated for a signal and can be calculated by dividing the m/z for a given signal by the difference in m/z . There are two ways to refer to mass accuracy. Absolute mass accuracy is the difference between the experimental m/z and the calculated m/z . Relative mass accuracy is usually reported in parts per million (ppm) and is the absolute mass accuracy divided by the m/z it is determined for.¹⁵

Metabolomics Data

Computer programs are used to not only control mass spectrometers but also aid in analyzing the large amounts of data collected by the instrument. Software programs such as Xcalibur™ (Thermo Fisher Scientific, San Jose, CA) allows for method setup, data acquisition, and data processing while also allowing users the ability to view the total ion chromatogram (TIC) and the extracted ion chromatogram (EIC). The TIC shows the sum of ionic intensities per spectrum verses retention time while the EIC shows the signal intensity at a selected m/z verses retention time.¹⁵ Data files produced by Xcalibur™ are in a RAW format and must be converted for analysis using programs like MSConvert by ProteoWizard.¹⁸ MSConvert changes the file format from a RAW file to a

mzML file that is readable by processing software such as MAVEN (<http://maven.princeton.edu>).¹⁹

Software programs such as MAVEN and XCMS Online (<https://xcmsonline.scripps.edu>) align mass spectrometry data from each sample in order to make processing easier. Data files obtained from samples analyzed with mass spectrometry platforms contain a large number of metabolites that were measured through a single analysis with untargeted analysis resulting in tens of thousands of spectral features.²⁰ MAVEN and XCMS Online are commonly used to align and group peaks across all samples correcting for factors such as retention time drift.¹⁹⁻²¹ MAVEN can be downloaded for use and is best used for matching detected metabolites to a known library while XCMS Online is better used for unknown analysis due to its additional features such as statistical analysis, visualizing metabolomics data, and metabolite assignment.^{19,21}

After determining the metabolites detected, intensities are normalized using either mass or volume before averaging the intensities of replicates to determine fold changes and statistical significance. Fold changes are found by dividing each treatment group by the control group. A student's t-test can be used to determine statistical significance between each treatment group and the control group with a resulting p value below 0.1 representing there is a 90% probability the differences between the groups did not occur by chance.²² Fold changes and statistical significance can be displayed on a heatmap, one of the most widely used bioinformatics graphic representations. A heatmap is a visualization tool in which fold changes of relative abundance are represented using a color intensity scale. Heatmaps can be used for visually recognizing patterns in changing intensities for finding interesting features.²⁰

Partial Least Squares-Discriminant Analysis (PLS-DA) plots are constructed to identify class differences from a multivariate dataset and are commonly used for classification purposes and biomarker selection.^{23,24} PLS-DA plots are based on PLS regression model in which the dependent variable represents the class of membership.^{24,25} PLS-DA plots can be made in programs such as RStudio (<https://www.rstudio.com/>)

or from metabolomics processing websites such as MetaboAnalyst²⁶. From PLS-DA plots, metabolites are assigned a variable importance in projection (VIP) score that is used to determine the most important variables and their contributions to the model. VIP scores above 1 are considered significant and represent the metabolites that are greatly influencing the separation between the groups in the model.^{27,28}

CHAPTER I
UNTARGETED METABOLOMICS OF *GALLERIA MELLONELLA*
INFECTED WITH ENTOMOPATHOGENIC NEMATODES

Abstract

An untargeted metabolomics experiment was performed on *Galleria mellonella* samples infected with entomopathogenic *Steinernema carpocapsae* nematodes to detect known and unknown spectral features. Samples were collected at various time points post infection then metabolites were extracted and analyzed by UPLC-HRMS. A total of 110 known metabolites were detected and over 54,000 unknown spectral features were detected. The amount of unknown spectral features was condensed using average intensity and p values. Fold changes and statistical differences in the intensity of both known and unknown metabolites were determined. Results showed that fold changes of intensity were more drastic as infection progressed. After initial processing of unknown metabolites, specific metabolites related to virulence and nicotinate and nicotinamide metabolism pathway were investigated in the untargeted spectral features.

Introduction

The greater wax moth *Galleria mellonella* (*G. mellonella*) has become an increasingly used model in recent years to study pathogenesis on non-mammal species.²⁹ *Steinernema carpocapsae* (*S. carpocapsae*) nematodes commonly infect *G. mellonella* along with other lepidopteron species.³⁰ With the help of *Xenorhabdus nematophila* (*X. nematophila*) bacteria, *S. carpocapsae* nematodes become pathogenic to a wide variety of insects.³⁰ *X. nematophila* alternates between a pathogenic stage of a variety of insects and a mutualistic stage with *S. carpocapsae*.³¹

S. carpocapsae colonized by *X. nematophila* are called infective juveniles (IJs). IJs enter an insect host through natural openings and release bacteria killing the insect. By day 5 post infection, IJs have developed into adult stages that reproduce within the insect cadaver. By approximately days 9-11, offspring has developed through multiple juvenile stages into adult stages. Reproduction continues until around day 16 when low nutrient availability and high nematode density signals IJ development, which are then colonized with *X. nematophila*. Once IJs are re-colonized, they leave the cadaver to find a new host to infect.³²

This model of parasite-host interactions between *X. nematophila*, *S. carpocapsae*, and *G. mellonella* can be used to study both mutualistic and pathogenic processes.³³ *G. mellonella* is a pest that lives in beehives and feeds off wax and pollen causing destruction of the hive and causing bee and wasp galleriosis.³⁴ A better understanding of *X. nematophila*-*S. carpocapsae*-*G. mellonella* interactions could lead to a safe and precise control of *G. mellonella* population through the improvement of bioinsecticides.³⁴ An insect model is often easier and cheaper to work with when studying pathogenesis as well as more ethically acceptable. An insect model can be used to better understand virulence factors before studying mammalian organisms. *G. mellonella* is commonly chosen as a model organism due to large larvae being easy to work with. A disadvantage to using *G. mellonella* is its genome is not fully sequenced and there are currently no methods to create mutant strains.³⁴

Materials and Methods

G. mellonella Samples

G. mellonella samples infected with entomopathogenic nematodes were collected from the Goodrich-Blair lab at the University of Tennessee, Knoxville. Samples were collected at 1 hour, 12 hours, 24 hours, 2 days, 4 days, 6 days, 8 days, 10 days, 12 days, and 16 days after infection. The 24-hour time point was split into two time points, 24 hours alive and 24 hours dead groups, to analyze differences between specimens that had succumb to infection and those that had not. There were 5 biological replicates of each time point and 5 uninfected *G. mellonella* samples were used as the control.

Metabolomics Extraction

Extraction procedures were adapted from Rabinowitz et al.³⁵ At 4°C, infected *G. mellonella* larvae were homogenized in 1.3 mL of extraction solvent made of HPLC grade 40/40/20 methanol, acetonitrile, and water with 0.1% formic acid. After homogenization, samples were placed on a vortex for 5 seconds before being placed in -20°C for 20 minutes. Samples were then centrifuged for 5 minutes to pack the sample

into a pellet. Supernatant was extracted into labeled Eppendorf tubes. An additional 0.2 mL of extraction solvent was added to the pellet for a second extraction in which samples were vortexed, placed in -20°C for 20 minutes, centrifuged, and supernatant was extracted. The supernatant was dried with a Thermo Fisher Savant ISS110 SpeedVac Concentrator and under nitrogen gas. Dried samples were suspended in 300 µL of Milli-Q water and placed in autosampler vials for analysis.³⁵

UPLC-HRMS

After extraction, samples were immediately analyzed in negative mode by UPLC-HRMS using a Thermo Fisher Exactive Plus Orbitrap Mass Spectrometer equipped with an UltiMate 3000 liquid chromatogram controlled by Xcalibur™. After cleaning and calibrating the instrument, samples were placed in the 4°C autosampler tray. An injection volume of 10µL of sample was separated on a 2.5-micron Synergi Hydro-RP 100, 100mm x 2 mm column (Phenomenex, Torrance, CA, USA) at 25°C with a constant flow rate of 200µL/minute. An acidic gradient was used with Solvent A consisting of 97:3 HPLC grade water:methanol with 15mM acetic acid and 10mM tributylamine used as an ion pairing agent. Solvent B was HPLC grade methanol. The gradient began at 0% B at 0 minutes and increased to 20% B at 5 minutes, 55% B at 13 minutes, and 95% B at 15.5 minutes. The percent methanol was decreased to 0% B from 15.5 minutes to 19 minutes and held at 0% B from 19 minutes to 25 minutes. Samples were analyzed with a scan window of 85 to 800 *m/z* from 0 to 9 min and 110 to 1000 *m/z* from 9 to 25 min and with a resolution of 140,000.

Known Metabolites Processing

Once samples were analyzed, RAW data files from the mass spectrometer were converted into MZML files using MSConvert. MZML files were opened with MAVEN¹⁹ and peaks were aligned and picked from the negative mode known compounds list containing approximately 260 metabolites. Metabolites were matched based on exact mass and retention time. The area of the peak represents the intensity of metabolites in the sample. Once all observable peaks were found, the data was exported to begin

processing in Microsoft Excel. Peak areas were normalized based on the amount of sample by taking the intensity and dividing it by the mass of each sample. Once samples were grouped by their respective time points, the average, standard error, and standard deviation of each group was determined. Fold changes were determined by dividing the average of each group by the average of the control group. P values were determined using a student's t-test and comparing each group to the control group. PLS-DA plots and heat maps were made to display the data using RStudio.

Unknown Metabolites Processing

Unprocessed MZML files were opened with MAVEN and analyzed for unknown spectral features at 10 ppm. The data was exported to an excel file then normalized, grouped, and averaged based on previously described methods. Due to the large number of spectral features detected, the list had to be reduced in order to process. In order to remain, at least 4 of the 12 groups had to have an average intensity over 10^5 . Next, the unknowns were reduced according to their p-value, which was determined by a student's t-test. In order to remain, at least one group had to have a p-value less than 0.005. Usually, a p value of less than 0.1 can be considered significant but due to the large number of unknowns a stricter p value was used.

The Goodrich-Blair lab provided a list of metabolites they were interested in determining their presence in the unknown spectral features. Using MAVEN, chemical formulas were searched and all observable peaks for that metabolite were picked. If multiple peaks were found at varying retention times, then all peaks were picked. The data was exported and processed using the same methods as described above. PLS-DA plots were made in R studio and an unknown heatmap was made with was made using Cluster 3.0 and Java TreeView 3.0.

Results and Discussion

Known Metabolites

A total of 111 known metabolites were detected throughout the infection model (Appendix, Tables 18-30). Table 1 displays the total number of known and unknown spectral features detected. When compared to the uninfected group, the number of statically varying metabolites increased as infection progressed reaching a peak of 63 statistically significant metabolites at 4 days after infection then decreasing to 38 statistically significant metabolites by day 16. The exact number of statistically significant metabolites for each time point is displayed in Figure 3. A p value below 0.1 was considered statistically significant. While there were no statistically significant metabolites at 1-hour post infection, 4 metabolites were significant at 12 hours after infection. These metabolites were guanine, uric acid, homocysteic acid, and glycinamide ribonucleotide (GAR). Four nematode samples were also compared to the uninfected group and resulted in 86 out of 111 metabolites being statistically significant.

Too many time points were present to include all time points on one PLS-DA plot so time points were grouped into early, middle, and late infection groups. PLS-DA plots for each infection group are shown in Figure 4. The early infection group contains samples from 1-hour post infection through 24 hours dead (Figure 4-A). The middle infection group contains samples from 2 days after infection through 8 days after infection (Figure 4-B). The late infection group contains samples from 10 days after infection through 16 days after infection (Figure 4-C). As these three PLS-DA plots

Table 1. *G. mellonella* detected features.

Result	Number of Features
Knowns detected	111
Unknowns detected	54259
Intensity over 10^5	25335
Significant p values	2199

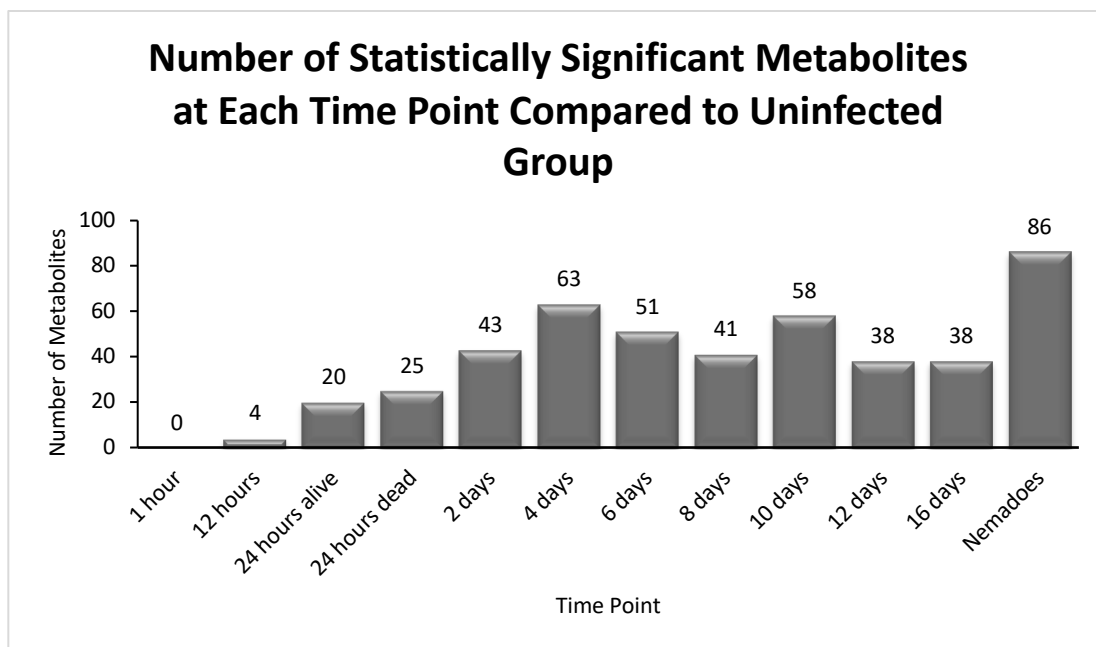


Figure 3. Number of Statistically significant metabolites.

show, separation between the time points increases as the length of infection increases. Although these plots do not display the z-axis, the uninfected groups were separated along the z-axis from the other time points in both the middle and late groups when plotted in 3-D PLS-DA plots (not shown).

Top VIP scores from each PLS-DA plot were determined and are displayed in Figure 5. In the early infection groups, 25 metabolites had a significant VIP score in both components. In the middle infection groups, 35 metabolites had a significant VIP score in both components. In the late infection groups, 38 metabolites had a significant VIP score in both components. An increase in the number of top VIP scores indicates more metabolites are differentiated by class as infection progresses.

There were 5 metabolites that had a VIP score above 1 in both components in all three PLS-DA plots (Table 2). All 5 metabolites listed in Table 1 have significant p values at multiple time points throughout infection with most significance being in the middle and late infection range. A full list of metabolites with VIP scores over 1 can be

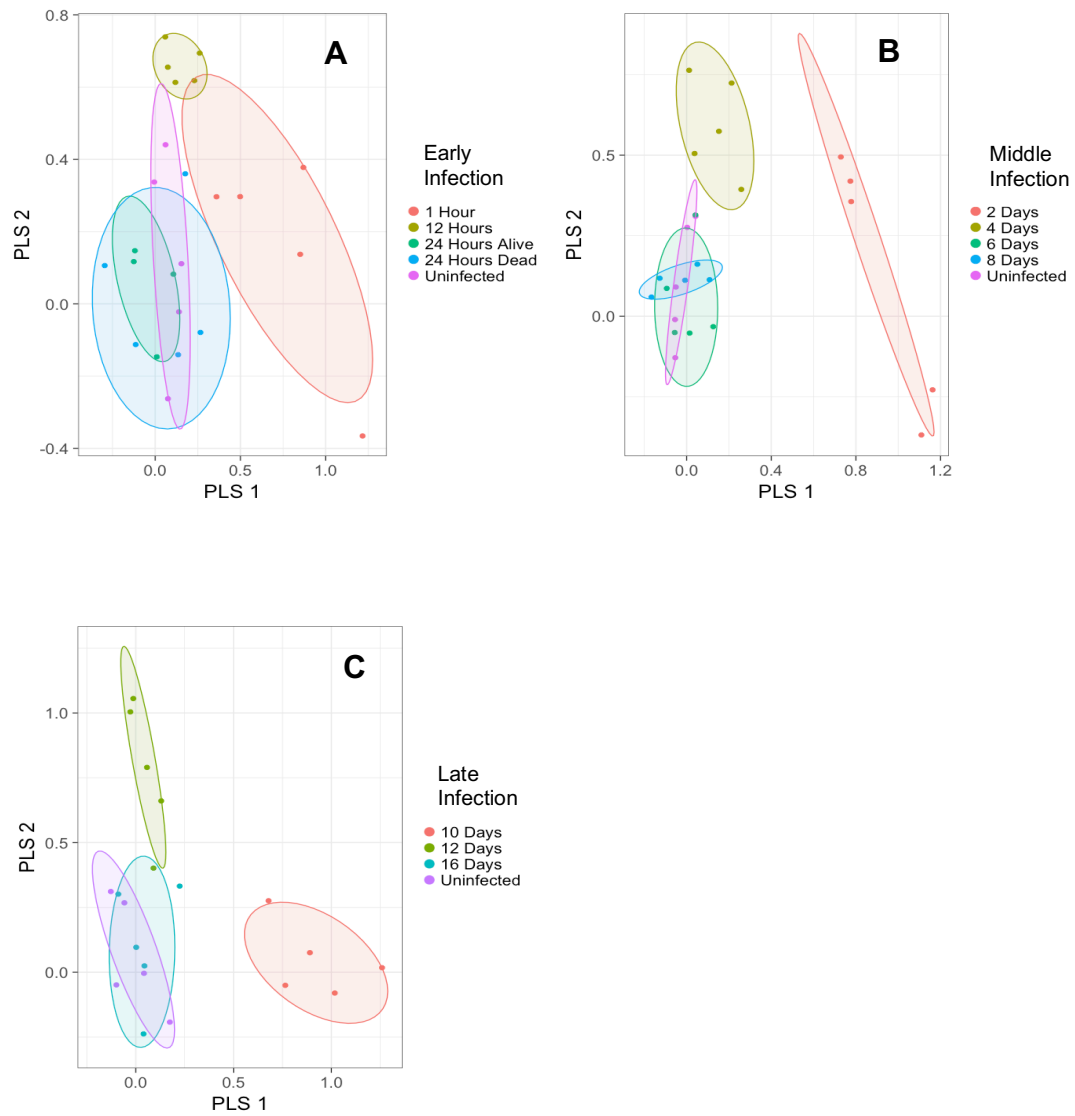


Figure 4. PLSDA plots of known metabolites in *G. mellonella* infected with entomopathogenic nematodes from early infection (A) to middle infection (B) and late infection (C).

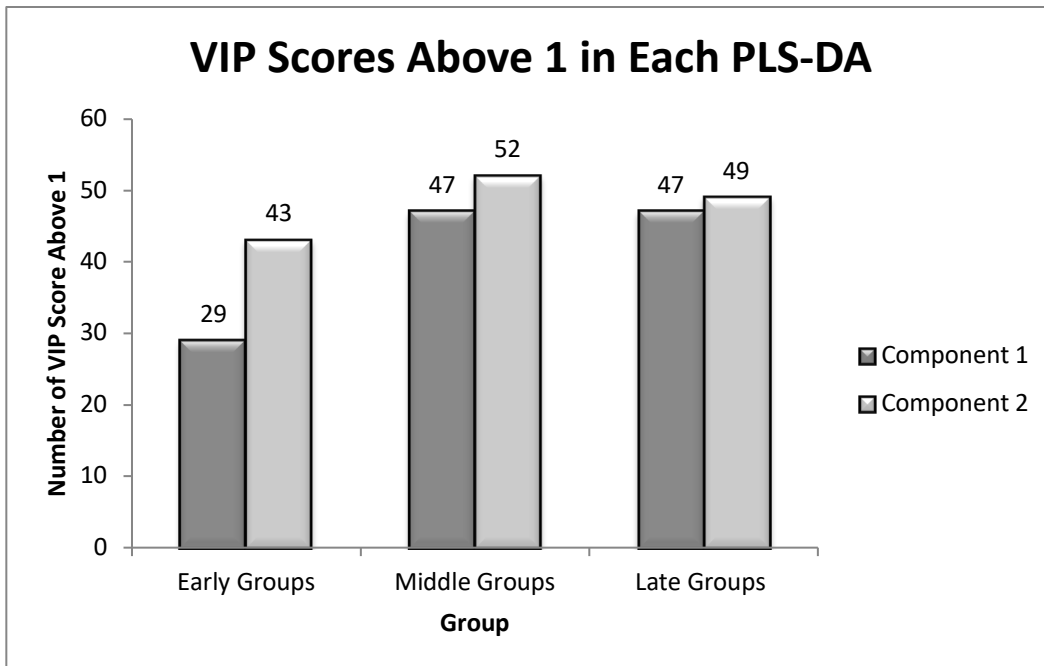


Figure 5. Number of significant VIP scores in *G. mellonella* groups.

Table 2. Metabolites with VIP scores above 1 in both components of all groups.

Metabolite	Early		Middle		Late	
	Comp 1	Comp 2	Comp 1	Comp 2	Comp 1	Comp 2
Phenyllactic acid	1.6505	1.3167	1.5087	1.1783	1.2511	1.1197
Phosphoenolpyruvate	1.1607	1.2045	1.5359	1.3461	1.2550	1.1412
Uracil	1.3847	1.0642	1.7937	1.5348	1.3799	1.1626
Uridine	2.2981	1.8439	1.3648	1.0639	1.0231	1.0409
Xylitol	2.3974	1.8718	1.3825	1.0741	1.1903	1.2219

found in the appendix in Tables 11-13. All of these metabolites in Table 1 except uracil also have a significant p value when compared to the nematode group. Uridine shows the most significant intensity changes with significant p values observed in 8 of 12 time points and in the nematodes. When all time points were analyzed, all 5 metabolites show significance at day 6 after infection. At or around day 6 of infection, IJs have developed into adult stages and should be reproducing. According to KEGG database (Kyoto Encyclopedia of Genes and Genomes), uracil and uridine are both involved in pyrimidine metabolism. Xylitol is involved in pentose and glucuronate interconversions. Phenyllactic acid and Phosphoenolpyruvate are both involved in phenylalanine, tyrosine, and tryptophan biosynthesis. All these pathways can be linked together through glycolysis and the pentose phosphate pathway.³⁶⁻³⁸

Fold changes were calculated to determine the change in intensity from each infected group compared to the uninfected group. Figure 6 is a heatmap displaying the fold changes and p values of all known metabolites detected for each group compared to the control group (Appendix, Tables 8-10). Fold changes in this heatmap are based on a log₂ scale of 5. The bright orange color represents the intensity is 32 times higher in the infected group compared to the uninfected group while the bright blue color means the intensity is 1/32 or 0.03125 times the intensity of the uninfected group. As infection progresses fold changes between the treatment groups and the uninfected group increase in either the positive or negative direction. The metabolites with increasing relative concentrations indicate more production as infection progresses. Since the insect itself dies within 48 hours of infection, these metabolites are likely being produced by either *S.*

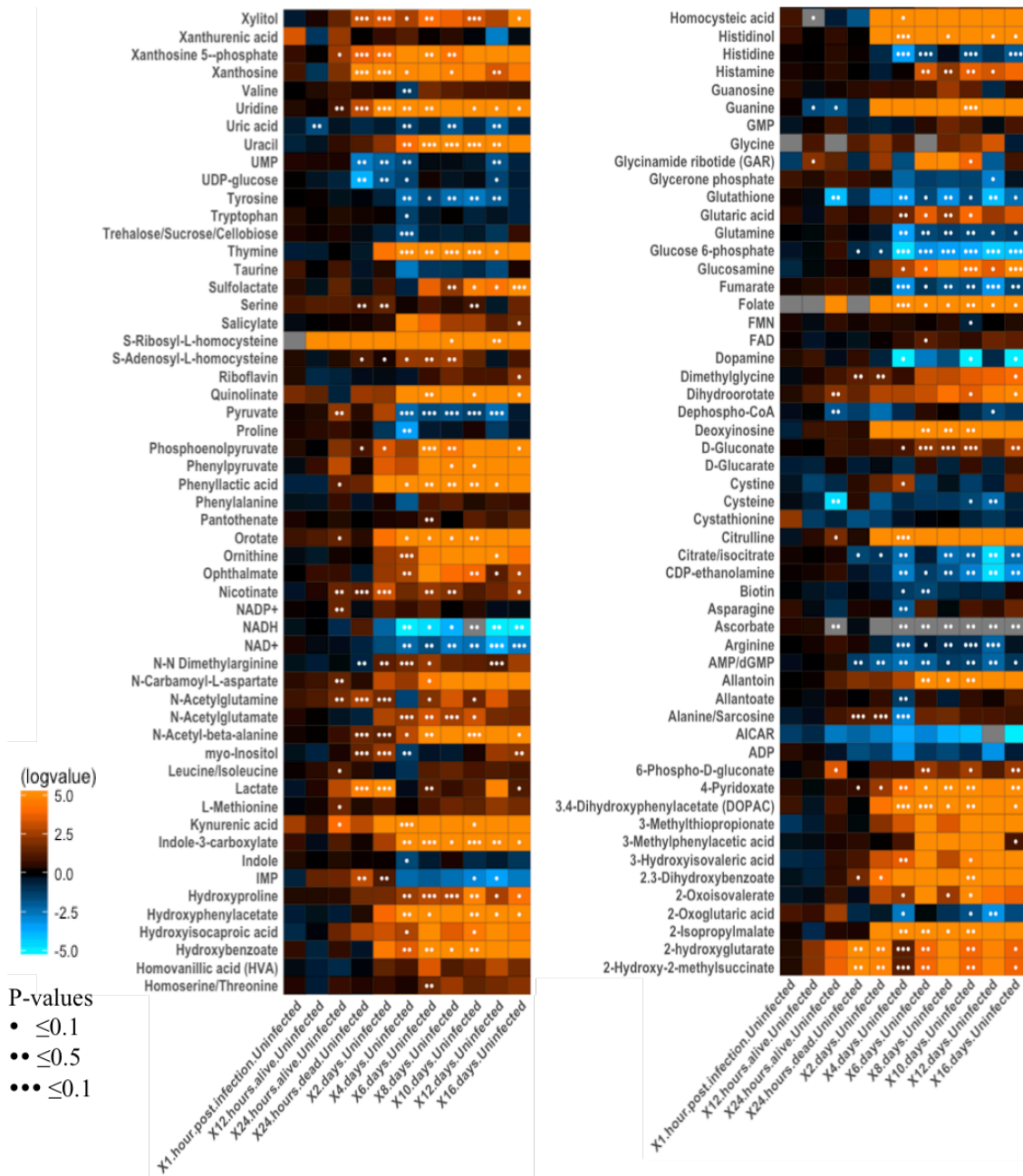


Figure 6. Heatmap displaying fold changes and p values of *G. mellonella* infected groups compared to the uninfected group on a log₂ scale of 5.

carpocapsae, *X. nematophila*, or both. Metabolites with decreasing relative concentrations indicate reduced production.

Visual inspection of average intestines across all groups revealed a subset of metabolites that were present in the infective juveniles but not present in the early infection groups of *G. mellonella* and other metabolites that were present in the early infection groups but not present in IJs. Folate and S-ribosyl-L-homocysteine were detected in the IJs but not in the uninfected, 1 hour, or 12 hour post infection groups. For both of these metabolites, the average intensity increases as infection increases with the highest average intensity at day 16 after infection. Glycinamide ribonucleotide (GAR), 5-Aminoimidazole-4-carboxamide ribonucleotide (AICAR), and Xanthosine 5-phosphate (XMP) were found in uninfected, 1 hour, and 12 hour groups but not in the IJs. The average intensity of AICAR decreases over time while the average intensity of XMP increases over time. According to the KEGG database, GAR, AICAR, and XMP are all involved in purine metabolism and the biosynthesis of secondary metabolites or metabolites that are not directly involved in normal growth, development, and reproduction.^{3,36-38}

Unknown Metabolites

During the untargeted, unknown metabolomics analysis over 54,000 spectral features were detected. This many spectral features cannot be processed so the number of spectral features was reduced by average intensity and p values as described in the methods section. Once reduced, a manageable number of just over 2,000 spectral features were analyzed.

PLS-DA plots are depicted for early, middle, and late groups in Figure 7. Although the early and middle infection groups do not show clear separation, the late groups are clearly separated. In the middle and late infection groups, the uninfected time point is separated in the z-direction that is not shown in a 2-D plot. Table 2 shows the total number of spectral features included in the PLS-DA plots and the number of spectral features with a VIP score over 1. In the early groups a total of 190 metabolites had VIP scores above 1 in both components while the middle and late groups had 549 and 491

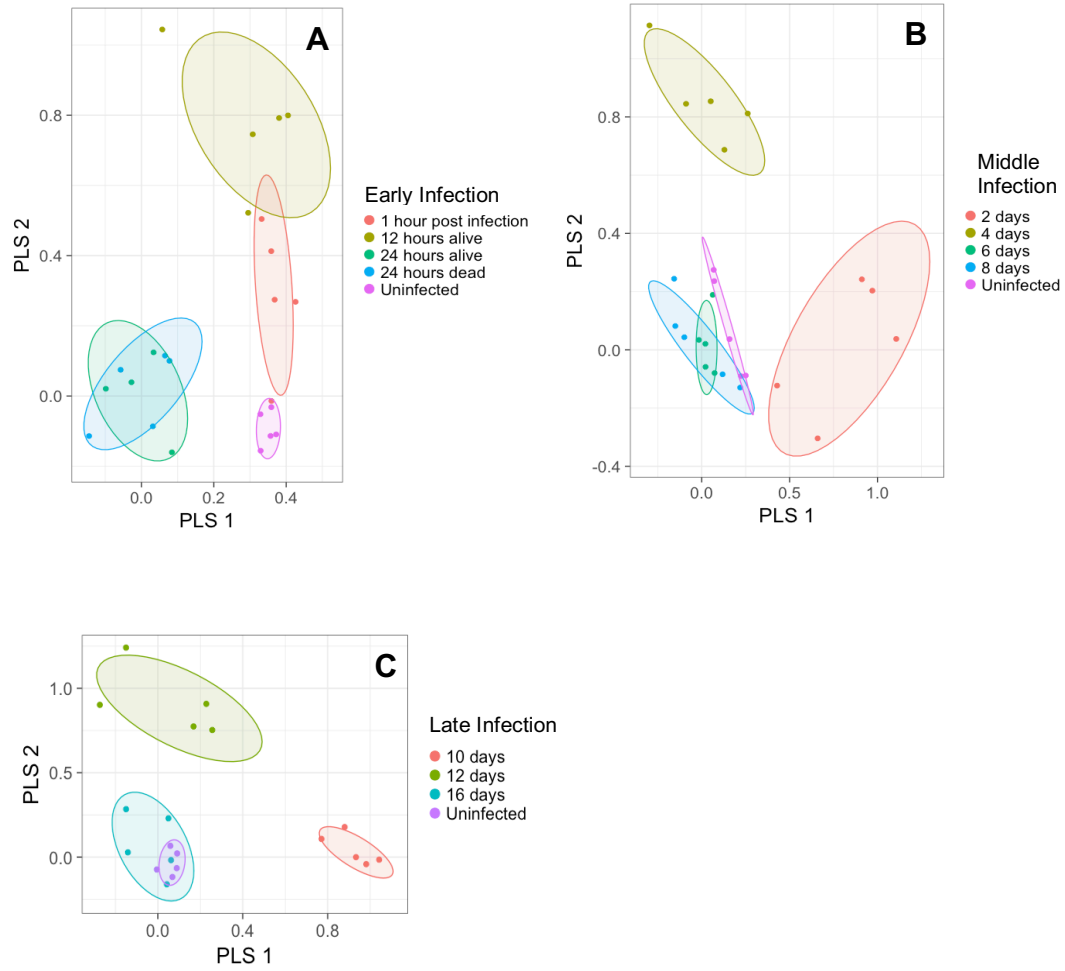


Figure 7. PLS-DA plots of unknown *G. mellonella* spectral features of early (A), middle (B), and late (C) groups compared to uninfected.

Table 3. Unknown spectral features of *G. mellonella* groups and number of VIP scores above 1.

Group	Number of Spectral Features	Top VIP scores in Component 1	Top VIP scores in Component 2
Early	1600	623	468
Middle	2049	1082	870
Late	2196	1161	854

metabolites with VIP scores above 1 in both components. An increase in the number of metabolites with a significant VIP score indicates more metabolic differences by class as infection progresses.

A heatmap of the reduced unknown spectral features was made without p values because of the large number of unknown spectral features (Figure 8). Most of the heatmap is blue representing a decrease in fold change from the infected time point to the uninfected group. This occurrence is due to the reduction of spectral features by significant p values compared to the uninfected group. Unknown spectral features displayed in the heatmap were searched through both HMDB and METLIN with inconclusive results. Most spectral features did not return any matches or returned multiple matches per spectral feature.

After initial analysis of the unknown data, the Goodrich-Blair lab provided two lists of metabolites they were interest in studying in more detail. The first list was related to virulence of the insect and the second list was related to nicotinate and nicotinamide metabolism. Using MAVEN, the chemical formula of each metabolite was matched to a m/z value in the unknown spectral features. After normalization, separate heatmaps were made of the metabolites detected (Figures 9 and 10). Several chemical formulas were found to have multiple peaks at varying retention times so all observable peaks were chosen to analyze. Although these chemical formulas of these spectral features matched the metabolites of interest, absolute identities of these spectral features cannot be

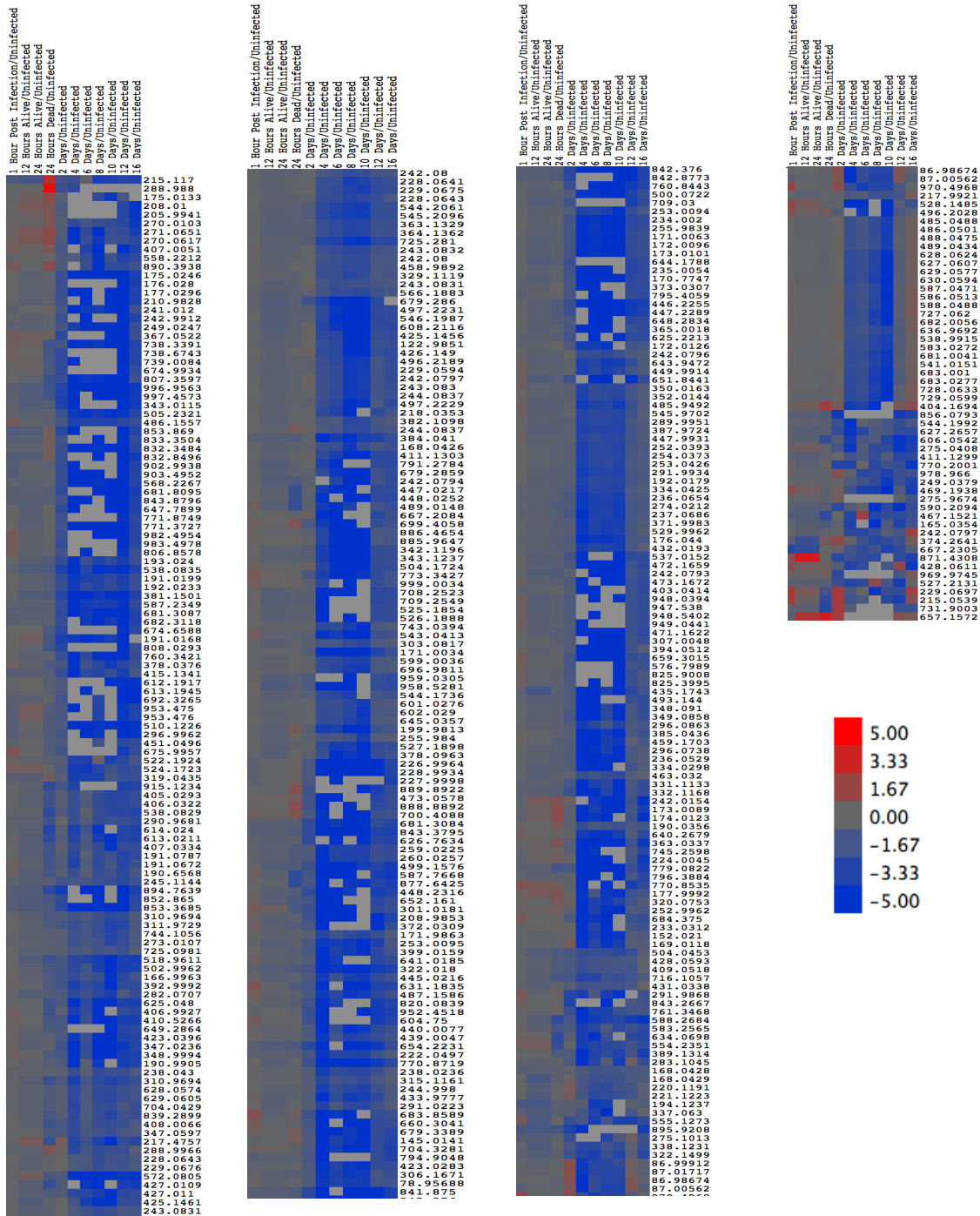


Figure 8. Heatmap of *G. mellonella* unknown spectral features compared to the uninfected group.

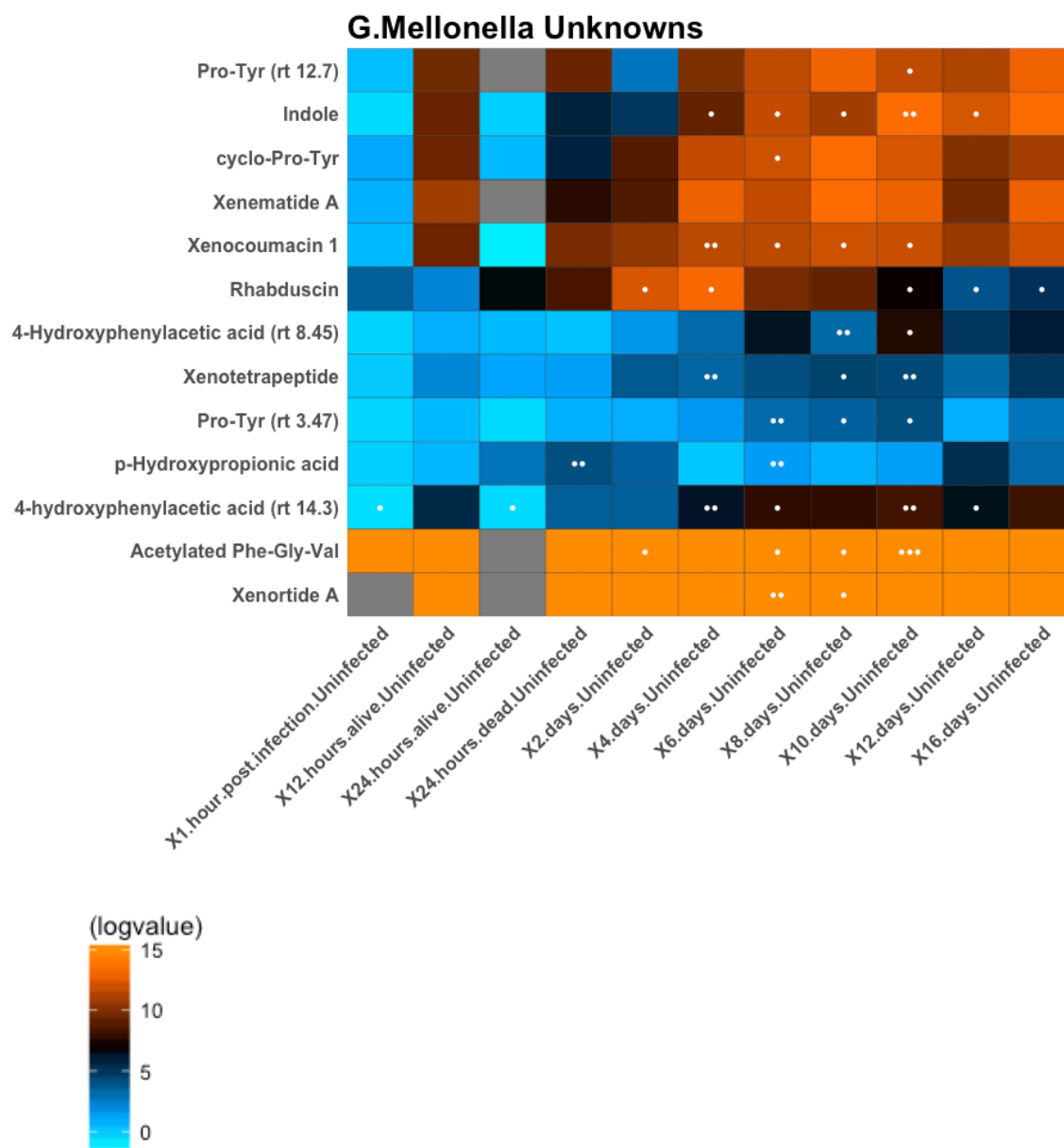


Figure 9. Heatmap of possible metabolites related to virulence matched by chemical formula.

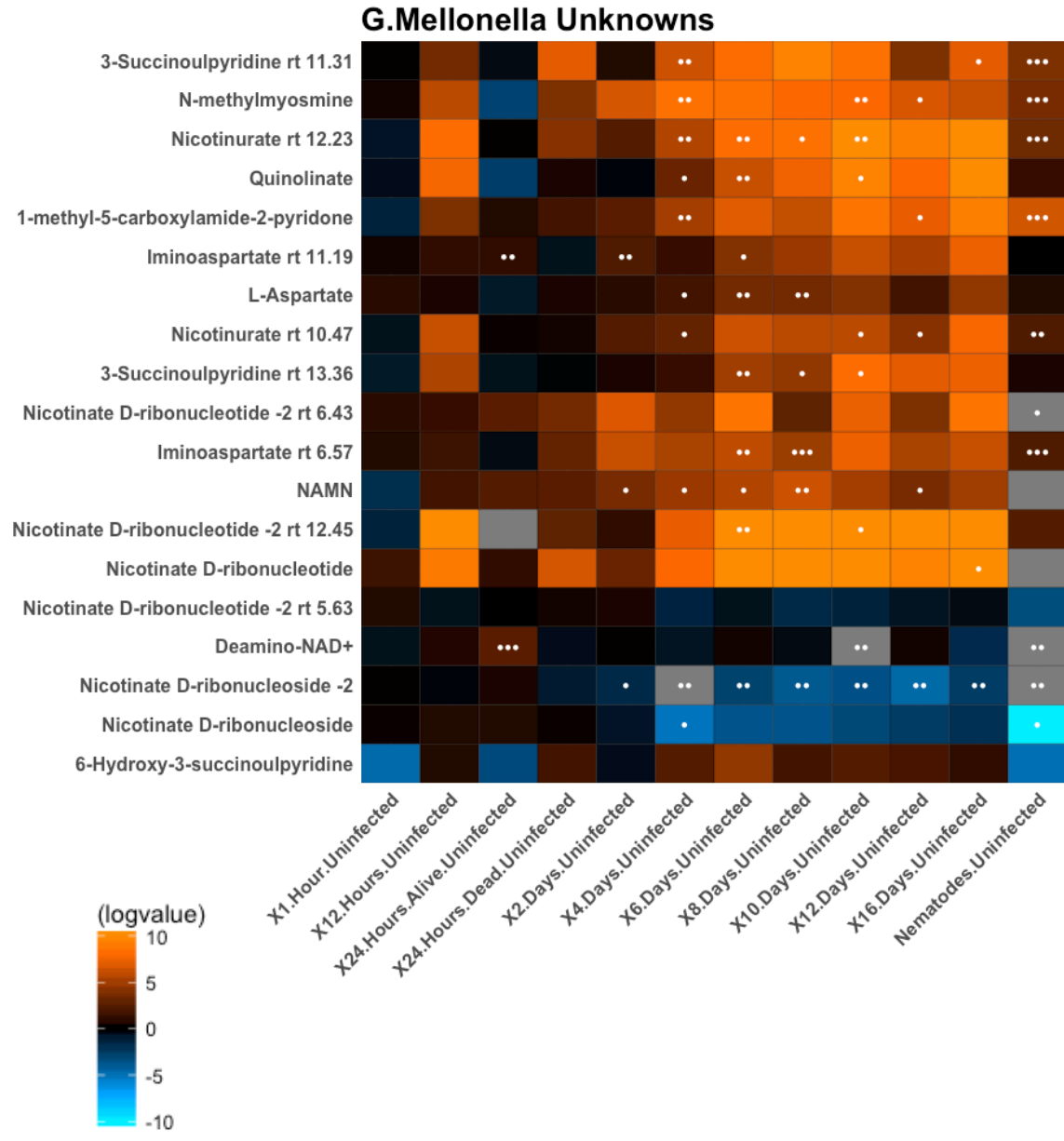


Figure 10. Heatmap of possible metabolites involved in nicotinate and nicotinamide metabolism matched by chemical formula.

confirmed without additional experiments in which high purity standards for each compound in the pathway are purchased or synthesized and analyzed using the same conditions as the samples to compare exact mass and retention time.

The metabolites related to virulence have increasing concentrations when compared to the uninfected as time progresses. Many metabolites in this heatmap show an increase in fold change at 12 hours after infection then a decrease in fold change at 24 hours alive. At 24 hours after infection, about half the *G. mellonella* samples had succumb to infection with all being deceased by 48 hours after infection. This change in intensities can also be seen in many of the known metabolites, which caused collaborators to develop an interest in the early infection time points for future studies.

The nicotinate and nicotinamide metabolism pathway includes known metabolites detected such as nicotinate, quinolinate, NAD⁺, NADP⁺, and NADH. Figure 10 shows unknown spectral features matched by chemical formula to a metabolite within this pathway. More than one peak was observed for several metabolites at both M-H and M-2H. Most metabolites show statistically significant fold changes in the middle and late infection groups as well as in the nematode samples, which correlates with the results from the known analysis.

Conclusion

Metabolite differences were detected between uninfected *G. mellonella* samples and samples infected with entomopathogenic *S. carpocapsae* nematodes. As time of infection and nematode development progressed, significant metabolites were revealed with most significant changes occurring between day 4 and day 10 after infection. Phenyllactic acid, phosphoenolpyruvate, uracil, uridine, and xylitol were determined to be among the most significant metabolites within this biological system. Unknown analysis resulted in a large number of spectral features that had to be reduced in order to align with current processing methods. This reduction, based on statistical significance and average intensity of infected time points compared to the uninfected group, could be causing important spectral features related to the IJs being removed leading to an incomplete model. Metabolites search by chemical formula relating to virulence and

nicotinate and nicotinamide metabolism were detected but cannot be confirmed without further experiments. Based on current results from this experiment, future experiments could focus on metabolite changes from beginning of infection until the insect host dies and confirming the presence of metabolites related to virulence and the nicotinate and nicotinamide pathway.

CHAPTER II
UNTARGETED METABOLOMICS OF *XENORHABDUS*
***NEMATOPHILA* WITH *NIL* LOCUS DELETION**

Abstract

Whole cell samples and supernatant samples of two strains of *Xenorhabdus nematophila* were analyzed by UPLC-HRMS using an untargeted metabolomics approach. In both strains the *nil* locus had been deleted but was complemented in the control strain. A total of 85 known metabolites were detected in the whole cell samples and 67 known metabolites were detected in the supernatant samples. Of the metabolites not detected in the supernatant samples, most had higher intensities in the control strain. Results of this metabolomics experiments was compared to the infection model of the previous chapter. A total of 7465 unknown spectral features were detected in the whole cell samples and 6181 unknown features were detected in the supernatant samples. Unknown spectral features were reduced by p value then exact masses were searched through online databases for potential matches.

Introduction

Xenorhabdus nematophila are gram-negative, gammaproteobacteria that have mutualistic relationship with *Steinernema carpocapsae* nematodes. Together, they work to infect and kill a host becoming a pathogen of a large variety of insects.^{33,39} *S. carpocapsae* nematodes carry between 50-200 colony-forming units of *X. nematophila* in a region known as the receptacle.^{39,40} The non-feeding, soil-dwelling IJs can survive for long periods of time without an insect host. Once a suitable host is found, the nematode enters the host through natural openings, sheds the outer cuticle, and migrates to the blood cavity. The ingestion of blood from the insect triggers the release of *X. nematophila*. *X. nematophila* multiply within the blood of the insect and work to produce compounds that suppress insect immunity leading to death of the insect along with producing compounds that protect the cadaver from other infections and ant scavengers. Hundreds of thousands of eggs can undergo development into the IJ stage within one insect cadaver. *X. nematophila* colonize the newly developed IJ's before they emerge from the cadaver to complete the cycle.³⁹

X. nematophila is thought to convert cadaver biomass into substrates that support nematode development. While both *X. nematophila* and *S. carpocapsae* both benefit from this mutualistic relationship, studies have shown that colonized IJs do not live as long as un-colonized IJs.³⁹ The basis of this colonization is believed to stem from the nematode intestine localization (*nil*) locus consisting of *nilA*, *nilB*, and *nilC*, located at symbiosis region 1 (SR1).^{30,40} *nilA* is an inner membrane protein consisting of 90 amino acids while *nilB* and *nilC* are outer membrane proteins consisting of 466 and 282 amino acids, respectively.⁴⁰ The location of *nilB* as a surface exposed beta barrel protein is thought to be responsible for colonization due to its interaction with the receptacle surface within the nematode.^{40,41}

Studies have shown that mutant strains lacking SR1 completely are not able to colonize a nematode host.⁴¹ Certain mutations in *nilA* lead to colonization of approximately 2.5% of the wild type level but *nilB* and *nilC* mutants are not able to colonize over the detection limit.⁴⁰ *X. nematophila* are known to specifically colonize *S. carpocapsae* nematodes in nature.³³ Interestingly, of all *Xenorhabdus* species, only *X. nematophila* have the *nil* locus but when *nil* loci were incorporated into the chromosomes of other *Xenorhabdus* bacteria, they were able to colonize *S. carpocapsae*.⁴²

Materials and Methods

X. Nematophila Samples

X. nematophila samples were supplied by the Goodrich-Blair lab from the University of Tennessee, Knoxville. Samples consisted of three biological replicates of two *X. nematophila* strains and three biological replicates of supernatant samples from the two strains. The strain considered the wild type or the control strain (1496) had the *nil* locus deleted but was complemented with SR1 in the Tn7 site. The mutant strain (1465) had the *nil* locus deleted but was not complemented with SR1. Cells were grown in minimal medium.

Metabolomics

Samples were extracted using the same procedures detailed in Chapter 1. After extraction, samples were dried under nitrogen gas before being suspended in 300 μ L of Milli-Q water. Samples were analyzed using UPLC-HRMS using the same mass spectrometer, protocols, and specifications as described in Chapter 1. For known metabolite analysis, RAW files were converted to MZML files using MS Convert before being loaded onto MAVEN to match peaks according to retention time and exact mass with metabolites from the known compound list.

For unknown analysis, RAW data files were uploaded to XCMS Online (Scripps Research Institute) for analysis. Dataset 1 was the control strain and dataset 2 was the 1495 strain. A pairwise job was chosen to compare the two whole cell strains. UPLC/Orbitrap parameters were used altering only the polarity to negative mode. Isotopes and adducts were removed from the unknown spectral features and punitive identities of remaining spectral features were given from the METLIN database. Unknown spectral features for the supernatant samples were then processed using the same procedures.

Results and Discussion

Known Metabolomics

A total of 85 known metabolites and 7465 unknown spectral features were detected in the whole cell samples (Appendix, Table 31). A total of 67 known metabolites and 6181 unknown spectral features were detected in the supernatant samples (Appendix, Table 32). Table 4 displays the total number of known and unknown metabolites detected in each sample set along with significant p values and VIP scores. Of the unknown spectral features detected, annotations were possible in 11.4% of whole cell unknown spectral features and 13.1% of supernatant unknown spectral features. Annotations were confirmed in 1.6% of whole cell unknown spectral features and 2.2% of supernatant unknown spectral features.

Table 4. Knowns and unknowns detected in *X. nematophila* samples.

	Whole Cell	Supernatant
Knowns detected	85	67
Knowns with significant p value	21	11
Knowns with significant VIP score	34	26
Unknowns detected	7465	6181
Unknowns with significant p value	743	908
Unknowns with significant VIP score	2962	2617
Percent of unknowns annotated	11.4%	13.1%
Percent of confirmed unknown annotations	1.6%	2.2%

All 67 metabolites from the supernatant samples were detected in the whole cell samples. Table 5 displays a list of metabolites that were detected in the whole cell samples but not in the supernatant samples. Of these metabolites listed, all but Xanthosine, NAD⁺, and sedoheptulose bisphosphate have a higher intensity in the control group compared to the 1495 strain. NAD⁺ is used in the nicotinate and nicotinamide pathway, which was studied in the infection model. Xanthosine was also detected in the infection model and is involved in purine metabolism. Although Xanthosine was not determined to be significant in the infection model, XMP, a precursor for Xanthosine, was significant.

Of the metabolites with higher intensities in the control samples, many belong to the same pathways. Alpha-ketoglutarate and UDP-glucuronate are involved in pentose and glucuronate interconversions. UDP-N-acetylglucosamine and glucosamine phosphate are involved in amino sugar and nucleotide sugar metabolism. Guanine, adenosine, AMP/dGMP, and GAR are involved in purine metabolism. Fumarate and FMN are involved in oxidative phosphorylation. Xylitol 5-phosphate is only involved in one reaction in which ATP reacts with Xylitol to form ADP and Xylitol 5-phosphate. CMP is involved in pyrimidine metabolism.³⁶⁻³⁸

PLS-DA plots shown in Figure 11 show clear separation between two strains in both whole cell and supernatant samples. In the whole cell samples, 34 metabolites had a VIP score above 1 in both components with 39 in component 1 and 46 in component 2

Table 5: Metabolites detected in *X. nemaophila* cells but not in supernatant.

Metabolite Name
alpha-Ketoglutarate
2-Hydroxy-2-methylsuccinate
Guanine
Xylitol 5-phosphate
Glucosamine phosphate
Adenosine
Xanthosine
Glycinamide ribonucleotide (GAR)
Octulose 8/1P
Cytidine monophosphate (CMP)
Trehalose/Sucrose/Cellobiose
AMP/dGMP
Sedoheptulose biphosphate
Flavin mononucleotide (FMN)
UDP-glucuronate
UDP-N-acetylglucosamine
NAD+
Fumarate

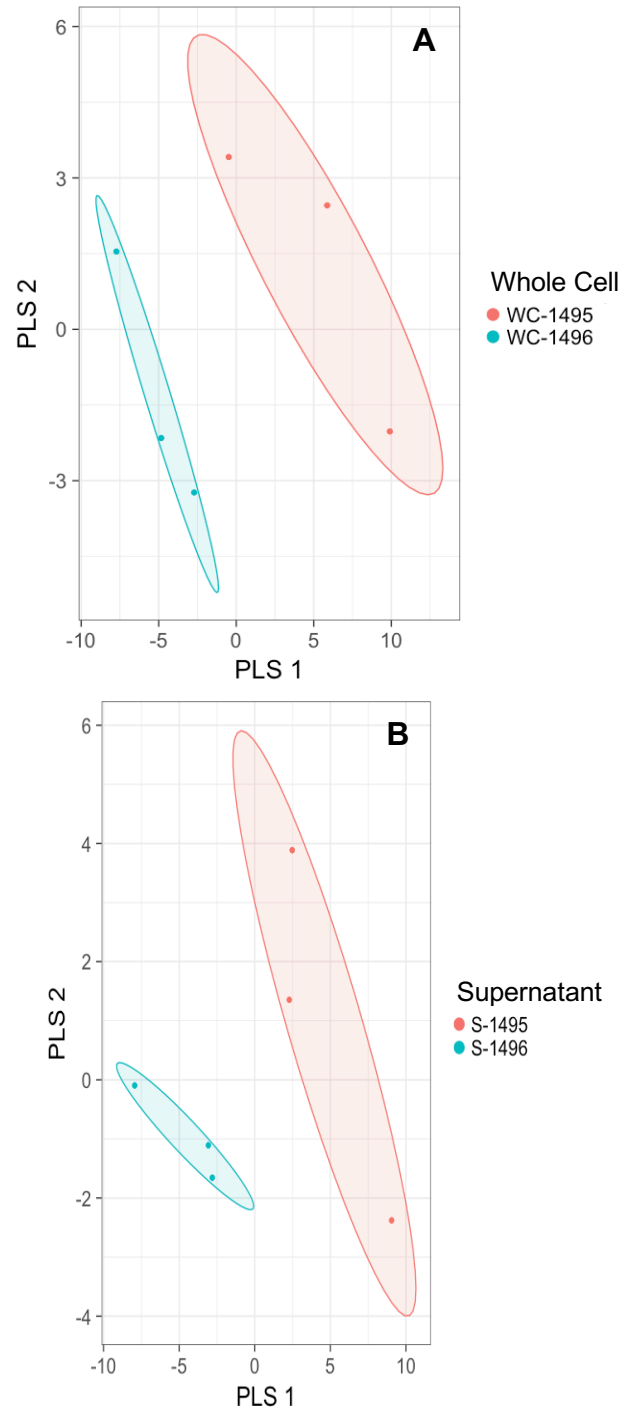


Figure 11. PLS-DA plots of known metabolites in *X. nematophila* whole cell (A) and supernatant samples (B).

(Appendix, Table 16). In the supernatant samples, 26 metabolites had a VIP score above 1 in both components with 29 in component 1 and 35 in component 2 (Appendix, Table 17). A complete list of these metabolites with significant VIP scores can be found in the appendix in Tables 14 and 15. Of the metabolites with VIP scores above 1 in both components, 9 metabolites were detected in both the whole cell and the supernatant samples. These metabolites are adenosine, citrate/isocitrate, deoxyribose phosphate, guanosine, phenylalanine, tryptophan, tyrosine, UDP-glucuronate, and uracil.

A heatmap of fold changes with significant p values is displayed in Figure 12 on a \log_2 scale of 3 (Appendix, Tables 14-15). Of the 21 metabolites in the whole cell samples with significant p values, 12 metabolites also had a significant VIP score. These metabolites are sedoheptulose 1/7-phosphate, UMP, guanosine, 6-phospho-D-gluconate, CMP, citrate/isocitrate, methionine, valine, D-gluconate, lipoate, uridine, acetylphosphate. Of the 11 metabolites with a significant p value in the supernatant samples, 5 metabolites also had a significant VIP score. These metabolites are uracil, alanine/sarcosine, thymine, 2-dehydro-D-gluconate, and pyruvate.

When significant metabolites from this experiment were compared to the significant metabolites from infection model experiment in Chapter 1, several metabolites were determined to be significant in both experiments. Uridine had a significant p value in all time points in the infection model except 1 hour, 12 hours, and 8 days as well as a significant VIP score in all PLS-DA plots. Uridine also had a significant p value and VIP score in the whole cells samples in experiment 2. Uridine is in the pyrimidine metabolism pathway and is involved in converting uracil to UMP and vice versa.³⁶⁻³⁸ Another pyrimidine metabolism pathway metabolite, uracil, had a significant p values and VIP scores in the infection model and was also detected and significant in the supernatant samples. Uridine and uracil both had a higher relative intensity in the control strain and increased in relative intensity as infection progressed in the infection model. Other metabolites from the pyrimidine pathway detected in the whole cell samples such as malate, thymine, dTDP, orotate, and UDP-glucose follow the same trend as having a lower intensity in the mutant strain. Since all these metabolites within this pathway have

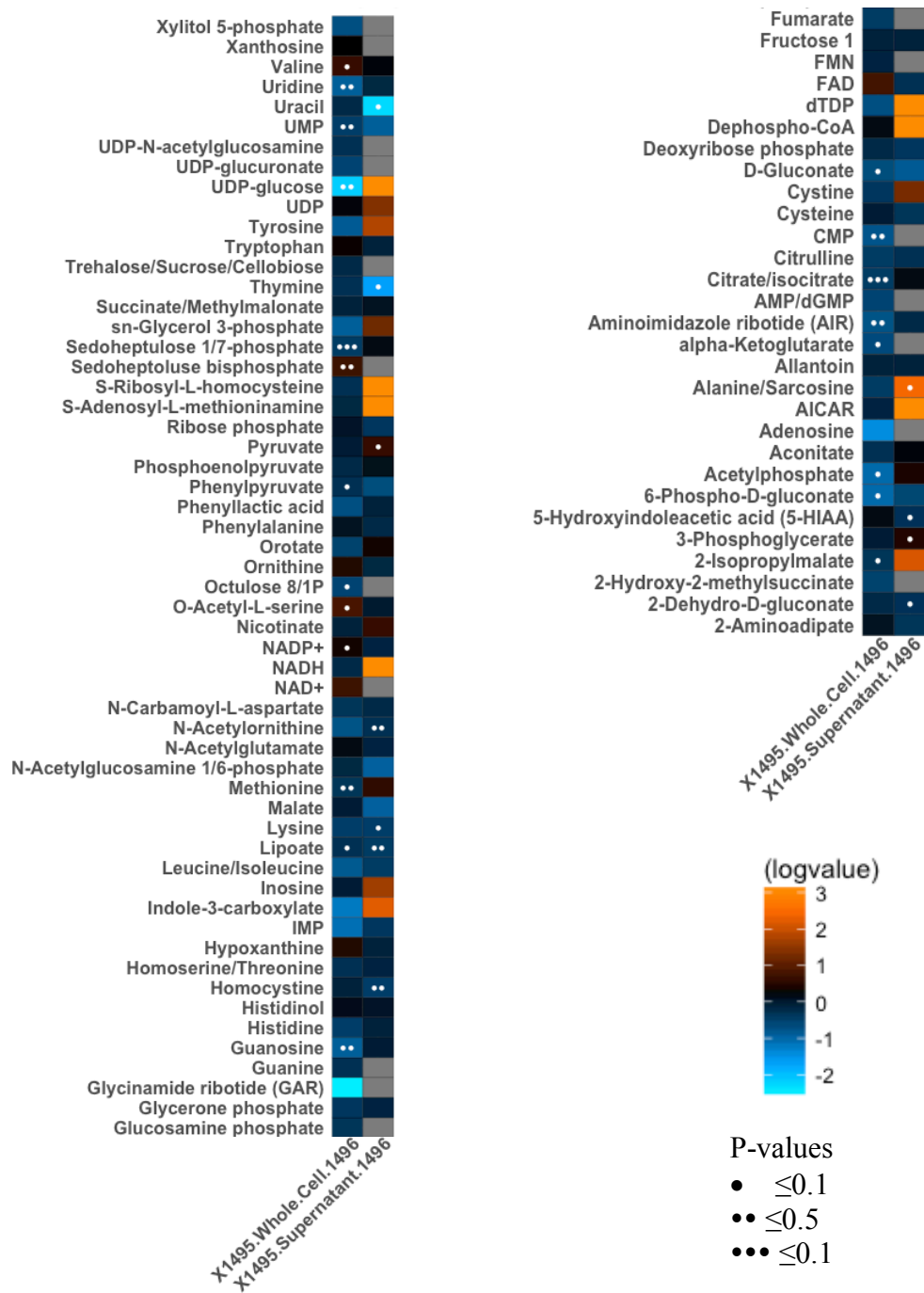


Figure 12. Heatmap of *X. nematophila* mutant strain compared to the control strain in whole cell and supernatant samples.

a lower relative intensity in the mutant strain, this is an indication that the deletion of the *nil* loci without complementing for the deletion affects the pyrimidine pathway. To confirm this hypothesis, a targeted metabolomics experiment should be performed to determine concentration changes of all the metabolites involved in the pyrimidine pathway.

Another pathway of interest determined to be meaningful in both experiments is the purine metabolism pathway. Xanthosine and XMP were both detected in *G. mellonella* but only XMP was detected in the whole cell samples. Other metabolites within this pathway that were also down regulated in the mutant strain are adenosine, AICAR, allantoin, AIR, GAR, IMP, and inosine. When compared to the infection model, adenosine, AIR, and inosine were not detected. XMP, Xanthosine, allantoin, and GAR all increased in relative concentration as infection progressed with AICAR and IMP decreasing. AICAR is also influenced by histidine metabolism and IMP is directly related to AICAR through FAICAR, which could explain the difference in intensity compared to other metabolites in the pathway.

Unknown Metabolomics

After processing from XCMS Online, the *X. nematophila* whole cell samples had a total of 7465 unknown spectral features with 743 having a p value of less than 0.1 and the supernatant samples had a total of 6181 unknown spectral features with 908 having a significant p value. After making PLS-DA plots of all spectral features, whole cell samples had 2962 spectral features with a VIP score above 1 in both components. Supernatant had 2617 spectral features with a VIP score above 1 in both components. None of the spectral features in the whole cell samples or supernatant samples had a significant p value and a significant VIP score indicating the model produced from the unknown spectral features is being heavily influenced by insignificant metabolites and is not an accurate model of metabolic changes.

To specifically analyze significant metabolites, the list of unknown spectral features was reduced to only spectral features with a significant p value. A second set of

PLS-DA plots were made for whole cell and supernatant samples (Figure 13). The whole cell samples had 306 metabolites with significant VIP score in both components (332 in component 1 and 339 in component 2). In supernatant samples, 404 metabolites had a significant VIP score above 1 in both components (421 in component 1 and 432 in component 2). With so many metabolites having a high VIP score, this model is more indicative of significant metabolites within the biological system.

Unknown spectral features with a significant p value and VIP score above 1 were then analyzed using HMDB to determine any punitive matches. While most matches resulted in numerous identities, 35 metabolites were identified in whole cell samples and 53 identified in supernatant samples. These matches from HMDB were also compared to the METLIN database for cross-validation with 9 confirmed in supernatant and 4 confirmed in whole cell. The *m/z*, compound identities, and chemical formulas of validated metabolites are shown in Tables 6 and 7.

Of the 4 metabolites in the whole cell samples identified by database matches, dCMP (deoxycytidine monophosphate) is the only metabolite identified that is likely to be present in the sample and is involved in pyrimidine metabolism. All other possible matches are extremely unlikely to be found in this biological system. Neoacrimarine G is an alkaloid found in citrus, chloropentafluoroethane is a chlorofluorocarbon once used as a refrigerant but has been banned by the Montreal Protocol since January 1, 1996, and (2*r*)-2-hydroxy-2-(4-hydroxyphenyl)ethyl glucosinolate is found in mustard family plants.

Table 6. Confirmed annotations for *X. nematophila* whole cell samples.

<i>m/z</i>	Compound Identity	Chemical formula
514.1533705	Neoacrimarine G	C ₂₉ H ₂₅ NO ₈
134.9433168	Chloropentafluoroethane	C ₂ ClF ₅
436.0340522	(2 <i>r</i>)-2-hydroxy-2-(4-hydroxyphenyl)ethyl glucosinolate	C ₁₅ H ₂₁ NO ₁₁ S ₂
288.0407888	dCMP	C ₉ H ₁₄ N ₃ O ₇ P

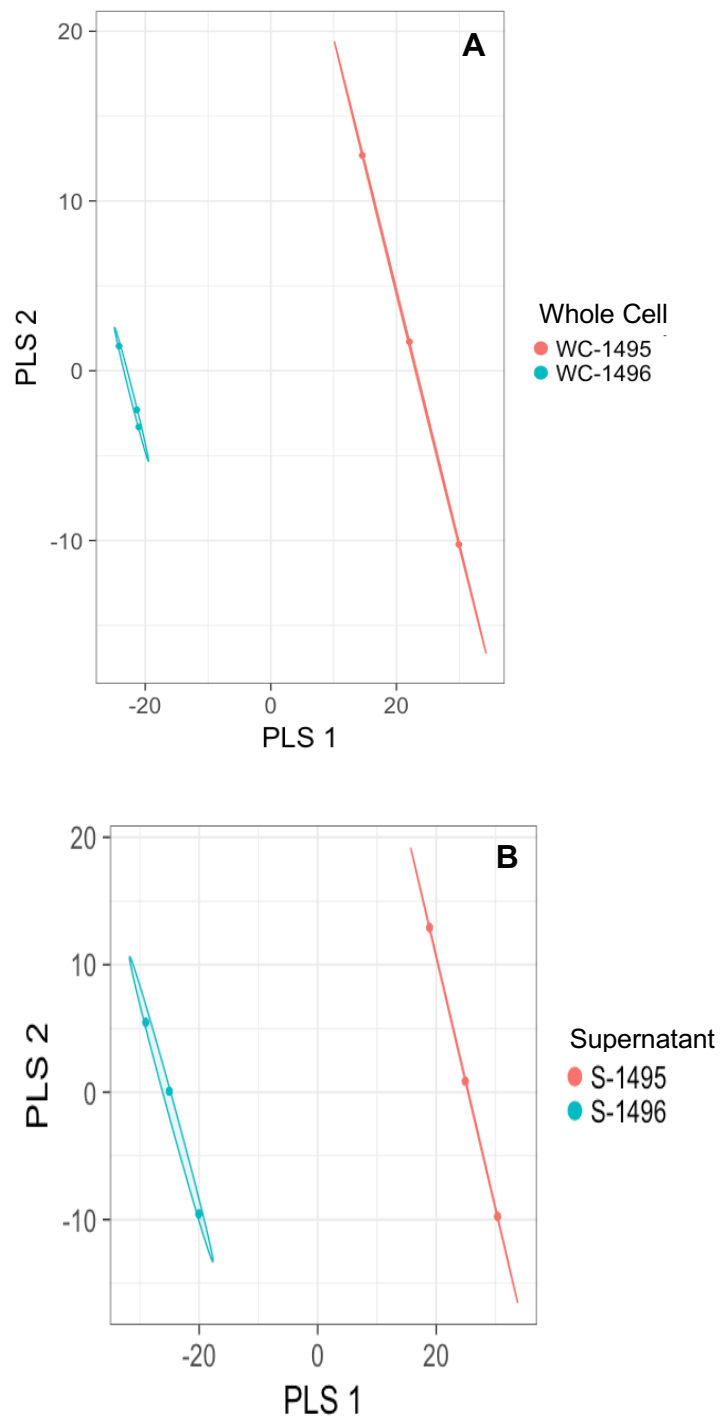


Figure 13. PLS-DA plots of *X. nematophila* unknown spectral features for whole cell (A) and supernatant (B) samples.

Table 7. Confirmed annotations for *X. nematophila* supernatant samples.

<i>m/z</i>	Compound Identity	Chemical formula
313.0442653	5'-phosphoribosyl-n-formylglycinamide (FGAR)	C ₈ H ₁₅ N ₂ O ₉ P
403.5555379	Acetyl-CoA	C ₂₃ H ₃₈ N ₇ O ₁₇ P ₃ S
311.1979392	Oseltamivir	C ₁₆ H ₂₈ N ₂ O ₄
366.2286597	Buspirone	C ₂₁ H ₃₁ N ₅ O ₂
141.016891	Naphthalene-2-thiol	C ₁₀ H ₈ S
201.0255251	5-hydroxy-2-oxo-4-ureido-2,5-dihydro-1h-imidazole-5-carboxylate	C ₅ H ₆ N ₄ O ₅
523.3749211	3beta-acetoxy-11alpha-methoxy-12-ursen-28-oic acid	C ₃₄ H ₅₄ O ₅
172.8989722	Bis(methylthio) selenide	C ₂ H ₆ S ₂ Se
255.179631	Lysyl-lysine	C ₁₂ H ₂₆ N ₄ O ₃

Metabolites identified by both databases in the supernatant samples show 6 metabolites that are likely to be present in the samples. FGAR is involved in aminoimidazole ribonucleotide biosynthesis and purine metabolism. Acetyl-CoA participates in biosynthesis of fatty acids and sterol as well as the oxidation of fatty acids and metabolism of many amino acids. Naphthalene-2-thiol is found in cell membranes, 5-hydroxy-2-oxo-4-ureido-2,5-dihydro-1h-imidazole-5-carboxylate exists in all living organisms, and 3beta-acetoxy-11alpha-methoxy-12-ursen-28-oic acid is found in cellular membranes and extracellular space. Lysyl-lysine is a dipeptide of two lysine residues resulting from the incomplete breakdown of protein digestion. Other metabolites matched by exact mass are unlikely to be present in the supernatant samples. Oseltamivir and Buspirone are both drugs that are only found when those drugs have been taken and Bis(methylthio) selenide is found in onion-family vegetables.

Out of the 711 unknown spectral features searched for, only 88 returned unique matches using HMDB. After validating with METLIN database, 13 *m/z* values had unique metabolite matches by both databases. Disregarding matches that do not reasonably apply to the biological system leaves less than 1% of significant unknown metabolites annotated by databases matches. This low annotation rate reveals one

disadvantage to unknown metabolomics analysis. Annotating unknown spectral features is extremely important to get a thorough representation of phenotype since known chemical libraries are generally small compared to the amount of detected spectral features. Building a large known metabolite library is not practical so better annotation tools for easily and accurately identifying unknown spectral features would be beneficial for unknown analysis.

Conclusion

Deletion of the *nil* locus of *X. nematophila* causes many metabolite differences in both whole cell and supernatant. When compared to the control strain, deletion of *nil* loci without complementing for the deletion caused a higher intensity in 21% of metabolites detected in the whole cell samples and about 42% of metabolites detected in the supernatant samples. Unfortunately, proteomics analysis revealed cell lyses within the supernatant that could lead to flawed conclusions. The 18 metabolites not detected in the supernatant is likely underrepresented with far fewer metabolites in supernatant that does not contain cell lyses. Many unknown spectral features had both significant p values and VIP scores, but the lack of unique database annotations hinders identification of these features.

CONCLUSION

In conclusion, using UPLC-HRMS to study metabolomics of mutualistic and pathogenic relations can offer great insight into the functions of a biological system. A detailed understanding of the relationships between *G. mellonella*, *S. carpocapsae*, and *X. nematophila* can lead to the development of bio insecticides to control insect populations. The purpose of an untargeted metabolomics approach is to detect as many spectral features as possible and develop new hypotheses for future studies. By studying both the complete biological system of *G. mellonella*, *S. carpocapsae*, and *X. nematophila*, then studying *X. nematophila* mutants in detail, we have been able to determine specific metabolic pathways that relate the two experiments.

The infection model consisted of *G. mellonella* infected with entomopathogenic nematodes carrying *X. nematophila* bacteria. By comparing statistical significance with significant VIP scores, several key metabolites were detected throughout the infection model. The metabolites belonged are involved in pyrimidine metabolism, pentose and glucuronate interconversions, and phenylalanine/tyrosine/tryptophan biosynthesis. Three metabolites were also detected within the infection model but was not detected in the IJs, which are involved in purine metabolism. Unknown analysis revealed many significant spectral features, but annotation was unsuccessful.

Several metabolic differences were detected between control and mutant strains of *X. nematophila*. In both strains the *nil* locus was deleted but this deletion was complemented for in the control strain. Whole cell samples and supernatant samples for both strains were analyzed. 18 more metabolites were detected in the whole cell samples that were not detected in the supernatant samples. Fold changes for metabolites detected in *X. nematophila* within pyrimidine and purine metabolism pathways had lower intensities in the mutant strain compared to the control strain. Of the significant unknown spectral features, less than 1% were annotated using HMDB and METLIN.

REFERENCES

- (1) Zhou, B.; Xiao, J. F.; Tuli, L.; Ressom, H. W. *Mol. Biosyst.* **2012**, *8*, 470–481.
- (2) Androulakis, I. P. *Crit. Rev. Biomed. Engineering* **2013**, *41* (3), 205–221.
- (3) Dettmer, K.; Aronov, P. A.; Hammock, B. D. *Mass Spectrom. Rev.* **2007**, *26* (1), 51–78.
- (4) Fiehn, O. *Plant Mol. Biol.* **2002**, *48*, 155–171.
- (5) Goodwin, C. R.; Sherrod, S. D.; Marasco, C. C.; Bachmann, B. O.; Schrammsapya, N.; Wikswo, J. P.; Mclean, J. A. *Anal. Chem.* **2014**, *86*, 6563–6571.
- (6) Goodacre, R.; Vaidyanathan, S.; Dunn, W. B.; Harrigan, G. G.; Kell, D. B. *TRENDS Biotechnol.* **2004**, *22* (5), 245–252.
- (7) Jurowski, K.; Kochan, K.; Walczak, J.; Baranska, M.; Piekoszewski, W.; Buszewski, B. *Crit. Rev. Anal. Chem.* **2017**, No. April.
- (8) Xiao, J. F.; Zhou, B.; Ressom, H. W. *Trends Anal. Chem.* **2012**, *32*, 1–14.
- (9) Patti, G. J.; Yanes, O.; Siuzdak, G. *Nat. Rev. Mol. Cell Biol.* **2012**, *13* (4), 263–269.
- (10) Wishart, D. S.; Tzur, D.; Knox, C.; Eisner, R.; Guo, A. C.; Young, N.; Cheng, D.; Jewell, K.; Arndt, D.; Sawhney, S.; Fung, C.; Nikolai, L.; Lewis, M.; Coutouly, M.; Forsythe, I.; Tang, P.; Shrivastava, S.; Jeroncic, K.; Stothard, P.; Amegbey, G.; Block, D.; Hau, D. D.; Wagner, J.; Miniaci, J.; Clements, M.; Gebremedhin, M.; Guo, N.; Zhang, Y.; Duggan, G. E.; Macinnis, G. D.; Weljie, A. M.; Dowlatabadi, R.; Bamforth, F.; Clive, D.; Greiner, R.; Li, L.; Marrie, T.; Sykes, B. D.; Vogel, H. J.; Querengesser, L. *Nucleic Acids Res.* **2007**, *35* (January), 521–526.
- (11) Patti, G. J.; Yanes, O.; Siuzdak, G. *Nat. Rev. Mol. Cell Biol.* **2012**, *13* (4), 263–269.
- (12) Want, E. J.; Wilson, I. D.; Gika, H.; Theodoridis, G.; Plumb, R. S.; Shockcor, J.; Holmes, E.; Nicholson, J. K. *Nat. Protoc.* **2010**, *5* (6), 1005–1018.
- (13) Miller, J. M. *Chromatography: Concepts and Contrasts*, Second Edi.; John Wiley & Sons, Inc.: Hoboken, New Jersey, 2005.
- (14) Gumustas, M.; Kurbanoglu, S.; Uslu, B.; Ozkan, S. A. *Chromatographia* **2013**, *76*, 1365–1427.
- (15) Gross, J. H. *Mass Spectrometry*, Second.; Springer: Heidelberg, 2011.
- (16) Hu, Q.; Noll, R. J.; Li, H.; Makarov, A.; Cooks, R. G. *J. Mass Spectrom.* **2005**, *40*, 430–443.
- (17) Strupat, K.; Scheibner, O.; Bromirski, M. *Thermo Fish. Sci.* **2013**.
- (18) Chambers, M. C.; Maclean, B.; Burke, R.; Amodei, D.; Runderman, D. L.; Neumann, S.; Gatto, L.; Fisher, B.; Pratt, B.; Egertson, J.; Hoff, K.; Kessner, D.; Tasman, N.; Shulman, N.; Frewen, B.; Baker, T. A.; Brusniak, M.-Y.; Paulse, C.; Creasy, D.; Flashner, L.; Kani, K.; Moulding, C.; Seymour, S. L.; Nuwaysir, L. M.; Lefebvre, B.; Kuhlmann, F.; Roark, J.; Rainer, P.; Detlev, S.; Hemenway, T.; Huhmer, A.; Langridge, J.; Conolly, B.; Chadick, T.; Holly, K.; Eckels, J.; Deutsch, E. W.; Mortiz, R. L.; Katz, J. E.; Agus, D. B.; MacCoss, M.; Tabb, D. L.; Mallick, P. *Nat. Biotechnol.* **2012**, *30* (10), 918–920.
- (19) Clasquin, M. F.; Melamud, E.; Rabinowitz, J. D. *Curr. Protoc. Bioinforma.* **2012**, 14.11.1-14.11.23.

- (20) Benton, P. H.; Ivanisevic, J.; Rinehart, D.; Epstein, A.; Kurczy, M. E.; Boska, M. D.; Gendelman, H. E.; Siuzdak, G. *Metabolomics* **2015**, *11* (4), 1029–1034.
- (21) Tautenhahn, R.; Patti, G. J.; Rinehart, D.; Siuzdak, G. *Anal. Chem.* **2012**, *84* (11), 5035–5039.
- (22) Wang, B.; Shi, Z.; Weber, G. F.; Kennedy, M. A. *Anal. Bioanal. Chem.* **2013**, *405* (26), 8419–8429.
- (23) Worley, B.; Powers, R. *Curr. Metabolomics* **2013**, *1* (1), 92–107.
- (24) Szymanska, E.; Saccenti, E.; Smilde, A. K.; Westerhuis, J. A. *Metabolomics* **2012**, *8*.
- (25) Smilde, A. K.; Velzen, Æ. E. J. J. Van; Duijnhoven, Æ. J. P. M. Van; Dorsten, F. A. Van. *Metabolomics* **2008**, *4* (1), 81–89.
- (26) Xia, J.; Psychogios, N.; Young, N.; Wishart, D. S. *Nucleic Acids Res.* **2009**, *37* (February), 652–660.
- (27) Banerjee, P.; Ghosh, S.; Dutta, M.; Subramani, E.; Khalpada, J.; RoyChoudhury, S.; Chakravarty, B.; Chaudhury, K. *PLoS One* **2013**, *8* (11).
- (28) Gromski, P. S.; Muhamadali, H.; Ellis, D. I.; Xu, Y.; Correa, E.; Turner, M. L.; Goodacre, R. *Anal. Chim. Acta* **2015**, *879*, 10–23.
- (29) Harding, C. R.; Schroeder, G. N.; Collins, J. W.; Frankel, G. *J. Vis. Exp.* **2013**, No. November, 1–10.
- (30) Goodrich-blair, H.; Clarke, D. J. *Mol. Microbiol.* **2007**, *64*, 260–268.
- (31) Cao, M.; Patel, T.; Rickman, T.; Goodrich-blair, H. *Appl. Environ. Microbiol.* **2017**, *83* (12).
- (32) Chaston, J. M.; Murfin, K. E.; Heath-heckman, E. A.; Goodrich-blair, H. *Cell. Microbiol.* **2013**, *15* (9), 1545–1559.
- (33) Chaston, J. M.; Suen, G.; Tucker, S. L.; Andersen, A. W.; Bhasin, A.; Bode, E.; Bode, H. B.; Brachmann, A. O.; Cowles, C. E.; Cowles, K. N.; Darby, C.; Drace, K.; Du, Z.; Givaudan, A.; Tran, E. E. H.; Jewell, K. A.; Knack, J. J.; Krasomil-osterfeld, K. C.; Kukor, R.; Lanois, A.; Latreille, P.; Nancy, K.; Lipke, C. M.; Liu, R.; Lu, X.; Martens, E. C.; Marri, P. R.; Menard, M. L.; Miller, N. M.; Morales-soto, N.; Norton, S.; Slominski, B.; Slominski, K.; Snyder, H.; Brian, C. *PLoS One* **2011**, *6* (11), E27909.
- (34) Wojda, I. *Insect Sci.* **2017**, *24*, 342–357.
- (35) Rabinowitz, J. D.; Kimball, E. *Anal. Chem.* **2007**, *79* (16), 6167–6173.
- (36) Kanehisa, M.; Goto, S. *Nucleic Acids Res.* **2000**, *28* (1), 27–30.
- (37) Kanehisa, M.; Sato, Y.; Kawashima, M.; Furumichi, M.; Tanabe, M. *Nucleic Acids Res.* **2016**, *44* (2016), 457–462.
- (38) Kanehisa, M.; Furumichi, M.; Tanabe, M.; Sato, Y.; Morishima, K. *Nucleic Acids Res.* **2017**, *45* (2017), 353–361.
- (39) Goodrich-blair, H. *Curr. Opin. Microbiol.* **2007**, *10* (3), 225–230.
- (40) Bhasin, A.; Chaston, J. M.; Goodrich-blair, H. *J. Bacteriol.* **2012**, *194* (7), 1763–1776.
- (41) Chaston, J.; Douglas, J. *Biol. Bull.* **2012**, *223* (1), 21–29.
- (42) Cowles, C. E.; Goodrich-blair, H. *J. Bacteriol.* **2008**, *190* (12), 4121–4128.

APPENDIX

Table 8. Fold changes and p values of early groups compared to uninfected group.

Metabolites	Fold Changes compared to uninfected				P values compared to uninfected			
	1 Hour	12 Hours	24 Hours Alive	24 Hours Dead	1 Hour	12 Hours	24 Hours Alive	24 Hours Dead
Glycine	0.000	2.075	0.001	2.316	0.3735	0.5325	0.3737	0.5105
Pyruvate	1.122	1.312	4.731	1.337	0.6689	0.3088	0.0447	0.5123
Alanine/Sarcosine	0.741	0.864	1.799	2.339	0.3298	0.7670	0.3037	0.0069
Lactate	0.774	1.228	7.479	24.826	0.3579	0.6129	0.3572	0.0001
Dimethylglycine	0.908	1.213	1.882	2.632	0.6671	0.4067	0.1122	0.0220
Serine	1.843	2.365	2.282	2.030	0.2104	0.1270	0.3016	0.0116
Histamine	1.156	1.035	1.371	1.012	0.5220	0.8693	0.2894	0.9502
Uracil	0.666	0.821	1.458	2.128	0.3576	0.6450	0.3103	0.2059
Proline	1.157	1.393	1.575	1.136	0.6479	0.1996	0.2998	0.6958
Fumarate	1.117	1.309	1.659	1.354	0.7158	0.5408	0.3889	0.3693
2-Oxoisovalerate	0.823	0.893	1.767	0.869	0.4866	0.6347	0.1796	0.6347
Indole	1.309	0.988	1.278	1.047	0.4799	0.9747	0.5132	0.9079
Valine	1.001	1.281	1.912	1.378	0.9962	0.2597	0.1161	0.1907
3-Hydroxyisovaleric acid	0.555	0.604	1.438	1.964	0.2285	0.2779	0.4083	0.4767
Homoserine/Threonine	1.231	0.678	1.643	1.233	0.7524	0.4240	0.2951	0.6555
3-Methylthiopropionate	0.442	0.722	1.424	0.925	0.3891	0.7332	0.4944	0.9222
Cysteine	0.895	0.641	0.045	1.357	0.7842	0.2826	0.0285	0.5712
Nicotinate	0.768	1.223	3.031	2.561	0.4054	0.5126	0.0266	0.0006
Taurine	1.817	0.982	1.826	0.780	0.2369	0.9751	0.3896	0.6544
Thymine	0.711	0.723	1.001	0.759	0.1459	0.3477	0.9946	0.2711
Hydroxyproline	1.253	1.256	1.364	3.181	0.3878	0.4970	0.1613	0.3944

Table 8. Continued.

Metabolites	Fold Changes compared to uninfected				P values compared to uninfected			
	1 Hour	12 Hours	24 Hours	24 Hours	1 Hour	12 Hours	24 Hours	24 Hours
			Alive	Dead			Alive	Dead
N-Acetyl-beta-alanine	1.101	1.030	1.593	3.114	0.7691	0.9149	0.1402	0.0027
Leucine/Isoleucine	1.039	1.384	2.230	1.345	0.9002	0.2447	0.0744	0.3477
Glutaric acid	1.411	0.871	1.891	1.219	0.4756	0.6700	0.3998	0.6956
Asparagine	1.446	0.919	0.513	1.182	0.6018	0.7396	0.2423	0.6785
Hydroxyisocaproic acid	0.558	0.938	2.932	6.639	0.3311	0.8995	0.2443	0.2579
Ornithine	0.899	0.755	1.090	0.998	0.7437	0.3600	0.7750	0.9958
Salicylate	0.890	0.989	1.078	1.095	0.6917	0.9654	0.7948	0.8058
Hydroxybenzoate	1.476	0.635	1.450	0.776	0.3666	0.2044	0.4440	0.4306
Histidinol	1.541	1.029	1.407	1.015	0.2724	0.8945	0.1011	0.9646
2-Oxoglutaric acid	2.040	1.602	5.479	0.581	0.2414	0.1493	0.3054	0.2993
Glutamine	0.976	0.931	1.392	0.937	0.9377	0.7993	0.2039	0.8221
2-hydroxyglutarate	1.245	4.345	13.648	49.553	0.6140	0.2105	0.2060	0.0167
2-Hydroxy-2-methylsuccinate	1.245	4.352	13.612	49.591	0.6154	0.2106	0.2061	0.0169
L-Methionine	0.952	1.120	3.145	1.265	0.8860	0.7107	0.0895	0.3634
Guanine	1.068	0.322	0.280	0.560	0.8807	0.0731	0.0619	0.2562
3-Methylphenylacetic acid	0.842	0.896	1.177	1.371	0.7410	0.8674	0.6492	0.6399
Hydroxyphenylacetate	0.701	0.835	0.712	1.263	0.1702	0.4725	0.1978	0.2971
Xylitol	0.735	1.148	2.904	8.280	0.2381	0.5052	0.1609	0.0000
Dopamine	1.292	1.696	0.872	1.416	0.5824	0.2083	0.8113	0.5249
2_3-Dihydroxybenzoate	0.844	0.650	1.451	3.356	0.7261	0.4275	0.4816	0.0833
Histidine	1.043	0.988	1.370	1.038	0.8439	0.9496	0.2799	0.8401
Orotate	1.756	2.131	2.860	1.379	0.4611	0.3478	0.0562	0.4526

Table 8. Continued.

Metabolites	Fold Changes compared to uninfected				P values compared to uninfected			
	1 Hour	12 Hours	24 Hours	24 Hours	1 Hour	12 Hours	24 Hours	24 Hours
			Alive	Dead			Alive	Dead
Dihydroorotate	1.245	2.157	4.168	2.825	0.6896	0.3756	0.0455	0.3847
Allantoin	1.000	1.045	2.254	3.971	0.9999	0.9396	0.4618	0.2413
Indole-3-carboxylate	1.572	0.872	2.102	1.139	0.4662	0.7296	0.1262	0.7446
Phenylpyruvate	0.875	1.638	7.916	1.093	0.7044	0.3614	0.1513	0.8264
Phenylalanine	0.828	0.799	1.555	0.776	0.6954	0.6523	0.3501	0.6243
Phenyllactic acid	0.622	0.600	2.621	3.038	0.4595	0.4175	0.0770	0.1726
Quinolate	3.606	2.735	0.641	5.119	0.4575	0.5198	0.5279	0.1249
Phosphoenolpyruvate	1.284	0.981	3.965	2.069	0.5767	0.9617	0.1815	0.0549
Uric acid	0.730	0.320	0.821	0.568	0.5801	0.0180	0.5575	0.1083
DOPAC	1.737	0.788	2.070	0.969	0.4609	0.3491	0.1617	0.9124
Sulfolactate	1.404	0.826	2.685	0.841	0.6190	0.5281	0.1525	0.5742
Glycerone phosphate	1.770	1.298	1.982	1.575	0.2052	0.5482	0.4195	0.2588
Arginine	1.004	1.097	1.571	1.173	0.9796	0.6556	0.2105	0.3164
Citrulline	0.821	1.366	3.466	1.237	0.5822	0.3560	0.0712	0.5542
Ascorbate	1.234	1.257	0.003	0.893	0.5451	0.7073	0.0235	0.8072
N-Carbamoyl-L-aspartate	1.405	1.722	2.775	1.325	0.4796	0.5026	0.0323	0.7239
Allantoate	1.032	0.904	1.205	0.982	0.9384	0.7036	0.6099	0.9617
2-Isopropylmalate	1.110	0.534	1.233	1.185	0.8656	0.1961	0.7486	0.7013
Glucosamine	0.585	0.930	1.170	1.045	0.1369	0.7950	0.6422	0.9010
myo-Inositol	0.840	0.606	1.190	2.818	0.5854	0.1148	0.7722	0.0001
Tyrosine	1.005	1.038	0.828	0.954	0.9863	0.8931	0.6257	0.8773
Homovanillic acid (HVA)	0.884	0.687	0.582	0.962	0.8514	0.3990	0.2222	0.9329
Homocysteic acid	1.815	0.000	0.697	0.277	0.6335	0.0805	0.6263	0.2015

Table 8. Continued.

Metabolites	Fold Changes compared to uninfected				P values compared to uninfected			
	1 Hour	12 Hours	24 Hours	24 Hours	1 Hour	12 Hours	24 Hours	24 Hours
			Alive	Dead			Alive	Dead
4-Pyridoxate	1.372	0.927	1.458	1.534	0.4069	0.7556	0.1284	0.0633
N-Acetylglutamine	1.793	2.199	3.501	6.045	0.4916	0.1958	0.0191	0.0052
Citrate/isocitrate	1.138	1.016	1.207	0.353	0.7173	0.9571	0.6696	0.0621
D-Gluconate	1.037	1.006	1.682	1.420	0.9068	0.9789	0.2023	0.2156
N-N Dimethylarginine	0.828	0.709	0.926	0.622	0.3164	0.1609	0.7091	0.0366
Tryptophan	1.293	1.035	1.313	1.124	0.4624	0.9208	0.4233	0.7361
Xanthurenic acid	10.219	0.440	4.993	1.024	0.3039	0.4973	0.3707	0.9808
D-Glucarate	0.715	0.632	1.125	0.697	0.4202	0.2917	0.7220	0.3986
Pantothenate	1.198	1.029	1.253	0.993	0.5907	0.9129	0.4632	0.9781
Cystathionine	4.703	0.406	0.629	0.296	0.2755	0.2885	0.5217	0.2169
Cystine	0.812	0.384	0.566	1.339	0.6146	0.1369	0.2581	0.5427
Uridine	1.293	1.053	2.094	7.836	0.4974	0.8292	0.0184	0.0009
Biotin	0.971	0.804	0.698	0.956	0.9334	0.4827	0.3267	0.8986
Deoxyinosine	0.668	1.684	1.773	1.326	0.6783	0.6719	0.5908	0.7768
Glucose 6-phosphate	0.769	0.932	1.583	0.578	0.3027	0.7248	0.3161	0.0645
S-Ribosyl-L-homocysteine	0.000	1.11E+07	2.11E+08	1.11E+07	#DIV/0!	0.3739	0.1269	0.3739
6-Phospho-D-gluconate	0.962	1.311	10.789	0.977	0.8856	0.4072	0.0873	0.9539
Guanosine	1.362	0.898	1.127	1.357	0.3776	0.7693	0.8057	0.3568
Xanthosine	1.886	0.467	3.867	197.576	0.5714	0.3095	0.4287	0.0005
Glycinamide ribotide (GAR)	0.406	4.340	2.741	0.574	0.4674	0.0523	0.1131	0.6397
Ophthalmate	1.009	1.637	1.561	0.721	0.9839	0.1807	0.3720	0.5125
Glutathione	1.111	0.915	0.055	0.491	0.8403	0.8641	0.0364	0.2132

Table 8. Continued.

Metabolites	Fold Changes compared to uninfected				P values compared to uninfected			
	1 Hour	12 Hours	24 Hours	24 Hours	1 Hour	12 Hours	24 Hours	24 Hours
			Alive	Dead			Alive	Dead
UMP	1.229	1.206	1.171	0.147	0.5310	0.5009	0.6873	0.0206
AICAR	0.402	0.551	0.156	0.207	0.4254	0.5767	0.2663	0.2947
Trehalose/Sucrose/Cellobiose	1.158	1.082	1.154	0.915	0.5129	0.7938	0.5458	0.6440
AMP/dGMP	0.865	0.978	1.290	0.397	0.6297	0.9264	0.4812	0.0471
IMP	0.657	2.794	3.110	7.889	0.4534	0.1188	0.2065	0.0197
GMP	0.823	1.056	1.808	0.736	0.5587	0.8291	0.1306	0.3464
Xanthosine 5--phosphate	1.587	1.025	5.190	12.913	0.3501	0.9531	0.0879	0.0069
Riboflavin	1.290	0.556	0.657	0.870	0.7055	0.1684	0.2493	0.6958
S-Adenosyl-L-homocysteine	1.272	0.818	1.255	2.118	0.6457	0.3348	0.6816	0.0850
ADP	1.369	1.145	0.766	0.314	0.5919	0.8410	0.6672	0.2350
Folate	0.000	0.000	4.57E+06	0.000	#DIV/0!	#DIV/0!	0.3910	#DIV/0!
CDP-ethanolamine	1.039	1.127	1.514	0.785	0.8931	0.6741	0.3627	0.4218
FMN	1.189	0.896	1.490	1.132	0.4610	0.6590	0.4711	0.6432
UDP-glucose	1.031	0.786	0.664	0.068	0.9434	0.4763	0.4042	0.0247
NAD+	1.157	0.923	0.872	0.614	0.6504	0.7782	0.5642	0.1864
NADH	0.828	1.009	0.534	2.146	0.6973	0.9827	0.4129	0.1857
Dephospho-CoA	0.856	0.972	0.272	0.397	0.6768	0.9260	0.0462	0.1025
NADP+	1.071	0.978	2.987	0.923	0.8288	0.9410	0.0407	0.8227
FAD	1.068	0.767	0.945	0.828	0.9084	0.6669	0.9242	0.7587
N-Acetylglutamate	1.220	1.024	0.800	0.643	0.6341	0.9587	0.5874	0.3429
Kynurenic acid	5.714	1.975	16.585	7.612	0.2766	0.2118	0.0542	0.2067

Table 9. Fold changes and p values of middle groups compared to uninfected group.

Metabolites	Fold Changes compared to the uninfected				P values compared to uninfected			
	2 Days	4 Days	6 Days	8 Days	2 Days	4 Days	6 Days	8 Days
Glycine	4.792	2.067	0.001	2.972	0.51052	0.58106	0.37392	0.45756
Pyruvate	6.409	0.200	0.328	0.286	0.51234	0.00163	0.00432	0.00307
Alanine/Sarcosine	2.547	0.132	2.972	3.208	0.00691	0.00691	0.28361	0.39061
Lactate	33.305	0.866	2.451	1.611	0.00012	0.66469	0.03176	0.22099
Dimethylglycine	2.915	1.599	8.413	7.686	0.02204	0.23466	0.13109	0.12141
Serine	2.718	1.124	2.042	1.339	0.01162	0.70979	0.13992	0.48825
Histamine	0.708	1.070	9.976	4.400	0.95021	0.89187	0.03294	0.03998
Uracil	4.394	16.293	100.473	93.704	0.20591	0.04228	0.00515	0.00237
Proline	0.473	0.094	0.725	0.793	0.69584	0.01812	0.38395	0.53966
Fumarate	0.826	0.111	0.459	0.281	0.36926	0.00882	0.05139	0.01616
2-Oxoisovalerate	7.444	5.049	45.681	5.119	0.63473	0.06135	0.27502	0.05421
Indole	1.035	0.325	0.722	1.177	0.90789	0.08085	0.50679	0.85735
Valine	1.199	0.420	3.358	2.552	0.19072	0.03848	0.23859	0.51087
3-Hydroxyisovaleric acid	9.084	12.066	92.980	7.524	0.47665	0.01535	0.12331	0.10206
Homoserine/Threonine	1.538	1.185	3.167	5.224	0.65552	0.64121	0.02501	0.28062
3-Methylthiopropionate	4.226	9.772	148.925	10.883	0.92223	0.20738	0.20707	0.32083
Cysteine	0.259	0.571	0.451	0.453	0.57115	0.25162	0.12901	0.15296
Nicotinate	9.210	3.191	5.023	3.947	0.00056	0.11202	0.01171	0.02336
Taurine	1.295	0.160	0.445	0.467	0.65444	0.10512	0.25720	0.32224
Thymine	19.165	114.556	302.136	269.657	0.27105	0.00890	0.02013	0.00931
Hydroxyproline	3.366	5.314	7.210	6.796	0.39440	0.03322	0.00300	0.00251

Table 9. Continued.

Metabolites	Fold Changes compared to the uninfected				P values compared to uninfected			
	2 Days	4 Days	6 Days	8 Days	2 Days	4 Days	6 Days	8 Days
N-Acetyl-beta-alanine	2.683	7.351	70.665	61.108	0.00270	0.05300	0.04994	0.25044
Leucine/Isoleucine	0.874	0.492	2.282	2.843	0.34767	0.12230	0.20158	0.47965
Glutaric acid	2.306	3.130	11.815	4.749	0.69556	0.02445	0.07333	0.01453
Asparagine	1.099	0.235	2.197	0.926	0.67846	0.01300	0.14360	0.84672
Hydroxyisocaproic acid	8.834	6.447	116.020	10.983	0.25789	0.08193	0.16961	0.25487
Ornithine	5.009	6.155	28.656	62.339	0.99584	0.00163	0.11175	0.31047
Salicylate	1.341	31.566	14.333	5.733	0.80576	0.31000	0.15179	0.33922
Hydroxybenzoate	21.561	11.108	61.260	34.617	0.43055	0.04212	0.03185	0.06085
Histidinol	77.448	343.644	106.747	64.686	0.96459	0.00802	0.25252	0.08561
2-Oxoglutaric acid	0.747	0.164	0.926	0.493	0.29934	0.05400	0.90553	0.19339
Glutamine	0.728	0.090	0.334	0.397	0.82209	0.01382	0.03563	0.04888
2-hydroxyglutarate	27.272	2.548	14.312	35.538	0.01672	0.00709	0.04671	0.27122
2-Hydroxy-2-methylsuccinate	27.260	2.550	14.346	35.625	0.01690	0.00720	0.04594	0.27111
L-Methionine	2.064	1.045	2.025	3.124	0.36341	0.91086	0.26663	0.40944
Guanine	42.531	211.056	908.328	499.976	0.25615	0.30159	0.19389	0.28031
3-Methylphenylacetic acid	1.030	2.015	544.929	80.221	0.63993	0.50735	0.17919	0.36781
Hydroxyphenylacetate	15.366	106.390	298.925	291.173	0.29706	0.02409	0.09366	0.12242
Xylitol	10.888	6.039	16.487	13.494	0.00003	0.05388	0.01841	0.10481
Dopamine	0.662	0.009	0.156	0.315	0.52487	0.08042	0.11852	0.23163
2_3-Dihydroxybenzoate	19.629	431.561	374.372	674.269	0.08331	0.10891	0.27523	0.24281
Histidine	0.546	0.090	0.335	0.862	0.84007	0.00136	0.00278	0.86056
Orotate	17.908	62.614	192.883	127.407	0.45255	0.07855	0.06108	0.05728
Dihydroorotate	6.824	6.522	8.572	17.943	0.38466	0.11281	0.10735	0.25847

Table 9. Continued.

Metabolites	Fold Changes compared to the uninfected				P values compared to uninfected			
	2 Days	4 Days	6 Days	8 Days	2 Days	4 Days	6 Days	8 Days
Allantoin	3.410	6.361	69.455	50.345	0.24131	0.17298	0.03317	0.05632
Indole-3-carboxylate	6.051	48.481	107.196	106.805	0.74457	0.01282	0.00365	0.05101
Phenylpyruvate	11.211	8.056	320.823	29.530	0.82642	0.12060	0.28221	0.07190
Phenylalanine	1.206	0.261	1.962	2.408	0.62425	0.11072	0.33706	0.51309
Phenyllactic acid	118.656	321.702	710.170	145.612	0.17260	0.05204	0.01641	0.04612
Quinolate	4.542	49.406	457.420	1123.157	0.12494	0.10754	0.02599	0.11338
Phosphoenolpyruvate	10.344	5.371	36.612	21.661	0.05493	0.12881	0.00390	0.04747
Uric acid	0.722	0.391	0.637	0.259	0.10834	0.02755	0.15243	0.01259
DOPAC	19.712	67.054	399.223	136.540	0.91242	0.00434	0.00111	0.07956
Sulfolactate	1.865	0.619	12.615	4.753	0.57417	0.18177	0.18006	0.04050
Glycerone phosphate	1.313	0.215	0.393	0.340	0.25883	0.11744	0.19737	0.17840
Arginine	0.662	0.290	0.694	0.494	0.31638	0.00176	0.05712	0.01212
Citrulline	41.678	65.756	312.333	171.161	0.55416	0.00182	0.20294	0.23443
Ascorbate	0.002	0.000	0.002	0.001	0.80717	0.02328	0.02337	0.02329
N-Carbamoyl-L-aspartate	7.981	5.088	22.889	32.337	0.72394	0.15983	0.09300	0.13994
Allantoate	1.448	0.410	1.511	0.708	0.96167	0.04922	0.48452	0.65862
2-Isopropylmalate	179.099	255.459	584.853	454.850	0.70127	0.03129	0.01129	0.05943
Glucosamine	3.401	6.899	17.109	36.100	0.90098	0.05300	0.07609	0.12901
myo-Inositol	5.255	0.408	0.765	0.727	0.00007	0.02893	0.33327	0.25749
Tyrosine	0.671	0.182	0.360	0.188	0.87732	0.02102	0.05194	0.02198
Homovanillic acid (HVA)	2.669	1.940	10.699	2.205	0.93293	0.12820	0.20677	0.17569
Homocysteic acid	86.493	1997.788	12078.719	495.383	0.20152	0.09063	0.33266	0.17748

Table 9. Continued.

Metabolites	Fold Changes compared to the uninfected				P values compared to uninfected			
	2 Days	4 Days	6 Days	8 Days	2 Days	4 Days	6 Days	8 Days
4-Pyridoxate	5.154	19.564	57.666	77.471	0.06328	0.03150	0.06271	0.03771
N-Acetylglutamine	3.363	0.359	3.900	10.001	0.00524	0.18438	0.06102	0.34041
Citrate/isocitrate	0.429	0.188	0.677	0.182	0.06214	0.03227	0.38929	0.03167
D-Gluconate	1.844	1.960	4.624	3.941	0.21557	0.07356	0.00000	0.00531
N-N Dimethylarginine	2.634	3.349	5.006	2.805	0.03661	0.00781	0.08934	0.17102
Tryptophan	1.057	0.384	0.791	1.019	0.73609	0.07430	0.57173	0.97972
Xanthurenic acid	1.641	2.259	1.038	1.358	0.98076	0.28515	0.97010	0.70499
D-Glucarate	0.923	0.506	1.499	0.670	0.39857	0.26408	0.36212	0.37628
Pantothenate	1.179	1.221	2.025	0.998	0.97814	0.48107	0.02351	0.99663
Cystathionine	0.403	0.775	0.963	0.999	0.21688	0.66738	0.94990	0.99828
Cystine	2.844	5.508	0.408	0.848	0.54273	0.08380	0.17188	0.76874
Uridine	56.301	246.279	504.667	373.328	0.00088	0.03610	0.04706	0.26154
Biotin	0.701	0.415	0.346	0.519	0.89865	0.06001	0.03921	0.16646
Deoxyinosine	123.288	1842.869	6062.509	3666.716	0.77676	0.10843	0.04260	0.03827
Glucose 6-phosphate	0.377	0.039	0.109	0.087	0.06451	0.00464	0.00550	0.00517
S-Ribosyl-L-homocysteine	1.61E+10	5.16E+09	6.61E+09	2.93E+09	0.37390	0.28146	0.31559	0.06872
6-Phospho-D-gluconate	2.079	2.023	5.269	3.127	0.95388	0.24139	0.04294	0.23053
Guanosine	1.555	1.478	1.818	5.202	0.35683	0.38841	0.18522	0.15072
Xanthosine	48.545	29.320	44.130	27.453	0.00050	0.07392	0.13650	0.09269
Glycinamide ribotide (GAR)	4.933	0.308	29.803	36.939	0.63972	0.41207	0.21219	0.20156
Ophthalmate	4.931	6.181	35.378	17.365	0.51249	0.04846	0.15629	0.11826
Glutathione	0.117	0.097	0.336	0.113	0.21320	0.04189	0.09603	0.04389

Table 9. Continued.

Metabolites	Fold Changes compared to the uninfected				P values compared to uninfected			
	2 Days	4 Days	6 Days	8 Days	2 Days	4 Days	6 Days	8 Days
UMP	0.217	0.312	0.920	0.884	0.02060	0.03918	0.83856	0.75138
AICAR	0.152	0.081	0.130	0.069	0.29472	0.23294	0.25434	0.22754
Trehalose/Sucrose/Cellobiose	0.631	0.271	0.720	0.638	0.64396	0.00567	0.29239	0.14309
AMP/dGMP	0.227	0.180	0.226	0.417	0.04713	0.01839	0.02019	0.05848
IMP	2.145	0.204	0.247	0.182	0.01970	0.12226	0.13900	0.11485
GMP	0.665	0.773	1.322	3.161	0.34635	0.50651	0.59308	0.18783
Xanthosine 5--phosphate	19.449	52.468	147.733	21.200	0.00688	0.33973	0.04360	0.04579
Riboflavin	0.898	0.773	1.657	3.151	0.69581	0.53213	0.28250	0.31463
S-Adenosyl-L-homocysteine	1.187	4.990	4.986	5.915	0.08497	0.06598	0.04512	0.03787
ADP	0.386	0.106	0.430	0.343	0.23502	0.14251	0.31985	0.25428
Folate	2.81E+08	2.68E+09	5.71E+09	1.72E+10	#DIV/0!	0.00274	0.09309	0.08407
CDP-ethanolamine	0.537	0.155	0.399	0.265	0.42183	0.01647	0.05535	0.02614
FMN	1.351	1.257	1.061	1.336	0.64325	0.36812	0.79650	0.45186
UDP-glucose	0.258	0.356	1.120	0.812	0.02469	0.07114	0.79310	0.64166
NAD+	0.309	0.200	0.312	0.158	0.18641	0.01256	0.02005	0.01121
NADH	0.223	0.024	0.039	0.067	0.18567	0.04903	0.05130	0.05466
Dephospho-CoA	0.186	0.529	1.357	1.052	0.10249	0.17794	0.48999	0.91004
NADP+	2.407	1.612	2.429	0.994	0.82268	0.31269	0.16649	0.98662
FAD	1.043	1.475	2.478	1.873	0.75866	0.50882	0.06953	0.31540
N-Acetylglutamate	6.512	4.915	9.298	5.726	0.34290	0.00770	0.01771	0.00386
Kynurenic acid	140.090	648.871	1937.756	2856.635	0.20668	0.00893	0.10627	0.11575

Table 10. Fold changes and p values of late groups compared to uninfected group.

Metabolites	Fold changes compared to the uninfected			P values compared to uninfected		
	10 Days	12 Days	16 Days	10 Days	12 Days	16 Days
Glycine	4.258	9.942	0.685	0.4932	0.1896	0.7949
Pyruvate	0.374	0.175	0.740	0.0059	0.0030	0.6172
Alanine/Sarcosine	2.026	2.039	1.716	0.4479	0.4959	0.6329
Lactate	2.353	28.355	2.180	0.1764	0.3647	0.0726
Dimethylglycine	11.472	13.655	16.762	0.1565	0.2508	0.1001
Serine	1.818	0.758	3.022	0.0358	0.5901	0.2352
Histamine	12.281	9.751	14.569	0.0238	0.0777	0.2373
Uracil	123.687	60.977	114.216	0.0061	0.0256	0.2715
Proline	1.182	0.419	0.773	0.6558	0.1107	0.6247
Fumarate	0.304	0.100	0.346	0.0179	0.0081	0.0336
2-Oxoisovalerate	31.558	20.332	12.962	0.0810	0.3346	0.3028
Indole	0.565	0.721	0.473	0.3733	0.6158	0.2285
Valine	2.007	2.009	1.724	0.5566	0.4570	0.6616
3-Hydroxyisovaleric acid	26.672	44.341	37.643	0.0591	0.1475	0.3212
Homoserine/Threonine	2.743	3.365	4.256	0.1711	0.3390	0.3952
3-Methylthiopropionate	173.653	118.922	314.975	0.3372	0.2298	0.1997
Cysteine	0.350	0.200	0.647	0.0857	0.0464	0.3951
Nicotinate	2.201	3.097	5.177	0.1574	0.2605	0.0867
Taurine	0.583	0.316	1.188	0.4551	0.1726	0.7356
Thymine	255.496	115.787	144.941	0.0065	0.0845	0.2907
Hydroxyproline	26.682	6.065	18.293	0.0111	0.0564	0.0957

Table 10. Continued.

Metabolites	Fold changes compared to the uninfected			P values compared to uninfected		
	10 Days	12 Days	16 Days	10 Days	12 Days	16 Days
N-Acetyl-beta-alanine	35.250	32.070	37.023	0.0092	0.1800	0.0801
Leucine/Isoleucine	2.007	2.208	1.925	0.5656	0.4619	0.6176
Glutaric acid	15.354	5.289	10.799	0.0952	0.1601	0.1654
Asparagine	2.011	1.418	2.947	0.2412	0.6278	0.2427
Hydroxyisocaproic acid	21.865	39.732	24.531	0.0664	0.1532	0.3379
Ornithine	34.781	45.329	19.233	0.2968	0.0600	0.2121
Salicylate	5.810	2.449	3.214	0.2559	0.2722	0.0957
Hydroxybenzoate	305.421	111.028	362.953	0.0353	0.2012	0.1076
Histidinol	60.620	32.374	42.209	0.2415	0.0752	0.0774
2-Oxoglutaric acid	0.293	0.109	0.324	0.0854	0.0458	0.1056
Glutamine	0.331	0.334	0.391	0.0352	0.0703	0.0542
2-hydroxyglutarate	14.582	27.552	13.872	0.0194	0.3012	0.0929
2-Hydroxy-2-methylsuccinate	14.644	27.614	13.972	0.0194	0.3011	0.0933
L-Methionine	2.704	4.711	3.303	0.4585	0.3321	0.4486
Guanine	89.340	56.306	129.946	0.0039	0.2368	0.1023
3-Methylphenylacetic acid	163.778	168.432	2.084	0.3699	0.3747	0.0728
Hydroxyphenylacetate	411.449	133.297	457.681	0.0348	0.0573	0.0976
Xylitol	9.882	6.643	31.981	0.0002	0.1393	0.0828
Dopamine	0.015	0.581	0.017	0.0816	0.5729	0.0820
2_3-Dihydroxybenzoate	297.354	263.830	502.594	0.0446	0.1500	0.1232
Histidine	0.304	0.487	0.251	0.0054	0.2119	0.0014

Table 10. Continued.

Metabolites	Fold changes compared to the uninfected			P values compared to uninfected		
	10 Days	12 Days	16 Days	10 Days	12 Days	16 Days
Allantoin	89.180	37.012	78.934	0.0172	0.1582	0.1169
Indole-3-carboxylate	357.678	160.493	277.190	0.0035	0.0301	0.0876
Phenylpyruvate	413.759	148.335	119.827	0.0571	0.2971	0.1103
Phenylalanine	1.312	1.694	1.589	0.7760	0.5444	0.6986
Phenyllactic acid	133.578	113.759	63.962	0.0158	0.0521	0.3039
Quinolate	4990.106	1609.825	10077.656	0.0887	0.1868	0.0708
Phosphoenolpyruvate	69.222	31.383	44.422	0.1334	0.2017	0.0629
Uric acid	0.543	0.216	0.614	0.1310	0.0108	0.3584
DOPAC	1045.916	389.290	877.422	0.0173	0.1443	0.0803
Sulfolactate	24.279	19.741	56.909	0.0712	0.0765	0.0099
Glycerone phosphate	0.366	0.145	0.811	0.1802	0.0921	0.7287
Arginine	0.481	0.217	0.824	0.0068	0.0018	0.6547
Citrulline	176.391	223.750	164.660	0.2869	0.1706	0.2978
Ascorbate	0.001	0.002	0.001	0.0234	0.0234	0.0234
N-Carbamoyl-L-aspartate	106.963	49.179	268.745	0.2229	0.3223	0.3277
Allantoate	1.454	1.108	2.143	0.5679	0.8838	0.3623
2-Isopropylmalate	1715.044	713.690	1764.979	0.0445	0.1586	0.1006
Glucosamine	21.719	11.875	50.631	0.0080	0.0545	0.0066
myo-Inositol	1.146	5.289	4.488	0.6049	0.3583	0.0163
Tyrosine	0.156	0.251	0.613	0.0192	0.0258	0.4731
Homovanillic acid (HVA)	3.132	7.208	3.279	0.1126	0.2717	0.3388

Table 10. Continued.

Metabolites	Fold changes compared to the uninfected			P values compared to uninfected		
	10 Days	12 Days	16 Days	10 Days	12 Days	16 Days
4-Pyridoxate	99.502	29.529	110.628	0.0309	0.2081	0.0255
N-Acetylglutamine	3.160	10.737	3.480	0.0776	0.3718	0.2769
Citrate/isocitrate	0.213	0.042	0.192	0.0355	0.0195	0.0313
D-Gluconate	5.375	2.788	7.319	0.0012	0.1631	0.0430
N-N Dimethylarginine	2.568	2.192	5.442	0.3259	0.0030	0.2650
Tryptophan	0.629	0.808	0.603	0.4234	0.7323	0.3645
Xanthurenic acid	0.936	0.146	0.877	0.9405	0.3174	0.8976
D-Glucarate	1.616	0.658	1.764	0.2083	0.4273	0.4712
Pantothenate	2.463	1.667	2.719	0.1128	0.2523	0.2935
Cystathionine	0.635	0.461	0.675	0.4991	0.3366	0.5878
Cystine	0.399	0.710	2.984	0.2071	0.6884	0.3603
Uridine	246.099	309.847	65.809	0.0717	0.0930	0.0958
Biotin	0.672	0.582	1.188	0.2657	0.1422	0.6731
Deoxyinosine	3527.064	1086.591	2116.136	0.0478	0.1849	0.3450
Glucose 6-phosphate	0.077	0.046	0.064	0.0052	0.0047	0.0050
S-Ribosyl-L-homocysteine	4.83E+09	5.50E+09	2.13E+10	0.2000	0.0215	0.2537
6-Phospho-D-gluconate	5.427	2.107	5.102	0.0584	0.3408	0.0361
Guanosine	2.626	0.580	1.333	0.1305	0.2309	0.4510
Xanthosine	27.111	9.649	21.699	0.1073	0.0426	0.3366
Glycinamide ribotide (GAR)	14.269	0.248	1.844	0.0875	0.3706	0.6249
Ophthalmate	14.317	2.551	6.548	0.0218	0.0689	0.0728

Table 10. Continued.

Metabolites	Fold changes compared to the uninfected			P values compared to uninfected		
	10 Days	12 Days	16 Days	10 Days	12 Days	16 Days
UMP	0.764	0.273	0.624	0.4312	0.0412	0.2389
AICAR	0.055	0.002	0.009	0.2221	0.2016	0.2043
Trehalose/Sucrose/Cellobiose	0.752	0.456	1.537	0.3469	0.1820	0.5144
AMP/dGMP	0.376	0.205	0.473	0.0418	0.0205	0.0890
IMP	0.132	0.093	0.157	0.0998	0.0892	0.1071
GMP	2.371	0.902	1.997	0.1188	0.9062	0.2518
Xanthosine 5--phosphate	403.992	149.259	274.389	0.2593	0.1164	0.1039
Riboflavin	1.986	1.951	4.368	0.1786	0.1190	0.0760
S-Adenosyl-L-homocysteine	2.739	0.813	2.015	0.1791	0.6711	0.2836
ADP	0.537	0.108	0.712	0.4098	0.1434	0.6597
Folate	5.34E+09	6.02E+09	1.85E+10	0.0319	0.0578	0.0612
CDP-ethanolamine	0.143	0.036	0.112	0.0173	0.0118	0.0145
FMN	0.658	1.004	1.255	0.0667	0.9917	0.7097
UDP-glucose	0.892	0.362	0.678	0.7482	0.0978	0.3336
NAD+	0.179	0.065	0.162	0.0129	0.0084	0.0098
NADH	0.003	0.031	0.023	0.0462	0.0501	0.0488
Dephospho-CoA	0.580	0.337	0.444	0.2235	0.0823	0.1405
NADP+	1.380	0.856	0.894	0.2859	0.6858	0.7879
FAD	1.426	2.977	2.587	0.4378	0.2124	0.1351
N-Acetylglutamate	8.838	3.296	3.122	0.0585	0.1524	0.1712
Kynurenic acid	3714.934	1043.830	668.726	0.0574	0.1675	0.3350

Table 11. Metabolites with VIP scores above 1 in *G. mellonella* early infection groups.

Metabolite	Component 1	Component 2
2-3-Dihydroxybenzoate	1.5869	1.2547
2-Hydroxy-2-methylsuccinate	2.2357	1.7410
2-hydroxyglutarate	2.2367	1.7417
2-Oxoglutaric acid	0.2764	1.0562
2-Oxoisovalerate	0.3018	1.0449
3-Hydroxyisovaleric-acid	1.0413	0.8204
6-Phospho-D-gluconate	0.5088	1.5479
ADP	1.2044	0.9568
Alanine/Sarcosine	1.7096	1.3124
Allantoin	1.1409	0.8779
AMP/dGMP	1.1497	1.3461
Ascorbate	0.9151	1.3537
Citrate/isocitrate	1.3093	1.2499
Citrulline	0.7014	1.3385
Cysteine	0.1700	1.2688
Dephospho-CoA	1.5255	1.2729
Dimethylglycine	1.9226	1.4751
Glucose-6-phosphate	0.3793	1.1412
Glutathione	1.0743	1.1795
GMP	0.0027	1.1881
Hydroxyisocaproic acid	1.5034	1.1533
Hydroxyphenylacetate	0.9852	1.0460
IMP	1.8978	1.4806
Kynurenic acid	0.9303	1.1735
L-Methionine	0.8580	1.3640
Lactate	2.2690	1.7879
Leucine/Isoleucine	0.7744	1.1339
myo-Inositol	1.9032	1.5627
N-Acetyl-beta-alanine	2.0101	1.5722
N-Acetylglutamine	1.8574	1.4248
NAD+	1.0673	0.8609
NADH	0.7192	1.0764
NADP+	0.3900	1.4325
Nicotinate	1.9260	1.6152
Phenyllactic acid	1.6506	1.3167
Phenylpyruvate	0.4665	1.2661

Table 11. Continued.

Metabolite	Component 1	Component 2
Phosphoenolpyruvate	1.1608	1.2046
Pyruvate	0.6499	1.4863
S-Ribosyl-L-homocysteine	0.7014	1.3681
UDP-glucose	1.8526	1.4801
UMP	1.7513	1.5589
Uracil	1.3847	1.0643
Uridine	2.2981	1.8439
Valine	0.9571	1.0844
Xanthosine	2.2370	1.9188
Xanthosine-5-phosphate	2.2546	1.7373
Xylitol	2.3975	1.8718

Table 12. Metabolites with VIP scores above 1 in *G. mellonella* middle infection groups.

Metabolite	Component 1	Component 2
2-Isopropylmalate	1.5248	1.1871
3-4-Dihydroxyphenylacetate (DOPAC)	1.7436	1.4597
3-Hydroxyisovaleric acid	1.1293	0.9594
4-Pyridoxate	1.4166	1.1114
6-Phospho-D-gluconate	1.0473	0.8986
ADP	0.7249	1.2095
AICAR	1.0346	1.0580
Allantoin	1.4607	1.3469
AMP/dGMP	1.0007	1.1633
Arginine	0.5502	1.2637
Ascorbate	1.5786	1.5895
Asparagine	0.3048	1.1124
Biotin	1.0826	0.9057
CDP-ethanolamine	0.9094	1.0994
Citrate/isocitrate	0.8538	1.2493
Citrulline	1.2375	0.9671
Creatinine	1.2335	0.9765
Cystine	0.3144	1.2624
D-Gluconate	1.6660	1.3972
Deoxyinosine	1.6059	1.2677
Dephospho-CoA	0.4148	1.0852
Dimethylglycine	1.1988	1.0838
Dopamine	0.9652	1.0429
FAD	1.0092	0.8260
Folate	1.2633	0.9814
Fumarate	0.7947	1.0874
Glucosamine	1.2807	1.0128
Glucose-6-phosphate	1.4496	1.4740
Glutamine	0.8161	1.1785
Glutaric acid	1.4200	1.1905
Glutathione	0.9395	1.4395
Guanine	1.1134	0.9052
Histamine	1.2110	1.3731
Histidine	0.6522	1.0409
Histidinol	0.6516	1.5178

Table 12. Continued.

Metabolite	Component 1	Component 2
Hydroxybenzoate	1.4315	1.1662
Hydroxyisocaproic acid	1.0166	0.9681
Hydroxyphenylacetate	1.3266	1.0348
Hydroxyproline	1.6513	1.3042
Indole-3-carboxylate	1.6935	1.3208
Kynurenic acid	1.3748	1.0706
N-Acetyl-beta-alanine	1.3496	1.2184
N-Acetylglutamate	1.3348	1.0555
N-Carbamoyl-L-aspartate	1.0631	0.8541
NAD ⁺	1.3386	1.3988
NADH	1.4399	1.3930
Ophthalmate	1.2818	1.0675
Ornithine	1.0276	0.8366
Orotate	1.5241	1.1980
Phenyllactic acid	1.5088	1.1783
Phenylpyruvate	1.0228	1.0159
Phosphoenolpyruvate	1.5359	1.3461
Proline	0.1203	1.4211
Quinolate	1.3176	1.1325
Sulfolactate	1.0324	1.1891
Thymine	1.7589	1.3729
Trehalose/Sucrose/Cellobiose	0.6078	1.0729
Tyrosine	1.1051	1.1166
UDP-glucose	0.0540	1.0075
UMP	0.0043	1.0181
Uracil	1.7937	1.5348
Uridine	1.3648	1.0640
Xanthosine-5-phosphate	1.1893	0.9888
Xylitol	1.3825	1.0741

Table 13. Metabolites with VIP scores above 1 in *G. mellonella* late infection groups.

Metabolite	Component 1	Component 2
2-3-Dihydroxybenzoate	1.0320	0.8792
2-Isopropylmalate	1.3026	1.2170
2-Oxoglutaric acid	1.3035	1.2662
3-4-Dihydroxyphenylacetate (DOPAC)	1.3602	1.2859
4-Pyridoxate	1.4160	1.4405
6-Phospho-D-gluconate	0.9082	1.1774
ADP	0.7134	1.1609
AICAR	1.4942	1.3018
Allantoin	1.2080	1.1331
AMP/dGMP	1.1334	1.2708
Arginine	0.8909	1.3022
Ascorbate	2.0234	1.7104
CDP-ethanolamine	1.7134	1.5556
Citrate/isocitrate	1.6885	1.6503
Creatinine	1.2483	1.2107
Cysteine	0.9511	1.1353
D-Gluconate	1.3744	1.4450
Deoxyinosine	1.1311	0.9658
Dopamine	1.2318	1.1108
Folate	1.2604	1.0862
Fumarate	1.4351	1.4405
Glucosamine	1.3690	1.3559
Glucose-6-phosphate	2.0301	1.7400
Glutamine	1.2314	1.1224
Glutaric acid	1.0303	0.9935
Glutathione	1.3890	1.3276
Glycerone phosphate	0.7610	1.0485
Histidinol	1.1034	0.9261
Homocysteic acid	0.8962	1.0255
Hydroxybenzoate	1.1602	1.2013
Hydroxyphenylacetate	1.2509	1.1862
Hydroxyproline	1.3826	1.4534
IMP	1.5350	1.3501
Indole-3-carboxylate	1.5819	1.4033
N-Acetyl-beta-alanine	1.1138	0.9329
N-Acetylglutamate	1.0512	0.9051
NAD+	1.8351	1.6522

Table 13. Continued.

Metabolite	Component 1	Component 2
NADH	1.8958	1.5881
Ophthalmate	1.0731	1.0745
Phenyllactic acid	1.2511	1.1197
Phenylpyruvate	1.1234	1.0432
Phosphoenolpyruvate	1.2550	1.1412
Pyruvate	1.1156	1.2633
Quinolate	1.2148	1.3644
S-Ribosyl-L-homocysteine	1.0276	0.8849
Serine	0.4471	1.1688
Sulfolactate	1.2581	1.2289
Thymine	1.3403	1.1227
Tyrosine	1.2468	1.1105
UMP	0.5836	1.0554
Uracil	1.3800	1.1627
Uric acid	0.9737	1.0744
Uridine	1.0231	1.0409
Xylitol	1.1903	1.2220

Table 14. *X. nematophila* whole cell fold changes and p values.

Metabolite	Fold Change	P Value
Sedoheptulose 1/7-phosphate	0.76	0.00128
Glucosamine phosphate	0.79	0.47906
Phenyllactic acid	0.63	0.25859
dTDP	0.62	0.34339
Xanthosine	1.20	0.81673
Guanine	0.81	0.18632
UMP	0.72	0.02615
Succinate/Methylmalonate	0.93	0.64195
AICAR	0.92	0.38993
N-Acetylglucosamine 1/6-phosphate	0.90	0.40928
Phenylalanine	1.07	0.31171
FAD	1.72	0.48248
Guanosine	0.54	0.01558
6-Phospho-D-gluconate	0.49	0.06740
UDP-glucuronate	0.68	0.18971
2-Hydroxy-2-methylsuccinate	0.70	0.10960
Tryptophan	1.24	0.15837
Malate	0.98	0.87020
CMP	0.59	0.04616
2-Dehydro-D-gluconate	0.86	0.31347
Deoxyribose phosphate	0.86	0.15399
Cysteine	0.98	0.66185
NADH	0.87	0.31984
Citrate/isocitrate	0.74	0.00801
Methionine	0.79	0.04967
Tyrosine	0.56	0.36929
Homoserine/Threonine	0.81	0.48235
Lysine	0.72	0.46062
Histidinol	1.11	0.67313
Adenosine	0.37	0.13234
Uracil	0.88	0.57351
Homocystine	0.96	0.63439
Fumarate	0.74	0.59933
2-Aminoadipate	1.07	0.80972
FMN	0.91	0.72816

Table 14. Continued.

Metabolite	Fold Change	P Value
Valine	1.56	0.07954
D-Gluconate	0.64	0.06387
Alanine/Sarcosine	0.75	0.19224
Lipoate	0.82	0.08314
Histidine	0.71	0.63894
Glycerone phosphate	0.77	0.35253
Ribose phosphate	1.04	0.77023
Uridine	0.54	0.03225
S-Adenosyl-L-methioninamine	0.90	0.24800
Acetylphosphate	0.49	0.09175
Allantoin	0.95	0.84082
Dephospho-CoA	1.13	0.58790
Citrulline	0.75	0.29892
Sedoheptoluse biphosphate	1.60	0.04071
Aconitate	0.82	0.66109
Leucine/Isoleucine	0.57	0.30088
Thymine	0.81	0.25397
UDP	1.15	0.10726
UDP-N-acetylglucosamine	0.81	0.55600
Ornithine	1.38	0.22683
Cystine	0.77	0.14722
alpha-Ketoglutarate	0.65	0.08855
N-Acetyloronithine	0.60	0.22501
Aminoimidazole ribotide (AIR)	0.60	0.02536
S-Ribosyl-L-homocysteine	0.82	0.24673
2-Isopropylmalate	0.79	0.08162
N-Carbamoyl-L-aspartate	0.78	0.29371
Phosphoenolpyruvate	0.89	0.13809
sn-Glycerol 3-phosphate	0.55	0.11985
3-Phosphoglycerate	0.97	0.88636
Nicotinate	0.95	0.57030
Pyruvate	0.97	0.74516
5-Hydroxyindoleacetic acid (5-HIAA)	1.12	0.68806
Fructose 1_6-bisphosphate	0.94	0.61374
Octulose 8/1P	0.68	0.07968

Table 14. Continued.

Metabolite	Fold Change	P Value
Hypoxanthine	1.39	0.59010
O-Acetyl-L-serine	1.74	0.09607
IMP	0.47	0.21822
Indole-3-carboxylate	0.44	0.38005
Trehalose/Sucrose/Cellobiose	0.87	0.56669
Inosine	0.97	0.89701
Phenylpyruvate	0.81	0.07534
N-Acetylglutamate	1.14	0.82379
Glycinamide ribotide (GAR)	0.18	0.34977
Xylitol 5-phosphate	0.63	0.37619
NAD+	1.59	0.18374
AMP/dGMP	0.68	0.47922
NADP+	1.29	0.09645
UDP-glucose	0.23	0.04314
Orotate	0.70	0.19850

Table 15. *X. nematophila* fold changes and p values in supernatant samples.

Metabolite	Fold Change	P Value
Alanine/Sarcosine	5.20	0.06791
Uracil	0.21	0.06578
Valine	1.17	0.43101
Succinate/Methylmalonate	1.08	0.67436
Homoserine/Threonine	0.91	0.53619
Thymine	0.32	0.08048
Leucine/Isoleucine	0.75	0.12441
Ornithine	0.90	0.58356
Acetylphosphate	1.33	0.26570
Histidinol	1.04	0.68347
Lysine	0.72	0.09591
O-Acetyl-L-serine	1.00	0.94217
Methionine	1.51	0.38199
Histidine	0.94	0.67606
Orotate	1.28	0.64708
Allantoin	0.93	0.55882
2-Aminoadipate	0.79	0.18348
Phenylpyruvate	0.64	0.12927
Phenylalanine	0.86	0.29660
Phenyllactic acid	0.93	0.67408
Aconitate	1.17	0.42953
N-Acetylornithine	0.82	0.04817
Citrulline	0.81	0.42511
N-Carbamoyl-L-aspartate	0.86	0.36051
2-Isopropylmalate	4.33	0.34999
Tyrosine	3.44	0.30039
3-Phosphoglycerate	1.34	0.06789
N-Acetylglutamate	0.92	0.72913
5-Hydroxyindoleacetic acid (5-HIAA)	0.80	0.09693
2-Dehydro-D-gluconate	0.80	0.07805
D-Gluconate	0.56	0.12419
Tryptophan	0.95	0.51508
Lipoate	0.75	0.02948
Deoxyribose phosphate	0.76	0.18628
Ribose phosphate	0.77	0.27434
Cystine	2.40	0.50162
Uridine	0.90	0.58695

Table 15. Continued.

Metabolite	Fold Change	P Value
S-Ribosyl-L-homocysteine	39.61	0.36545
Homocystine	0.71	0.04432
Inosine	3.04	0.15467
6-Phospho-D-gluconate	0.67	0.12300
Guanosine	0.98	0.90710
Aminoimidazole ribotide (AIR)	0.86	0.57086
N-Acetylglucosamine 1/6-phosphate	0.53	0.17174
UMP	0.55	0.43299
AICAR	155.19	0.35298
Fructose 1-6-bisphosphate	0.93	0.50633
IMP	0.76	0.24101
S-Adenosyl-L-methioninamine	4700.60	0.38085
dTDP	16410.75	0.38681
UDP	2.58	0.36245
UDP-glucose	79.48	0.36736
NADH	16.67	0.41368
Dephospho-CoA	287.28	0.42297
NADP+	0.91	0.86773
FAD	0.82	0.15527
Pyruvate	1.53	0.08027
Cysteine	0.79	0.12319
Nicotinate	1.53	0.15976
Malate	0.53	0.15475
Hypoxanthine	0.93	0.56312
Indole-3-carboxylate	4.49	0.14188
Phosphoenolpyruvate	1.10	0.63250
Glycerone phosphate	0.91	0.30988
sn-Glycerol 3-phosphate	2.29	0.19390
Citrate/isocitrate	1.12	0.51990
Sedoheptulose 1/7-phosphate	1.12	0.51990

Table 16. *X. nematophila* whole cell top VIP scores.

Metabolite	Component 1	Component 2
Sedoheptulose-1-7-phosphate	1.66968	1.63180
Glucosamine phosphate	1.57479	1.41781
Xanthosine	1.56944	1.37976
N-Acetylglucosamine-1-6-phosphate	1.50243	1.29932
Guanine	1.50208	1.36583
AICAR	1.50206	1.30604
dTDP	1.49856	1.39025
Succinate/Methylmalonate	1.49764	1.30887
FAD	1.45132	1.24881
Guanosine	1.42062	1.22071
UDP-glucuronate	1.41112	1.21236
UMP	1.40906	1.33120
Phenylalanine	1.39964	1.21857
Tryptophan	1.39940	1.20299
CMP	1.37684	1.18199
2-Hydroxy-2-methylsuccinate	1.34826	1.19411
Tyrosine	1.30842	1.12363
Deoxyribose phosphate	1.30651	1.14087
Methionine	1.30122	1.12507
Lysine	1.30011	1.11473
Citrate/isocitrate	1.28548	1.11829
Histidinol	1.28216	1.11433
FMN	1.25433	1.08018
Homocystine	1.23846	1.06614
NADH	1.22256	1.09975
Glycerone phosphate	1.21841	1.04605
S-Adenosyl-L-methioninamine	1.18527	1.02807
Lipoate	1.17091	1.01205
Ribose phosphate	1.16526	0.99911
Uridine	1.14919	1.04710
Histidine	1.11666	1.03669
Acetylphosphate	1.10824	1.03810
UDP-N-acetylglucosamine	1.10323	0.94880
Citrulline	1.10294	0.99247
Uracil	1.08479	1.10097
Allantoin	1.06258	1.03374

Table 16. Continued.

Metabolite	Component 1	Component 2
Adenosine	1.05546	1.08837
Sedoheptulose biphosphate	1.04062	0.95559
Leucine/Isoleucine	1.00898	0.96469
Alanine/Sarcosine	0.97716	1.05681
D-Gluconate	0.90413	1.04520
Dephospho-CoA	0.89718	1.00083
Phenyllactic acid	0.86806	1.35070
Malate	0.56711	1.13021
Valine	0.55355	1.07655
Cysteine	0.48347	1.12674
Homoserine/Threonine	0.41919	1.13215
2-Dehydro-D-gluconate	0.35256	1.12877
Fumarate	0.32495	1.07013
2-Aminoadipate	0.19590	1.05751
6-Phospho-D-gluconate	0.08055	1.22786

Table 17. *X. nematophila* supernatant top VIP scores.

Metabolites	Component 1	Component 2
Valine	1.56439	1.42869
Leucine/Isoleucine	1.53484	1.40497
Uracil	1.49572	1.45030
Deoxyribose phosphate	1.47138	1.30673
Inosine	1.44952	1.29413
Phosphoenolpyruvate	1.42618	1.26056
O-Acetyl-L-serine	1.40388	1.24111
Citrulline	1.40197	1.30565
Tryptophan	1.36852	1.21813
N-Acetylglutamate	1.35695	1.21030
Phenylalanine	1.35167	1.55223
6-Phospho-D-gluconate	1.34402	1.20394
2-Dehydro-D-gluconate	1.34070	1.18615
UDP glucose	1.31546	1.20901
D-Gluconate	1.30653	1.16868
Citrate/isocitrate	1.27542	1.14331
Nicotinate	1.26601	1.11930
Malate	1.22379	1.16489
Guanosine	1.20259	1.07568
Pyruvate	1.20054	1.12470
Ornithine	1.19638	1.05909
Hypoxanthine	1.17702	1.05332
Ribose phosphate	1.16857	1.04021
Fructose-1-6-bisphosphate	1.10632	1.04797
Phenylpyruvate	1.09177	0.97723
UDP	1.04696	1.02680
3-Phosphoglycerate	1.03688	0.98286
Tyrosine	1.03133	1.09314
Xylitol-5-phosphate	1.00944	0.90164
Dephospho-CoA	0.90985	1.05237
NADP+	0.75328	1.04958
Thymine	0.57284	1.19543
N-Acetylglucosamine-1-6-phosphate	0.48750	1.15191
Uridine	0.30100	1.07233
Alanine/Sarcosine	0.25544	1.39027

Table 18. Intensities of *G. mellonella* replicates in uninfected group.

Metabolite	Uninfected-1	Uninfected-2	Uninfected-3	Uninfected-4	Uninfected-5
Glyoxylate	0.00E+00	0.00E+00	0.00E+00	2.10E+03	5.29E+06
Glycine	8.98E+04	1.00E+05	7.59E+04	2.09E+05	2.64E+08
Pyruvate	3.72E+08	6.15E+08	3.48E+08	5.10E+08	2.47E+08
Alanine/Sarcosine	5.66E+08	9.27E+08	5.53E+08	1.33E+09	6.29E+08
Lactate	3.58E+08	3.63E+08	3.42E+08	8.62E+08	4.73E+08
Dimethylglycine	2.21E+07	2.24E+07	2.25E+07	2.74E+07	2.37E+07
Serine	2.97E+07	4.15E+07	2.01E+07	4.84E+07	5.55E+07
Histamine	2.38E+05	3.74E+05	2.00E+05	3.43E+05	2.41E+05
Uracil	1.90E+07	6.39E+06	1.34E+07	4.04E+07	1.55E+07
Creatinine	7.71E+03	2.51E+04	0.00E+00	1.92E+03	2.26E+03
Proline	5.25E+09	1.44E+10	4.45E+09	7.66E+09	8.04E+09
Fumarate	9.34E+07	1.38E+08	7.53E+07	2.10E+08	1.22E+08
2-Oxoisovalerate	8.73E+06	1.02E+07	5.81E+06	1.47E+07	4.31E+06
Indole	1.72E+06	4.73E+06	1.19E+06	3.97E+06	9.57E+05
Valine	7.58E+08	1.34E+09	4.69E+08	1.10E+09	4.61E+08
3-Hydroxyisovaleric acid	1.13E+07	2.17E+07	1.10E+07	4.33E+07	8.72E+06
Homoserine/Threonine	1.17E+08	2.53E+08	8.89E+07	2.20E+08	2.83E+07
3-Methylthiopropionate	8.74E+04	2.07E+05	1.70E+05	8.51E+05	1.48E+04
Cysteine	1.45E+06	2.16E+06	1.36E+06	5.13E+06	3.35E+06
Nicotinate	4.76E+07	1.68E+07	3.85E+07	7.21E+07	4.05E+07
Taurine	7.79E+05	2.72E+06	1.68E+06	6.98E+06	1.07E+06

Table 18. Continued.

Metabolite	Uninfected-1	Uninfected-2	Uninfected-3	Uninfected-4	Uninfected-5
Thymine	8.18E+06	1.18E+07	8.83E+06	1.11E+07	4.58E+06
Hydroxyproline	1.10E+06	2.08E+06	1.86E+06	1.13E+06	1.08E+06
N-Acetyl-beta-alanine	4.92E+06	1.25E+07	5.29E+06	1.25E+07	6.03E+06
Leucine/Isoleucine	1.93E+09	4.87E+09	1.18E+09	2.23E+09	2.09E+09
Glutaric acid	3.95E+07	1.49E+08	4.85E+07	1.42E+08	5.81E+07
Asparagine	1.57E+08	3.49E+08	1.56E+08	2.75E+08	1.10E+08
Hydroxyisocaproic acid	4.75E+07	1.27E+08	3.35E+07	2.38E+08	4.01E+07
Ornithine	2.83E+06	5.20E+06	2.53E+06	8.34E+06	5.00E+06
Salicylate	1.12E+07	3.77E+07	1.85E+07	2.45E+07	1.51E+07
Hydroxybenzoate	7.35E+05	1.87E+06	6.44E+05	2.29E+06	1.08E+06
Histidinol	4.68E+04	6.71E+04	3.23E+04	4.79E+04	3.48E+04
2-Oxoglutaric acid	2.84E+08	7.80E+08	2.83E+08	2.88E+08	1.23E+08
Glutamine	1.09E+09	3.00E+09	1.14E+09	1.62E+09	1.60E+09
2-hydroxyglutarate	6.11E+07	1.45E+08	6.51E+07	1.42E+08	6.97E+07
2-Hydroxy-2-methylsuccinate	6.08E+07	1.45E+08	6.48E+07	1.42E+08	6.93E+07
L-Methionine	4.49E+07	9.11E+07	2.34E+07	4.99E+07	3.70E+07
Guanine	1.04E+04	4.32E+04	9.91E+04	1.11E+05	3.85E+04
3-Methylphenylacetic acid	1.38E+06	3.34E+06	1.38E+06	4.52E+06	4.04E+05
Hydroxyphenylacetate	1.19E+06	1.89E+06	3.12E+06	1.56E+06	1.03E+06
Xylitol	1.05E+07	6.26E+06	7.95E+06	1.38E+07	1.02E+07
Dopamine	7.13E+07	7.78E+08	1.23E+08	3.79E+08	1.38E+08
2,3-Dihydroxybenzoate	4.86E+04	8.39E+03	2.30E+05	1.71E+05	1.31E+05

Table 18. Continued.

Metabolite	Uninfected-1	Uninfected-2	Uninfected-3	Uninfected-4	Uninfected-5
Histidine	3.76E+08	5.20E+08	2.99E+08	4.70E+08	3.67E+08
Orotate	4.59E+05	3.30E+06	5.06E+05	3.96E+06	2.48E+06
Dihydroorotate	4.63E+05	1.20E+06	4.75E+05	1.46E+06	2.31E+05
Allantoin	1.12E+07	3.53E+06	7.47E+06	6.04E+06	2.88E+06
Indole-3-carboxylate	1.52E+05	5.44E+05	1.66E+05	6.94E+05	2.92E+05
Phenylpyruvate	9.53E+05	2.75E+06	1.83E+06	2.42E+06	1.29E+06
Phenylalanine	9.98E+08	4.14E+09	9.82E+08	1.64E+09	7.29E+08
Phenyllactic acid	1.83E+06	6.46E+06	2.34E+06	1.45E+07	1.77E+06
Quinolate	5.22E+03	2.17E+05	2.88E+04	1.61E+05	1.70E+05
Phosphoenolpyruvate	1.74E+06	5.34E+06	1.07E+06	2.51E+06	2.16E+06
Uric acid	7.08E+08	9.28E+08	6.02E+08	1.61E+09	7.24E+08
3_4-Dihydroxyphenylacetate (DOPAC)	1.68E+05	3.52E+05	1.92E+05	2.42E+05	1.29E+05
Sulfolactate	2.58E+06	4.23E+06	1.47E+06	2.88E+06	3.03E+06
Glycerone phosphate	5.84E+06	4.25E+07	8.52E+06	9.75E+06	2.20E+07
Arginine	7.31E+07	1.19E+08	8.82E+07	7.87E+07	7.44E+07
Citrulline	1.65E+06	1.67E+06	1.06E+06	2.66E+06	9.54E+05
Ascorbate	2.79E+08	1.27E+09	4.72E+08	4.89E+08	5.90E+08
N-Carbamoyl-L-aspartate	1.29E+06	5.39E+06	1.21E+06	5.14E+06	2.10E+06
Allantoate	5.61E+08	8.20E+08	5.50E+08	2.71E+08	2.79E+08
2-Isopropylmalate	1.49E+06	4.20E+06	1.00E+07	3.04E+06	4.86E+06
Glucosamine	7.15E+05	9.21E+05	1.26E+06	2.37E+05	4.41E+05

Table 18. Continued.

Metabolite	Uninfected-1	Uninfected-2	Uninfected-3	Uninfected-4	Uninfected-5
myo-Inositol	3.02E+07	3.13E+07	2.30E+07	5.94E+07	3.45E+07
Tyrosine	1.04E+09	2.59E+09	8.48E+08	1.90E+09	8.50E+08
Homovanillic acid (HVA)	1.58E+07	3.74E+07	1.39E+07	4.52E+07	8.50E+06
Homocysteic acid	2.44E+03	0.00E+00	0.00E+00	3.85E+03	2.40E+03
4-Pyridoxate	3.53E+06	6.81E+06	3.57E+06	6.27E+06	3.05E+06
N-Acetylglutamine	1.01E+07	6.94E+07	7.26E+06	2.13E+07	2.89E+07
Citrate/isocitrate	1.82E+10	4.48E+10	1.29E+10	1.74E+10	2.23E+10
D-Gluconate	1.33E+08	2.49E+08	8.31E+07	2.26E+08	1.49E+08
N-N Dimethylarginine	4.46E+05	5.16E+05	4.60E+05	7.69E+05	4.79E+05
Tryptophan	5.34E+08	1.31E+09	3.80E+08	1.09E+09	3.21E+08
Xanthurenic acid	1.75E+07	5.37E+06	1.27E+07	1.67E+08	5.40E+06
D-Glucarate	2.00E+09	2.96E+09	6.08E+08	2.79E+09	3.68E+09
Pantothenate	9.43E+08	2.11E+09	7.89E+08	1.66E+09	9.17E+08
Cystathionine	1.48E+07	4.43E+06	3.57E+06	3.56E+07	3.44E+06
Cystine	6.39E+05	2.47E+05	9.47E+05	1.47E+06	1.60E+05
Uridine	1.36E+05	3.96E+05	1.96E+05	2.95E+05	2.03E+05
Biotin	2.23E+06	2.64E+06	2.83E+06	5.22E+06	9.59E+05
Deoxyinosine	3.36E+03	2.16E+03	0.00E+00	0.00E+00	0.00E+00
Glucose 6-phosphate	3.73E+08	2.75E+08	3.61E+08	4.45E+08	4.51E+08
S-Ribosyl-L-homocysteine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
6-Phospho-D-gluconate	4.72E+06	3.79E+06	7.52E+06	4.79E+06	2.80E+06
Guanosine	9.26E+06	9.44E+06	9.38E+06	1.49E+07	1.07E+07

Table 18. Continued.

Metabolite	Uninfected-1	Uninfected-2	Uninfected-3	Uninfected-4	Uninfected-5
Xanthosine	1.50E+05	2.93E+05	7.89E+04	2.69E+05	6.27E+05
Glycinamide ribotide (GAR)	2.48E+04	1.91E+05	0.00E+00	3.38E+04	0.00E+00
Ophthalmate	2.01E+06	4.54E+06	1.32E+06	1.33E+06	1.39E+06
Glutathione	1.29E+08	4.00E+08	6.89E+07	3.50E+08	3.69E+08
UMP	1.58E+08	4.38E+08	1.46E+08	3.06E+08	2.97E+08
AICAR	5.74E+06	2.67E+07	7.18E+05	3.96E+06	7.04E+05
Trehalose/Sucrose/Cellobiose	2.70E+07	3.06E+07	2.90E+07	1.69E+07	2.80E+07
AMP/dGMP	1.97E+09	1.29E+09	1.90E+09	2.50E+09	2.78E+09
IMP	3.36E+07	2.44E+07	2.37E+07	1.41E+08	3.34E+07
GMP	1.26E+08	7.27E+07	1.05E+08	2.28E+08	1.66E+08
Xanthosine 5--phosphate	3.32E+04	2.96E+04	0.00E+00	5.75E+04	3.02E+04
Riboflavin	2.75E+06	3.39E+06	3.89E+06	7.44E+06	1.29E+06
S-Adenosyl-L-homocysteine	7.97E+04	7.65E+04	5.25E+04	1.03E+05	5.36E+04
ADP	2.10E+08	1.33E+09	2.21E+08	2.05E+08	2.34E+08
Folate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CDP-ethanolamine	4.20E+06	1.14E+07	4.71E+06	5.49E+06	6.31E+06
FMN	7.96E+06	1.27E+07	6.48E+06	9.70E+06	5.90E+06
UDP-glucose	8.72E+07	2.42E+08	4.50E+07	1.86E+08	8.92E+07
NAD+	4.06E+07	1.03E+08	4.29E+07	6.68E+07	5.30E+07
NADH	2.24E+06	1.46E+06	3.18E+06	5.05E+06	6.42E+06
Dephospho-CoA	9.34E+05	1.98E+06	7.16E+05	2.07E+06	2.12E+06
NADP+	5.14E+06	1.24E+07	6.66E+06	4.11E+06	3.30E+06

Table 18. Continued.

Metabolite	Uninfected-1	Uninfected-2	Uninfected-3	Uninfected-4	Uninfected-5
FAD	8.93E+05	6.34E+06	5.33E+05	7.90E+05	2.61E+06
N-Acetylglutamate	5.59E+07	2.48E+08	5.92E+07	1.01E+08	1.66E+08
Kynurenic acid	1.17E+05	1.65E+05	6.45E+04	3.99E+05	9.87E+04

Table 19. Intensities of *G. mellonella* replicates in 1-Hour post infection group.

Metabolite	1 Hour-1	1 Hour-2	1 Hour-3	1 Hour-4	1 Hour-5
Glyoxylate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Glycine	7.21E+04	4.83E+04	2.26E+04	3.28E+04	1.86E+04
Pyruvate	5.61E+08	7.10E+08	3.96E+08	1.98E+08	5.17E+08
Alanine/Sarcosine	3.96E+08	7.99E+08	1.06E+09	3.97E+08	4.61E+08
Lactate	4.66E+08	3.48E+08	4.64E+08	3.63E+08	3.80E+08
Dimethylglycine	1.95E+07	3.19E+07	1.70E+07	1.61E+07	2.95E+07
Serine	1.79E+08	4.25E+07	5.17E+07	8.45E+07	6.20E+07
Histamine	4.63E+05	4.18E+05	3.27E+05	1.90E+05	3.10E+05
Uracil	5.10E+06	6.65E+06	1.87E+07	1.35E+07	2.27E+07
Creatinine	2.36E+04	3.01E+04	1.20E+04	5.77E+03	2.08E+04
Proline	1.68E+10	9.07E+09	1.07E+10	5.16E+09	8.38E+09
Fumarate	1.62E+08	2.44E+08	1.60E+08	7.69E+07	1.13E+08
2-Oxoisovalerate	7.36E+06	1.13E+07	8.25E+06	4.83E+06	4.95E+06
Indole	4.75E+06	2.76E+06	3.99E+06	7.18E+05	4.24E+06
Valine	9.86E+08	1.03E+09	8.93E+08	5.86E+08	7.85E+08
3-Hydroxyisovaleric acid	1.53E+07	1.43E+07	9.81E+06	9.40E+06	6.49E+06
Homoserine/Threonine	1.09E+08	4.72E+08	1.90E+08	3.31E+07	3.11E+07
3-Methylthiopropionate	2.73E+05	1.64E+05	1.09E+04	1.40E+05	1.50E+04
Cysteine	1.26E+06	2.36E+06	3.18E+06	1.70E+06	4.60E+06
Nicotinate	1.88E+07	2.11E+07	5.68E+07	3.84E+07	4.34E+07
Taurine	5.45E+06	3.93E+06	3.95E+06	1.76E+06	8.82E+06
Thymine	7.99E+06	1.01E+07	4.60E+06	5.65E+06	4.36E+06

Table 19. Continued.

Metabolite	1 Hour-1	1 Hour-2	1 Hour-3	1 Hour-4	1 Hour-5
Hydroxyproline	2.59E+06	1.43E+06	1.82E+06	1.05E+06	2.60E+06
N-Acetyl-beta-alanine	1.23E+07	1.54E+07	7.69E+06	3.82E+06	7.84E+06
Leucine/Isoleucine	3.90E+09	2.47E+09	3.15E+09	1.82E+09	2.43E+09
Glutaric acid	2.56E+08	1.95E+08	1.05E+08	2.64E+07	5.61E+07
Asparagine	1.66E+08	8.94E+08	2.46E+08	8.57E+07	1.08E+08
Hydroxyisocaproic acid	1.22E+08	6.55E+07	4.37E+07	2.92E+07	1.93E+07
Ornithine	5.73E+06	2.42E+06	6.58E+06	2.76E+06	5.81E+06
Salicylate	2.65E+07	2.92E+07	1.43E+07	1.52E+07	1.56E+07
Hydroxybenzoate	2.50E+06	3.77E+06	1.35E+06	5.81E+05	1.91E+06
Histidinol	6.41E+04	9.75E+04	3.91E+04	3.81E+04	1.25E+05
2-Oxoglutaric acid	1.53E+09	1.03E+09	1.97E+08	1.86E+08	6.52E+08
Glutamine	2.90E+09	1.10E+09	2.43E+09	1.17E+09	1.40E+09
2-hydroxyglutarate	2.91E+08	1.38E+08	6.97E+07	6.46E+07	7.45E+07
2-Hydroxy-2-methylsuccinate	2.91E+08	1.37E+08	6.96E+07	6.45E+07	7.42E+07
L-Methionine	4.58E+07	7.74E+07	3.77E+07	1.79E+07	6.27E+07
Guanine	1.03E+05	9.72E+04	9.24E+04	0.00E+00	3.09E+04
3-Methylphenylacetic acid	4.05E+06	2.92E+06	6.96E+05	1.07E+06	5.91E+05
Hydroxyphenylacetate	1.65E+06	1.56E+06	1.02E+06	1.10E+06	1.05E+06
Xylitol	5.25E+06	5.88E+06	1.09E+07	6.99E+06	9.73E+06
Dopamine	5.30E+08	4.83E+08	4.71E+08	9.01E+07	3.87E+08
2_3-Dihydroxybenzoate	1.26E+04	1.66E+05	3.92E+04	2.34E+05	1.14E+05
Histidine	5.94E+08	5.72E+08	3.72E+08	2.66E+08	4.46E+08
Orotate	4.75E+06	1.10E+07	3.32E+06	1.12E+05	7.32E+05

Table 19. Continued.

Metabolite	1 Hour-1	1 Hour-2	1 Hour-3	1 Hour-4	1 Hour-5
Dihydroorotate	1.02E+06	2.20E+06	9.70E+05	2.90E+05	2.19E+05
Allantoin	1.40E+06	2.99E+06	1.77E+07	6.23E+05	7.31E+06
Indole-3-carboxylate	9.38E+05	1.41E+06	2.54E+05	1.68E+05	2.43E+05
Phenylpyruvate	3.30E+06	2.39E+06	1.19E+06	5.99E+05	9.36E+05
Phenylalanine	1.28E+09	1.73E+09	2.02E+09	9.22E+07	1.85E+09
Phenyllactic acid	4.76E+06	6.64E+06	2.31E+06	7.21E+05	2.06E+06
Quinolate	4.49E+04	2.00E+06	1.33E+05	3.12E+04	3.33E+04
Phosphoenolpyruvate	7.63E+06	3.62E+06	2.50E+06	1.20E+06	2.64E+06
Uric acid	3.29E+07	2.05E+09	7.60E+08	2.97E+07	4.33E+08
3_4-Dihydroxyphenylacetate (DOPAC)	2.39E+05	1.09E+06	1.89E+05	7.69E+04	2.65E+05
Sulfolactate	3.18E+06	1.22E+07	1.94E+06	7.30E+05	2.63E+06
Glycerone phosphate	4.21E+07	3.61E+07	3.20E+07	9.51E+06	5.16E+07
Arginine	1.16E+08	7.59E+07	9.25E+07	8.79E+07	9.77E+07
Citrulline	7.38E+05	7.72E+05	2.91E+06	8.89E+05	1.45E+06
Ascorbate	1.50E+09	6.60E+08	5.87E+08	7.71E+08	7.30E+08
N-Carbamoyl-L-aspartate	5.21E+06	5.85E+06	8.32E+06	3.76E+05	2.06E+06
Allantoate	4.67E+08	3.22E+08	1.10E+09	7.23E+07	6.00E+08
2-Isopropylmalate	3.46E+06	1.52E+07	4.53E+06	1.11E+06	2.47E+06
Glucosamine	5.49E+05	1.75E+05	3.10E+05	6.01E+05	6.04E+05
myo-Inositol	3.40E+07	5.74E+07	2.11E+07	2.07E+07	2.60E+07
Tyrosine	1.48E+09	1.98E+09	1.74E+09	6.28E+08	1.60E+09
Homovanillic acid (HVA)	1.13E+07	6.74E+07	1.28E+07	5.63E+06	6.54E+06

Table 19. Continued.

Metabolite	1 Hour-1	1 Hour-2	1 Hour-3	1 Hour-4	1 Hour-5
Homocysteic acid	0.00E+00	1.40E+04	2.20E+03	0.00E+00	0.00E+00
4-Pyridoxate	8.42E+06	1.22E+07	3.40E+06	4.38E+06	4.70E+06
N-Acetylglutamine	1.78E+08	2.79E+07	3.15E+07	7.94E+06	2.73E+07
Citrate/isocitrate	4.78E+10	3.56E+10	2.11E+10	1.12E+10	2.52E+10
D-Gluconate	2.41E+08	2.96E+08	1.49E+08	7.35E+07	1.57E+08
N-N Dimethylarginine	5.92E+05	5.89E+05	3.80E+05	5.04E+05	3.39E+05
Tryptophan	1.36E+09	8.48E+08	1.11E+09	2.43E+08	1.17E+09
Xanthurenic acid	3.02E+08	1.55E+09	4.89E+07	1.39E+07	5.11E+07
D-Glucarate	2.60E+09	2.85E+09	1.14E+09	1.57E+09	1.68E+09
Pantothenate	1.83E+09	2.74E+09	1.15E+09	7.35E+08	1.50E+09
Cystathionine	3.15E+06	1.66E+08	3.63E+06	2.65E+06	9.28E+07
Cystine	3.51E+05	4.60E+05	6.07E+05	6.01E+05	7.84E+05
Uridine	3.90E+05	6.15E+05	2.34E+05	1.34E+05	2.79E+05
Biotin	1.28E+06	4.78E+06	2.46E+06	1.89E+06	2.91E+06
Deoxyinosine	0.00E+00	2.17E+03	0.00E+00	1.62E+03	0.00E+00
Glucose 6-phosphate	1.97E+08	2.15E+08	3.51E+08	4.33E+08	4.47E+08
S-Ribosyl-L-homocysteine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
6-Phospho-D-gluconate	4.73E+06	2.99E+06	3.81E+06	3.56E+06	8.10E+06
Guanosine	2.72E+07	2.19E+07	5.62E+06	1.30E+07	1.17E+07
Xanthosine	2.32E+05	2.35E+06	2.66E+05	3.25E+04	1.53E+05
Glycinamide ribotide (GAR)	4.35E+04	8.54E+03	1.81E+04	6.56E+03	2.52E+04
Ophthalmate	1.92E+06	4.20E+06	1.62E+06	7.86E+05	2.36E+06
Glutathione	4.44E+08	7.07E+08	1.05E+08	6.01E+07	2.79E+08

Table 19. Continued.

Metabolite	1 Hour-1	1 Hour-2	1 Hour-3	1 Hour-4	1 Hour-5
UMP	4.07E+08	5.54E+08	3.14E+08	1.57E+08	3.48E+08
AICAR	6.49E+05	8.03E+06	4.70E+06	1.13E+05	1.07E+06
Trehalose/Sucrose/Cellobiose	3.68E+07	3.64E+07	2.15E+07	2.73E+07	4.29E+07
AMP/dGMP	1.55E+09	1.18E+09	2.82E+09	1.85E+09	2.67E+09
IMP	3.42E+07	3.54E+07	5.08E+07	3.00E+07	2.61E+07
GMP	9.35E+07	7.01E+07	1.85E+08	1.06E+08	1.75E+08
Xanthosine 5--phosphate	1.02E+05	6.34E+04	2.64E+04	6.99E+03	5.27E+04
Riboflavin	1.25E+06	1.37E+07	2.90E+06	1.27E+06	3.97E+06
S-Adenosyl-L-homocysteine	1.81E+04	1.08E+05	7.44E+04	3.85E+04	2.28E+05
ADP	1.27E+09	9.03E+08	3.47E+08	1.87E+08	4.22E+08
Folate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CDP-ethanolamine	1.10E+07	6.91E+06	7.29E+06	4.14E+06	6.79E+06
FMN	1.04E+07	1.34E+07	1.16E+07	5.27E+06	1.17E+07
UDP-glucose	2.15E+08	2.55E+08	7.72E+07	4.38E+07	1.01E+08
NAD+	9.94E+07	1.21E+08	5.39E+07	3.75E+07	6.27E+07
NADH	2.53E+06	8.86E+05	4.10E+06	3.80E+06	6.44E+06
Dephospho-CoA	1.36E+06	7.43E+05	2.68E+06	1.05E+06	1.69E+06
NADP+	1.14E+07	8.18E+06	5.54E+06	4.71E+06	5.33E+06
FAD	4.92E+06	3.08E+06	1.35E+06	4.91E+05	3.21E+06
N-Acetylglutamate	2.72E+08	2.47E+08	1.36E+08	4.83E+07	1.44E+08
Kynurenic acid	6.40E+05	3.31E+06	5.23E+05	6.95E+04	1.88E+05

Table 20. Intensities of *G. mellonella* replicates in 12-Hour post infection group

Metabolite	12 Hours-1	12 Hours-2	12 Hours-3	12 Hours-4	12 Hours-5
Glyoxylate	0.00E+00	5.10E+06	5.23E+06	3.58E+03	3.16E+03
Glycine	1.19E+05	7.22E+08	3.80E+08	1.06E+04	5.74E+04
Pyruvate	1.17E+09	4.98E+08	5.92E+08	3.94E+08	6.53E+08
Alanine/Sarcosine	1.03E+09	4.32E+08	3.07E+08	3.89E+08	1.58E+09
Lactate	9.03E+08	5.77E+08	3.97E+08	4.89E+08	1.06E+09
Dimethylglycine	3.76E+07	3.23E+07	2.74E+07	3.50E+07	3.95E+07
Serine	1.63E+08	4.34E+07	7.04E+07	1.19E+08	1.63E+08
Histamine	2.74E+05	4.69E+05	2.89E+05	3.54E+05	3.61E+05
Uracil	4.21E+07	1.07E+07	8.36E+06	3.14E+07	8.29E+06
Creatinine	4.66E+04	1.24E+04	9.05E+03	8.37E+03	1.95E+04
Proline	1.47E+10	1.82E+10	1.16E+10	1.29E+10	1.27E+10
Fumarate	3.40E+08	1.28E+08	1.04E+08	1.11E+08	3.02E+08
2-Oxoisovalerate	1.58E+07	1.17E+07	5.64E+06	7.05E+06	7.86E+06
Indole	3.56E+06	6.38E+06	1.46E+06	1.55E+06	2.59E+06
Valine	1.98E+09	1.45E+09	1.18E+09	8.93E+08	1.03E+09
3-Hydroxyisovaleric acid	1.67E+07	2.06E+07	8.43E+06	9.24E+06	1.43E+07
Homoserine/Threonine	1.66E+08	3.38E+08	4.41E+07	5.06E+07	4.37E+07
3-Methylthiopropionate	1.94E+05	1.30E+04	2.28E+04	2.65E+04	5.83E+05
Cysteine	2.14E+06	3.42E+06	1.62E+06	2.35E+06	1.75E+06
Nicotinate	1.27E+08	4.68E+07	2.95E+07	7.94E+07	5.06E+07
Taurine	7.77E+06	2.02E+06	3.41E+05	5.52E+06	1.13E+06
Thymine	8.18E+06	2.74E+06	2.57E+06	1.11E+07	1.04E+07
Hydroxyproline	3.25E+06	2.05E+06	7.82E+05	4.10E+06	1.28E+06

Table 20. Continued.

Metabolite	12 Hours-1	12 Hours-2	12 Hours-3	12 Hours-4	12 Hours-5
N-Acetyl-beta-alanine	1.30E+07	1.03E+07	6.50E+06	9.28E+06	1.17E+07
Leucine/Isoleucine	5.19E+09	3.67E+09	4.21E+09	3.94E+09	3.91E+09
Glutaric acid	8.94E+07	1.22E+08	5.88E+07	9.85E+07	9.19E+07
Asparagine	3.13E+08	4.18E+08	1.38E+08	1.76E+08	1.73E+08
Hydroxyisocaproic acid	1.04E+08	2.84E+08	3.79E+07	4.85E+07	9.94E+07
Ornithine	4.03E+06	6.83E+06	3.87E+06	4.76E+06	3.57E+06
Salicylate	3.43E+07	3.39E+07	2.40E+07	1.63E+07	2.31E+07
Hydroxybenzoate	1.31E+06	9.06E+05	7.94E+05	9.99E+05	1.07E+06
Histidinol	5.33E+04	6.56E+04	4.37E+04	5.50E+04	6.22E+04
2-Oxoglutaric acid	1.24E+09	6.01E+08	6.58E+08	5.55E+08	4.30E+08
Glutamine	3.17E+09	2.26E+09	1.35E+09	1.35E+09	1.89E+09
2-hydroxyglutarate	3.02E+08	2.37E+08	2.38E+08	3.23E+08	1.04E+09
2-Hydroxy-2-methylsuccinate	3.01E+08	2.36E+08	2.38E+08	3.23E+08	1.04E+09
L-Methionine	9.19E+07	5.91E+07	3.86E+07	6.56E+07	7.58E+07
Guanine	3.86E+04	2.31E+04	1.16E+04	2.28E+03	3.59E+04
3-Methylphenylacetic acid	2.82E+06	5.89E+05	9.48E+05	5.21E+05	4.82E+06
Hydroxyphenylacetate	1.31E+06	3.25E+06	1.89E+06	1.08E+06	1.39E+06
Xylitol	2.02E+07	1.40E+07	9.16E+06	1.49E+07	1.21E+07
Dopamine	1.10E+09	6.05E+08	3.76E+08	5.17E+08	5.38E+08
2_3-Dihydroxybenzoate	1.37E+05	0.00E+00	1.75E+05	1.83E+04	1.12E+05
Histidine	4.93E+08	4.95E+08	4.16E+08	4.93E+08	5.17E+08
Orotate	5.56E+06	3.40E+06	2.19E+06	2.82E+06	1.14E+07
Dihydroorotate	1.42E+06	1.17E+06	8.28E+05	7.68E+05	4.01E+06
Allantoin	2.92E+07	6.95E+06	2.17E+06	1.97E+06	3.54E+06

Table 20. Continued.

Metabolite	12 Hours-1	12 Hours-2	12 Hours-3	12 Hours-4	12 Hours-5
Indole-3-carboxylate	6.71E+05	3.70E+05	1.89E+05	2.25E+05	4.99E+05
Phenylpyruvate	1.02E+07	6.79E+06	6.68E+05	9.25E+05	2.35E+06
Phenylalanine	2.08E+09	3.93E+09	2.10E+08	1.81E+09	9.12E+08
Phenyllactic acid	4.52E+06	6.25E+06	1.16E+06	2.81E+06	4.32E+06
Quinolate	6.38E+04	4.20E+03	1.88E+06	1.45E+04	7.60E+04
Phosphoenolpyruvate	2.36E+06	7.04E+05	3.26E+06	4.66E+06	3.41E+06
Uric acid	3.74E+08	9.42E+08	1.07E+08	7.32E+07	3.84E+08
3_4-Dihydroxyphenylacetate (DOPAC)	2.75E+05	2.72E+05	1.24E+05	1.38E+05	2.19E+05
Sulfolactate	3.50E+06	4.28E+06	1.13E+06	2.43E+06	3.37E+06
Glycerone phosphate	1.89E+07	3.16E+07	4.75E+07	2.14E+07	2.62E+07
Arginine	1.36E+08	9.70E+07	1.10E+08	1.01E+08	1.24E+08
Citrulline	5.86E+06	1.98E+06	9.89E+05	3.09E+06	1.84E+06
Ascorbate	5.36E+08	6.40E+08	5.06E+08	6.41E+08	1.86E+09
N-Carbamoyl-L-aspartate	3.58E+06	4.28E+06	3.22E+06	1.96E+06	1.36E+07
Allantoate	9.99E+08	7.05E+08	3.15E+08	3.17E+08	4.65E+08
2-Isopropylmalate	2.95E+06	1.49E+06	5.76E+06	1.94E+06	2.81E+06
Glucosamine	9.00E+05	6.10E+05	7.12E+05	8.05E+05	8.12E+05
myo-Inositol	3.26E+07	2.28E+07	2.51E+07	1.85E+07	3.07E+07
Tyrosine	1.74E+09	2.74E+09	1.23E+09	1.52E+09	1.83E+09
Homovanillic acid (HVA)	2.24E+07	5.06E+07	8.17E+06	7.01E+06	1.68E+07
Homocysteic acid	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
4-Pyridoxate	6.34E+06	6.06E+06	3.18E+06	4.26E+06	5.81E+06
N-Acetylglutamine	1.10E+08	2.18E+08	1.90E+07	5.08E+07	3.90E+07
Citrate/isocitrate	3.47E+10	3.63E+10	2.42E+10	2.47E+10	2.78E+10

Table 20. Continued.

Metabolite	12 Hours-1	12 Hours-2	12 Hours-3	12 Hours-4	12 Hours-5
D-Gluconate	3.02E+08	2.37E+08	1.52E+08	1.69E+08	1.99E+08
N-N Dimethylarginine	2.92E+05	3.49E+05	5.44E+05	5.49E+05	4.71E+05
Tryptophan	1.05E+09	1.78E+09	4.91E+08	4.88E+08	8.43E+08
Xanthurenic acid	2.68E+07	3.71E+07	9.80E+06	9.77E+06	2.28E+07
D-Glucarate	1.87E+09	2.43E+09	2.73E+09	1.48E+09	1.57E+09
Pantothenate	2.07E+09	1.69E+09	1.27E+09	1.14E+09	1.77E+09
Cystathionine	5.19E+06	4.31E+06	4.31E+06	4.96E+06	7.99E+06
Cystine	5.99E+05	5.64E+04	1.33E+05	3.43E+05	3.42E+05
Uridine	4.92E+05	2.75E+05	2.52E+05	2.73E+05	3.04E+05
Biotin	2.65E+06	2.73E+06	1.78E+06	2.51E+06	2.91E+06
Deoxyinosine	1.96E+03	0.00E+00	0.00E+00	0.00E+00	5.90E+03
Glucose 6-phosphate	5.99E+08	4.74E+08	4.85E+08	5.32E+08	2.38E+08
S-Ribosyl-L-homocysteine	0.00E+00	0.00E+00	0.00E+00	1.22E+04	0.00E+00
6-Phospho-D-gluconate	1.46E+07	2.67E+06	3.93E+06	9.95E+06	5.93E+06
Guanosine	3.73E+06	8.87E+06	1.25E+07	1.03E+07	1.77E+07
Xanthosine	4.28E+05	1.38E+05	8.11E+04	1.50E+05	1.66E+05
Glycinamide ribotide (GAR)	1.97E+05	6.27E+05	1.95E+05	9.16E+04	2.21E+05
Ophthalmate	5.99E+06	8.82E+06	2.74E+06	4.62E+06	1.34E+06
Glutathione	8.23E+07	2.51E+08	2.96E+08	2.10E+08	5.31E+08
UMP	3.57E+08	5.12E+08	3.63E+08	3.63E+08	4.25E+08
AICAR	2.05E+06	2.43E+07	2.06E+06	5.14E+05	8.65E+05
Trehalose/Sucrose/Cellobiose	2.81E+07	2.66E+07	3.47E+07	3.08E+07	4.51E+07
AMP/dGMP	3.02E+09	3.21E+09	2.88E+09	2.55E+09	1.75E+09
IMP	4.26E+08	9.91E+07	4.73E+07	2.58E+08	9.15E+07

Table 20. Continued.

Metabolite	12 Hours-1	12 Hours-2	12 Hours-3	12 Hours-4	12 Hours-5
GMP	3.10E+08	1.95E+08	1.55E+08	1.98E+08	1.16E+08
Xanthosine 5--phosphate	1.71E+04	5.75E+04	4.13E+04	7.24E+04	1.20E+04
Riboflavin	2.36E+06	6.42E+06	1.92E+06	1.83E+06	9.54E+05
S-Adenosyl-L-homocysteine	1.37E+05	1.19E+05	4.16E+04	6.89E+04	3.27E+04
ADP	4.28E+08	3.59E+08	4.56E+08	3.10E+08	1.11E+09
Folate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CDP-ethanolamine	9.44E+06	8.40E+06	6.85E+06	9.45E+06	9.83E+06
FMN	1.84E+07	1.65E+07	5.34E+06	8.62E+06	3.28E+06
UDP-glucose	1.21E+08	1.26E+08	1.38E+08	1.29E+08	1.05E+08
NAD+	5.30E+07	7.82E+07	7.12E+07	5.32E+07	8.01E+07
NADH	2.46E+06	5.00E+06	6.27E+06	6.77E+06	3.61E+06
Dephospho-CoA	3.14E+06	3.19E+06	1.23E+06	1.97E+06	1.10E+06
NADP+	1.12E+07	5.05E+06	5.58E+06	8.06E+06	6.86E+06
FAD	1.67E+06	2.91E+06	2.02E+06	1.09E+06	2.90E+06
N-Acetylglutamate	1.42E+08	1.87E+08	1.09E+08	9.95E+07	2.46E+08
Kynurenic acid	8.74E+05	4.53E+05	8.35E+04	1.80E+05	4.62E+05

Table 21. Intensities of *G. mellonella* replicates in 24 hours alive group.

Metabolite	24 HA-1	24 HA-3	24 HA-4	24 HA-5
Glyoxylate	0.00E+00	0.00E+00	4.42E+03	0.00E+00
Glycine	1.20E+05	4.75E+04	6.02E+04	6.32E+04
Pyruvate	1.07E+09	2.44E+09	2.94E+09	1.06E+09
Alanine/Sarcosine	2.18E+09	4.91E+08	3.38E+09	4.36E+08
Lactate	9.24E+08	6.96E+08	1.54E+10	4.07E+08
Dimethylglycine	5.42E+07	5.00E+07	6.92E+07	1.27E+07
Serine	6.21E+07	9.56E+07	2.52E+08	4.92E+06
Histamine	4.25E+05	4.95E+05	4.16E+05	1.72E+05
Uracil	2.03E+07	3.55E+07	2.77E+07	1.88E+07
Creatinine	2.76E+03	5.26E+04	1.40E+04	2.51E+03
Proline	7.89E+09	1.84E+10	1.69E+10	6.22E+09
Fumarate	2.43E+08	9.52E+07	5.67E+08	6.05E+07
2-Oxoisovalerate	8.73E+06	1.78E+07	1.24E+07	1.46E+07
Indole	2.97E+06	4.17E+06	3.25E+06	1.56E+06
Valine	1.43E+09	1.90E+09	2.31E+09	5.65E+08
3-Hydroxyisovaleric acid	1.22E+07	1.78E+07	3.81E+07	3.12E+07
Homoserine/Threonine	1.98E+08	3.32E+08	1.78E+08	1.15E+08
3-Methylthiopropionate	3.89E+05	2.46E+05	4.87E+05	2.71E+05
Cysteine	3.49E+05	0.00E+00	2.63E+05	0.00E+00
Nicotinate	1.59E+08	1.23E+08	2.17E+08	4.58E+07
Taurine	1.23E+07	3.09E+06	4.21E+06	8.11E+05
Thymine	6.95E+06	1.06E+07	1.01E+07	5.35E+06
Hydroxyproline	2.87E+06	1.91E+06	2.26E+06	9.07E+05

Table 21. Continued.

Metabolite	24 HA-1	24 HA-3	24 HA-4	24 HA-5
N-Acetyl-beta-alanine	1.73E+07	9.96E+06	2.30E+07	5.14E+06
Leucine/Isoleucine	5.76E+09	7.13E+09	6.92E+09	2.20E+09
Glutaric acid	4.71E+08	4.16E+07	1.35E+08	7.34E+07
Asparagine	3.19E+08	2.07E+06	1.85E+08	8.81E+05
Hydroxyisocaproic acid	8.73E+07	7.23E+07	7.54E+08	2.38E+08
Ornithine	8.81E+06	5.32E+06	5.27E+06	2.28E+06
Salicylate	2.63E+07	1.95E+07	4.15E+07	8.93E+06
Hydroxybenzoate	1.05E+06	3.09E+06	2.12E+06	9.59E+05
Histidinol	6.55E+04	5.94E+04	1.01E+05	3.40E+04
2-Oxoglutaric acid	4.56E+08	4.49E+09	5.68E+08	7.56E+08
Glutamine	3.16E+09	2.54E+09	2.26E+09	1.43E+09
2-hydroxyglutarate	1.23E+09	3.74E+08	4.40E+09	1.67E+08
2-Hydroxy-2-methylsuccinate	1.22E+09	3.73E+08	4.38E+09	1.67E+08
L-Methionine	1.34E+08	2.26E+08	1.90E+08	5.55E+07
Guanine	3.24E+03	1.92E+04	4.28E+04	3.92E+03
3-Methylphenylacetic acid	3.12E+06	2.65E+06	2.91E+06	1.12E+06
Hydroxyphenylacetate	1.16E+06	1.33E+06	1.75E+06	5.91E+05
Xylitol	2.43E+07	1.87E+07	7.31E+07	9.11E+06
Dopamine	3.04E+08	3.91E+08	2.75E+08	4.97E+07
2_3-Dihydroxybenzoate	3.27E+05	9.01E+03	3.09E+05	1.12E+05
Histidine	6.05E+08	7.22E+08	5.95E+08	2.66E+08
Orotate	1.00E+07	7.69E+06	4.85E+06	2.79E+06
Dihydroorotate	6.12E+06	2.28E+06	3.28E+06	1.17E+06
Allantoin	4.71E+07	2.56E+06	6.54E+06	3.71E+06

Table 21. Continued.

Metabolite	24 HA-1	24 HA-3	24 HA-4	24 HA-5
Indole-3-carboxylate	5.77E+05	1.10E+06	7.56E+05	4.83E+05
Phenylpyruvate	4.73E+06	1.94E+07	2.92E+06	1.97E+07
Phenylalanine	3.56E+09	3.55E+09	1.98E+09	9.84E+08
Phenyllactic acid	6.30E+06	1.60E+07	1.50E+07	1.21E+07
Quinolate	4.14E+04	4.17E+04	2.79E+05	9.17E+03
Phosphoenolpyruvate	1.06E+07	1.90E+07	5.86E+06	3.08E+06
Uric acid	1.16E+09	1.40E+08	9.68E+08	7.59E+08
3_4-Dihydroxyphenylacetate (DOPAC)	3.64E+05	6.53E+05	3.29E+05	2.74E+05
Sulfolactate	1.66E+07	8.25E+06	6.28E+06	1.62E+06
Glycerone phosphate	1.56E+07	7.58E+07	3.82E+07	8.60E+06
Arginine	1.10E+08	1.85E+08	1.25E+08	8.96E+07
Citrulline	1.12E+07	4.33E+06	5.20E+06	1.96E+06
Ascorbate	8.84E+06	2.10E+05	8.41E+05	2.73E+05
N-Carbamoyl-L-aspartate	1.53E+07	6.47E+06	6.75E+06	5.21E+06
Allantoate	1.20E+09	5.25E+08	3.98E+08	2.54E+08
2-Isopropylmalate	2.85E+06	1.19E+07	5.23E+06	1.63E+06
Glucosamine	1.36E+06	9.28E+05	7.03E+05	2.89E+05
myo-Inositol	2.39E+07	2.16E+07	1.32E+08	1.39E+07
Tyrosine	2.07E+09	1.01E+09	1.98E+09	1.11E+08
Homovanillic acid (HVA)	1.26E+07	1.67E+07	1.10E+07	1.00E+07
Homocysteic acid	2.55E+03	2.38E+03	0.00E+00	0.00E+00
4-Pyridoxate	9.04E+06	6.20E+06	9.66E+06	2.70E+06
N-Acetylglutamine	9.52E+07	1.22E+08	1.29E+08	4.79E+07

Table 21. Continued.

Metabolite	24 HA-1	24 HA-3	24 HA-4	24 HA-5
Citrate/isocitrate	2.23E+10	4.54E+10	2.43E+10	1.44E+10
D-Gluconate	2.32E+08	3.46E+08	4.81E+08	9.88E+07
N-N Dimethylarginine	4.94E+05	5.70E+05	4.42E+05	3.67E+05
Tryptophan	8.75E+08	1.20E+09	1.02E+09	4.83E+08
Xanthurenic acid	1.71E+07	5.11E+08	4.49E+07	6.62E+07
D-Glucarate	2.99E+09	3.31E+09	3.08E+09	1.84E+09
Pantothenate	1.79E+09	2.04E+09	1.88E+09	6.36E+08
Cystathionine	1.20E+07	2.14E+06	1.81E+07	1.45E+06
Cystine	5.58E+05	2.87E+05	3.73E+05	2.38E+05
Uridine	5.80E+05	4.94E+05	7.94E+05	2.40E+05
Biotin	2.74E+06	1.21E+06	3.59E+06	4.96E+05
Deoxyinosine	6.02E+03	0.00E+00	2.63E+03	0.00E+00
Glucose 6-phosphate	3.07E+08	9.05E+08	5.27E+08	4.88E+08
S-Ribosyl-L-homocysteine	0.00E+00	4.77E+04	2.07E+04	5.68E+04
6-Phospho-D-gluconate	1.50E+07	7.21E+07	3.30E+07	4.88E+07
Guanosine	2.95E+06	2.12E+07	1.51E+07	5.96E+06
Xanthosine	5.26E+05	2.16E+05	5.35E+06	1.73E+04
Glycinamide ribotide (GAR)	1.89E+05	1.08E+05	5.93E+04	1.30E+05
Ophthalmate	3.67E+06	5.12E+06	2.03E+06	1.52E+06
Glutathione	3.96E+07	7.24E+05	3.10E+07	2.44E+06
UMP	3.72E+08	4.82E+08	2.36E+08	1.51E+08
AICAR	2.06E+06	6.31E+05	1.39E+06	6.33E+05
Trehalose/Sucrose/Cellobiose	2.30E+07	3.53E+07	3.39E+07	2.40E+07
AMP/dGMP	2.34E+09	3.93E+09	2.32E+09	1.83E+09

Table 21. Continued.

Metabolite	24 HA-1	24 HA-3	24 HA-4	24 HA-5
IMP	2.89E+08	4.93E+07	3.67E+08	2.00E+07
GMP	2.71E+08	3.33E+08	3.23E+08	1.02E+08
Xanthosine 5--phosphate	1.16E+05	1.88E+05	3.28E+05	3.30E+04
Riboflavin	3.80E+06	1.88E+06	3.01E+06	1.03E+06
S-Adenosyl-L-homocysteine	1.70E+05	3.37E+04	2.17E+05	3.35E+03
ADP	3.34E+08	4.22E+08	3.66E+08	1.76E+08
Folate	0.00E+00	0.00E+00	4.20E+03	0.00E+00
CDP-ethanolamine	1.00E+07	1.51E+07	1.03E+07	3.27E+06
FMN	7.51E+06	2.23E+07	1.17E+07	5.17E+06
UDP-glucose	8.64E+07	1.51E+08	2.76E+07	4.54E+07
NAD+	5.73E+07	4.51E+07	8.30E+07	3.26E+07
NADH	1.76E+06	8.83E+04	8.53E+06	7.29E+04
Dephospho-CoA	6.14E+05	2.85E+05	1.04E+06	7.20E+04
NADP+	1.68E+07	2.29E+07	1.37E+07	1.45E+07
FAD	3.92E+06	8.51E+05	4.51E+06	7.05E+05
N-Acetylglutamate	1.39E+08	1.11E+08	1.48E+08	4.03E+07
Kynurenic acid	7.70E+05	3.72E+06	4.30E+06	1.62E+06

Table 22. Intensities of *G. mellonella* replicates in 24 hours dead group.

Metabolite	24 HD-1	24 HD-2	24 HD-3	24 HD-4	24 HD-5
Glyoxylate	5.58E+06	0.00E+00	0.00E+00	0.00E+00	5.94E+06
Glycine	3.58E+08	6.18E+04	0.00E+00	6.07E+04	4.33E+08
Pyruvate	8.73E+08	1.40E+09	1.59E+08	4.90E+08	3.03E+08
Alanine/Sarcosine	1.81E+09	2.64E+09	2.39E+09	2.00E+09	1.65E+09
Lactate	1.87E+10	1.34E+10	1.53E+10	1.37E+10	9.10E+09
Dimethylglycine	7.92E+07	9.64E+07	1.06E+08	5.70E+07	3.09E+07
Serine	1.43E+08	1.08E+08	8.53E+07	1.31E+08	4.47E+07
Histamine	2.89E+05	4.30E+05	3.83E+05	2.81E+05	2.25E+05
Uracil	1.15E+07	9.96E+07	5.09E+07	2.89E+07	2.85E+07
Creatinine	0.00E+00	5.65E+04	3.68E+04	1.53E+04	8.09E+03
Proline	1.15E+10	1.54E+10	1.61E+10	8.62E+09	3.54E+09
Fumarate	1.58E+08	3.74E+08	1.91E+08	2.58E+08	7.07E+07
2-Oxoisovalerate	5.29E+06	9.24E+06	1.51E+07	7.49E+06	4.76E+06
Indole	1.97E+06	3.88E+06	5.29E+06	1.91E+06	1.43E+06
Valine	1.28E+09	1.51E+09	1.79E+09	1.52E+09	5.42E+08
3-Hydroxyisovaleric acid	1.08E+07	2.40E+07	1.43E+08	1.70E+07	1.20E+07
Homoserine/Threonine	8.92E+07	3.17E+08	3.51E+08	6.45E+07	9.37E+07
3-Methylthiopropionate	4.09E+04	1.31E+05	7.89E+05	2.94E+05	7.73E+04
Cysteine	4.59E+06	1.05E+05	7.34E+06	2.14E+06	5.54E+06
Nicotinate	1.20E+08	1.54E+08	1.36E+08	1.55E+08	7.82E+07
Taurine	4.29E+06	9.96E+05	1.16E+06	1.63E+06	2.78E+06
Thymine	3.54E+06	1.02E+07	1.06E+07	1.28E+07	2.48E+06
Hydroxyproline	1.59E+06	2.24E+06	1.38E+06	1.32E+06	1.25E+07

Table 22. Continued.

Metabolite	24 HD-1	24 HD-2	24 HD-3	24 HD-4	24 HD-5
N-Acetyl-beta-alanine	2.15E+07	3.64E+07	3.46E+07	3.27E+07	2.05E+07
Leucine/Isoleucine	3.15E+09	4.93E+09	5.82E+09	4.29E+09	1.61E+09
Glutaric acid	4.79E+07	1.39E+08	2.92E+08	5.92E+07	5.58E+07
Asparagine	1.32E+08	3.22E+08	5.78E+08	1.48E+08	1.61E+08
Hydroxyisocaproic acid	1.29E+08	5.33E+08	2.52E+09	3.24E+08	9.83E+07
Ornithine	4.27E+06	4.77E+06	4.39E+06	5.11E+06	7.08E+06
Salicylate	2.37E+07	3.43E+07	5.23E+07	2.00E+07	7.58E+06
Hydroxybenzoate	2.15E+06	1.25E+06	1.38E+06	1.19E+06	3.91E+05
Histidinol	7.23E+04	4.76E+04	1.09E+05	3.00E+04	1.63E+04
2-Oxoglutaric acid	2.55E+08	5.33E+08	1.15E+08	2.21E+08	6.30E+07
Glutamine	1.50E+09	2.11E+09	2.27E+09	1.31E+09	1.63E+09
2-hydroxyglutarate	5.23E+09	5.81E+09	1.04E+10	5.59E+09	1.57E+09
2-Hydroxy-2-methylsuccinate	5.23E+09	5.80E+09	1.04E+10	5.57E+09	1.56E+09
L-Methionine	1.11E+08	4.96E+07	9.15E+07	9.27E+07	3.42E+07
Guanine	0.00E+00	6.54E+04	3.09E+04	1.76E+04	4.87E+04
3-Methylphenylacetic acid	1.68E+06	2.40E+06	9.55E+06	2.91E+06	4.72E+05
Hydroxyphenylacetate	4.05E+06	2.76E+06	2.82E+06	2.25E+06	1.06E+06
Xylitol	1.04E+08	1.08E+08	1.04E+08	1.10E+08	5.44E+07
Dopamine	4.67E+08	3.17E+08	1.08E+09	3.06E+08	2.28E+08
2_3-Dihydroxybenzoate	4.04E+05	9.93E+05	2.84E+05	5.97E+05	1.38E+05
Histidine	4.34E+08	5.72E+08	6.18E+08	4.26E+08	3.49E+08
Orotate	7.54E+06	4.60E+06	3.72E+06	1.45E+06	1.32E+06
Dihydroorotate	1.06E+07	9.92E+05	8.21E+05	7.83E+05	5.15E+05
Allantoin	4.73E+06	2.98E+07	1.44E+07	5.12E+06	5.04E+07

Table 22. Continued.

Metabolite	24 HD-1	24 HD-2	24 HD-3	24 HD-4	24 HD-5
Indole-3-carboxylate	3.02E+05	8.34E+05	7.43E+05	5.35E+05	1.19E+05
Phenylpyruvate	1.20E+06	4.42E+06	3.90E+06	1.53E+06	6.11E+05
Phenylalanine	1.17E+09	1.95E+09	2.95E+09	2.69E+08	7.98E+08
Phenyllactic acid	1.40E+07	2.35E+07	4.31E+07	8.48E+06	3.13E+06
Quinolate	2.95E+04	4.06E+05	3.14E+05	2.03E+06	8.70E+05
Phosphoenolpyruvate	6.94E+06	8.70E+06	5.10E+06	3.72E+06	5.26E+06
Uric acid	3.06E+08	8.21E+08	9.80E+08	2.78E+08	4.29E+08
3_4-Dihydroxyphenylacetate (DOPAC)	1.47E+05	3.86E+05	3.36E+05	2.30E+05	9.92E+04
Sulfolactate	1.79E+06	4.58E+06	3.77E+06	3.78E+06	8.41E+05
Glycerone phosphate	4.66E+07	2.90E+07	4.92E+07	2.07E+07	2.31E+07
Arginine	1.02E+08	1.39E+08	1.22E+08	1.31E+08	8.64E+07
Citrulline	1.23E+06	3.24E+06	1.50E+06	1.63E+06	2.51E+06
Ascorbate	4.34E+08	8.34E+05	9.90E+08	7.81E+08	8.09E+08
N-Carbamoyl-L-aspartate	1.95E+07	1.71E+06	1.61E+06	9.37E+05	1.89E+06
Allantoate	1.94E+08	7.59E+08	5.52E+08	2.22E+08	6.61E+08
2-Isopropylmalate	3.74E+06	1.42E+07	4.34E+06	7.88E+06	2.93E+06
Glucosamine	8.25E+05	1.19E+06	4.03E+05	5.28E+05	9.15E+05
myo-Inositol	1.31E+08	1.14E+08	1.23E+08	1.81E+08	6.29E+07
Tyrosine	1.81E+09	1.63E+09	2.61E+09	1.22E+09	6.98E+08
Homovanillic acid (HVA)	2.95E+07	2.56E+07	5.75E+07	1.89E+07	3.81E+06
Homocysteic acid	0.00E+00	0.00E+00	0.00E+00	3.83E+03	0.00E+00
4-Pyridoxate	5.63E+06	9.26E+06	9.52E+06	9.27E+06	6.07E+06
N-Acetylglutamine	1.88E+08	2.76E+08	2.63E+08	1.33E+08	1.21E+08

Table 22. Continued.

Metabolite	24 HD-1	24 HD-2	24 HD-3	24 HD-4	24 HD-5
Citrate/isocitrate	9.99E+09	1.26E+10	1.80E+10	9.74E+09	1.04E+09
D-Gluconate	2.70E+08	3.92E+08	3.89E+08	2.84E+08	1.02E+08
N-N Dimethylarginine	3.56E+05	3.39E+05	3.62E+05	5.05E+05	3.31E+05
Tryptophan	6.64E+08	1.16E+09	1.53E+09	6.42E+08	5.06E+08
Xanthurenic acid	1.87E+07	5.05E+07	1.46E+08	8.40E+06	4.68E+06
D-Glucarate	1.58E+09	3.16E+09	2.73E+09	3.04E+09	5.20E+08
Pantothenate	1.35E+09	1.48E+09	2.42E+09	1.61E+09	6.42E+08
Cystathionine	6.33E+06	2.06E+06	4.48E+06	2.85E+06	3.59E+06
Cystine	5.04E+05	5.52E+05	5.76E+05	1.81E+06	1.24E+06
Uridine	1.84E+06	2.07E+06	2.10E+06	3.30E+06	1.80E+06
Biotin	3.33E+06	2.24E+06	5.81E+06	2.49E+06	1.07E+06
Deoxyinosine	0.00E+00	5.33E+03	2.29E+03	0.00E+00	0.00E+00
Glucose 6-phosphate	2.92E+08	2.94E+08	2.50E+08	4.23E+08	1.20E+08
S-Ribosyl-L-homocysteine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	7.22E+03
6-Phospho-D-gluconate	4.16E+06	1.22E+07	5.05E+06	4.32E+06	9.54E+05
Guanosine	1.75E+07	1.63E+07	3.15E+07	2.07E+07	4.13E+06
Xanthosine	7.81E+07	8.01E+07	9.55E+07	9.59E+07	3.37E+07
Glycinamide ribotide (GAR)	3.08E+04	0.00E+00	0.00E+00	0.00E+00	8.12E+04
Ophthamate	1.29E+06	3.47E+06	3.34E+06	9.74E+05	3.59E+04
Glutathione	1.41E+08	2.75E+07	4.08E+08	7.91E+07	1.11E+08
UMP	5.39E+07	7.90E+07	5.92E+07	2.68E+07	1.97E+07
AICAR	4.15E+05	1.24E+06	5.62E+06	5.41E+05	5.74E+05
Trehalose/Sucrose/Cellobiose	2.66E+07	3.90E+07	2.64E+07	3.35E+07	1.72E+07
AMP/dGMP	9.86E+08	1.05E+09	1.57E+09	8.21E+08	5.54E+08

Table 22. Continued.

Metabolite	24 HD-1	24 HD-2	24 HD-3	24 HD-4	24 HD-5
IMP	4.30E+08	6.10E+08	7.86E+08	4.24E+08	1.22E+08
GMP	1.20E+08	1.60E+08	1.73E+08	1.24E+08	4.94E+07
Xanthosine 5--phosphate	4.72E+05	3.79E+05	7.78E+05	5.30E+05	2.00E+05
Riboflavin	4.67E+06	2.82E+06	6.56E+06	3.81E+06	1.02E+06
S-Adenosyl-L-homocysteine	1.08E+05	2.58E+05	2.61E+05	9.68E+04	1.20E+05
ADP	1.29E+08	1.95E+08	2.17E+08	1.89E+08	7.71E+07
Folate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CDP-ethanolamine	7.44E+06	6.27E+06	8.71E+06	6.79E+06	2.06E+06
FMN	8.72E+06	1.17E+07	1.58E+07	2.08E+07	2.72E+06
UDP-glucose	1.30E+07	1.45E+07	8.96E+06	1.21E+07	4.61E+06
NAD+	4.22E+07	5.09E+07	9.02E+07	2.60E+07	1.36E+07
NADH	9.75E+06	2.41E+06	1.99E+07	7.10E+06	8.18E+06
Dephospho-CoA	3.17E+05	4.53E+05	2.20E+06	6.42E+05	2.25E+05
NADP+	4.43E+06	1.24E+07	7.08E+06	6.73E+06	2.70E+06
FAD	2.85E+06	4.21E+06	1.64E+06	8.44E+04	1.82E+06
N-Acetylglutamate	8.61E+07	1.17E+08	1.51E+08	7.45E+07	6.02E+07
Kynurenic acid	1.04E+05	4.35E+06	2.22E+06	3.90E+05	1.42E+05

Table 23. Intensities of *G. mellonella* replicates in 2 days post infection group.

Metabolite	2 Days-1	2 Days-2	2 Days-3	2 Days-4	2 Days-5
Glyoxylate	0.00E+00	7.15E+06	0.00E+00	7.81E+03	5.24E+06
Glycine	3.88E+04	3.59E+08	5.99E+04	3.87E+04	1.08E+09
Pyruvate	1.12E+08	4.43E+07	7.89E+09	4.26E+07	5.74E+09
Alanine/Sarcosine	2.10E+08	1.21E+08	4.84E+09	9.96E+07	5.09E+09
Lactate	4.07E+08	2.75E+08	3.45E+10	3.11E+08	4.54E+10
Dimethylglycine	5.99E+07	3.12E+07	1.06E+08	6.77E+07	9.07E+07
Serine	9.95E+07	7.42E+07	1.87E+08	6.25E+07	1.41E+08
Histamine	1.27E+05	3.23E+04	4.07E+05	3.59E+04	4.23E+05
Uracil	1.93E+08	8.34E+07	5.30E+06	8.94E+07	3.91E+07
Creatinine	2.73E+04	1.53E+04	2.26E+04	6.25E+04	5.18E+03
Proline	2.51E+08	9.41E+07	1.35E+10	1.36E+08	7.00E+09
Fumarate	1.10E+07	4.96E+06	3.04E+08	4.25E+06	2.36E+08
2-Oxoisovalerate	1.45E+08	7.82E+07	4.76E+07	2.06E+07	2.20E+07
Indole	3.99E+05	5.99E+05	2.95E+06	1.97E+05	7.64E+06
Valine	8.24E+08	5.86E+08	1.96E+09	2.92E+08	1.27E+09
3-Hydroxyisovaleric acid	3.53E+08	1.18E+08	9.42E+07	1.06E+08	1.85E+08
Homoserine/Threonine	1.27E+08	4.81E+07	3.84E+08	6.89E+07	4.19E+08
3-Methylthiopropionate	2.58E+06	1.18E+06	3.86E+05	1.13E+06	4.31E+03
Cysteine	1.75E+06	3.99E+05	1.72E+04	1.70E+06	1.35E+04
Nicotinate	7.50E+08	3.28E+08	3.82E+08	3.50E+08	2.27E+08
Taurine	2.28E+06	4.32E+06	1.56E+06	4.46E+06	2.22E+06
Thymine	1.83E+08	2.52E+08	2.20E+07	2.85E+08	3.74E+06
Hydroxyproline	5.91E+06	6.94E+06	2.38E+06	5.15E+06	1.84E+06

Table 23. Continued.

Metabolite	2 Days-1	2 Days-2	2 Days-3	2 Days-4	2 Days-5
N-Acetyl-beta-alanine	1.77E+07	1.07E+07	4.00E+07	1.85E+07	2.64E+07
Leucine/Isoleucine	7.99E+08	9.64E+08	5.42E+09	5.59E+08	3.40E+09
Glutaric acid	1.95E+08	1.75E+08	2.58E+08	1.59E+08	1.94E+08
Asparagine	7.34E+06	1.86E+07	3.19E+08	6.90E+06	7.18E+08
Hydroxyisocaproic acid	6.14E+08	2.86E+08	1.46E+09	2.75E+08	1.57E+09
Ornithine	1.67E+07	2.97E+07	1.68E+07	2.24E+07	2.53E+07
Salicylate	2.74E+07	1.16E+07	6.11E+07	2.27E+07	2.88E+07
Hydroxybenzoate	3.70E+07	4.52E+07	3.39E+06	4.28E+07	1.42E+06
Histidinol	5.34E+06	3.78E+06	9.45E+04	7.87E+06	3.96E+04
2-Oxoglutaric acid	4.53E+07	3.57E+07	1.07E+09	2.52E+07	2.55E+08
Glutamine	2.24E+08	6.49E+07	2.50E+09	4.84E+07	3.44E+09
2-hydroxyglutarate	5.05E+08	1.79E+08	8.42E+09	1.63E+08	4.82E+09
2-Hydroxy-2-methylsuccinate	5.05E+08	1.79E+08	8.39E+09	1.63E+08	4.81E+09
L-Methionine	3.14E+07	1.09E+07	2.16E+08	1.72E+07	2.42E+08
Guanine	1.02E+06	6.54E+06	1.64E+05	1.62E+06	1.68E+04
3-Methylphenylacetic acid	1.49E+06	5.91E+05	2.29E+06	6.47E+06	4.82E+05
Hydroxyphenylacetate	3.82E+06	1.18E+07	2.22E+06	1.09E+08	1.91E+06
Xylitol	8.98E+07	4.76E+07	1.81E+08	9.15E+07	1.41E+08
Dopamine	5.90E+06	5.90E+06	6.05E+08	6.69E+06	4.07E+08
2_3-Dihydroxybenzoate	1.05E+07	5.07E+05	2.28E+06	5.33E+05	4.22E+05
Histidine	1.19E+08	2.00E+07	5.68E+08	1.77E+07	4.55E+08
Orotate	1.15E+08	4.31E+07	1.22E+07	2.72E+07	8.87E+06
Dihydroorotate	1.01E+07	9.41E+05	1.07E+07	1.52E+06	5.00E+06
Allantoin	1.33E+07	1.28E+07	4.92E+07	2.47E+07	6.24E+06

Table 23. Continued.

Metabolite	2 Days-1	2 Days-2	2 Days-3	2 Days-4	2 Days-5
Indole-3-carboxylate	1.27E+06	4.40E+06	2.17E+06	1.36E+06	4.04E+05
Phenylpyruvate	3.11E+07	3.52E+07	1.13E+07	1.13E+07	4.20E+06
Phenylalanine	2.39E+08	1.45E+08	2.96E+09	2.96E+08	6.03E+09
Phenyllactic acid	9.83E+08	7.84E+08	1.13E+08	8.33E+08	1.77E+08
Quinolate	6.90E+05	2.32E+05	1.69E+06	5.80E+05	4.55E+04
Phosphoenolpyruvate	3.87E+07	2.72E+07	2.64E+07	3.06E+07	1.07E+07
Uric acid	5.94E+08	8.47E+07	1.28E+09	2.84E+08	1.22E+09
3_4-Dihydroxyphenylacetate (DOPAC)	2.98E+06	8.71E+06	7.15E+05	4.29E+06	4.68E+05
Sulfolactate	5.88E+06	3.62E+06	4.45E+06	6.14E+06	6.64E+06
Glycerone phosphate	1.92E+07	1.64E+06	5.67E+07	2.30E+07	3.33E+07
Arginine	2.43E+07	1.05E+07	1.30E+08	1.09E+07	1.20E+08
Citrulline	6.80E+07	1.08E+08	1.43E+07	7.73E+07	1.81E+07
Ascorbate	3.67E+05	1.90E+05	1.83E+05	1.67E+05	5.63E+06
N-Carbamoyl-L-aspartate	3.93E+07	2.84E+07	2.06E+07	1.81E+07	1.11E+07
Allantoate	8.60E+08	7.71E+08	6.88E+08	8.77E+08	2.19E+08
2-Isopropylmalate	2.09E+09	7.99E+08	8.79E+06	1.47E+09	5.41E+06
Glucosamine	3.31E+06	2.69E+06	6.56E+05	4.46E+06	2.35E+05
myo-Inositol	9.63E+06	7.59E+06	5.02E+08	8.95E+06	4.51E+08
Tyrosine	3.18E+08	9.95E+07	1.15E+09	2.77E+08	2.77E+09
Homovanillic acid (HVA)	1.07E+08	3.09E+07	3.68E+07	4.40E+07	9.37E+07
Homocysteic acid	1.35E+05	2.45E+05	0.00E+00	3.15E+05	0.00E+00
4-Pyridoxate	2.62E+07	2.28E+07	1.62E+07	2.30E+07	2.41E+07
N-Acetylglutamine	1.16E+07	5.76E+06	1.55E+08	2.05E+06	2.93E+08
Citrate/isocitrate	7.88E+09	5.92E+09	1.98E+10	6.34E+09	1.18E+10

Table 23. Continued.

Metabolite	2 Days-1	2 Days-2	2 Days-3	2 Days-4	2 Days-5
D-Gluconate	2.41E+08	1.12E+08	7.11E+08	1.42E+08	4.38E+08
N-N Dimethylarginine	1.86E+06	1.66E+06	6.49E+05	2.09E+06	4.64E+05
Tryptophan	1.61E+08	2.28E+08	9.90E+08	8.37E+07	2.07E+09
Xanthurenic acid	9.52E+07	7.37E+07	4.57E+07	1.27E+07	7.11E+07
D-Glucarate	3.34E+09	1.13E+09	2.65E+09	2.30E+09	2.86E+09
Pantothenate	2.01E+09	8.85E+08	2.32E+09	1.18E+09	1.42E+09
Cystathionine	2.16E+06	2.68E+06	5.68E+06	1.75E+06	9.87E+06
Cystine	3.76E+06	4.94E+05	2.54E+05	5.46E+06	0.00E+00
Uridine	1.21E+07	2.61E+07	4.13E+06	1.50E+07	1.99E+06
Biotin	2.80E+06	5.81E+05	2.70E+06	5.88E+05	3.00E+06
Deoxyinosine	1.92E+05	1.68E+05	0.00E+00	2.22E+05	0.00E+00
Glucose 6-phosphate	2.27E+07	8.47E+06	3.29E+08	9.78E+06	3.78E+08
S-Ribosyl-L-homocysteine	1.30E+07	1.51E+06	0.00E+00	2.60E+06	1.06E+04
6-Phospho-D-gluconate	1.93E+07	8.27E+06	7.31E+06	7.02E+06	6.25E+06
Guanosine	3.63E+07	1.41E+07	1.18E+07	1.69E+07	8.04E+06
Xanthosine	1.20E+07	1.21E+07	2.74E+07	1.43E+07	1.31E+07
Glycinamide ribotide (GAR)	0.00E+00	0.00E+00	9.68E+05	0.00E+00	3.49E+05
Ophthalmate	1.47E+07	7.60E+06	4.91E+06	2.06E+07	4.35E+06
Glutathione	1.06E+07	6.92E+06	1.05E+08	7.41E+06	4.77E+07
UMP	1.43E+07	5.08E+07	5.53E+07	5.30E+06	1.43E+08
AICAR	4.30E+05	1.26E+06	1.89E+06	2.73E+05	1.27E+06
Trehalose/Sucrose/Cellobiose	2.10E+07	1.41E+07	2.07E+07	2.11E+07	8.45E+06
AMP/dGMP	1.07E+08	2.39E+08	3.22E+08	4.52E+07	1.49E+09
IMP	3.84E+06	3.57E+06	4.19E+08	1.37E+06	1.68E+08

Table 23. Continued.

Metabolite	2 Days-1	2 Days-2	2 Days-3	2 Days-4	2 Days-5
GMP	1.49E+07	5.20E+07	7.93E+07	9.00E+06	2.73E+08
Xanthosine 5--phosphate	7.62E+04	2.88E+05	1.22E+06	2.44E+04	1.29E+06
Riboflavin	2.65E+06	9.11E+05	4.93E+06	1.10E+06	6.55E+06
S-Adenosyl-L-homocysteine	7.49E+04	1.08E+05	5.93E+03	1.07E+05	8.43E+04
ADP	2.09E+08	4.06E+07	3.48E+08	7.70E+07	2.33E+08
Folate	7.17E+04	1.00E+05	0.00E+00	5.15E+04	0.00E+00
CDP-ethanolamine	2.81E+05	5.50E+05	8.12E+06	1.18E+05	8.66E+06
FMN	1.85E+07	5.44E+06	7.24E+06	1.03E+07	1.63E+07
UDP-glucose	2.14E+07	3.46E+07	4.96E+07	2.28E+07	3.10E+07
NAD+	1.50E+07	8.60E+06	4.21E+07	7.23E+06	2.64E+07
NADH	3.38E+04	2.26E+04	2.79E+06	3.01E+04	1.85E+06
Dephospho-CoA	3.45E+05	1.05E+05	2.72E+05	9.89E+04	6.95E+05
NADP+	2.97E+07	9.70E+06	1.38E+07	1.78E+07	7.17E+06
FAD	4.84E+06	1.26E+06	2.79E+06	2.70E+06	1.60E+06
N-Acetylglutamate	7.06E+08	1.39E+09	2.14E+08	1.35E+09	1.78E+08
Kynurenic acid	2.50E+07	4.39E+07	2.50E+06	2.65E+07	1.29E+06

Table 24. Intensities of *G. mellonella* replicates in 4 days post infection group.

Metabolite	4 Days-1	4 Days-2	4 Days-3	4 Days-4	4 Days-5
Glyoxylate	8.07E+07	0.00E+00	2.74E+08	1.10E+04	6.06E+03
Glycine	8.45E+08	1.73E+04	2.00E+08	1.44E+05	4.13E+04
Pyruvate	5.61E+07	6.47E+07	2.45E+08	7.88E+07	3.07E+07
Alanine/Sarcosine	1.11E+08	4.42E+07	9.56E+07	1.87E+08	1.67E+08
Lactate	5.41E+08	2.78E+08	3.34E+08	9.27E+08	3.84E+08
Dimethylglycine	5.03E+07	2.19E+07	1.98E+07	8.27E+07	4.80E+07
Serine	6.26E+07	3.59E+07	3.27E+07	8.26E+07	5.75E+07
Histamine	1.87E+05	1.21E+05	2.25E+04	7.24E+05	6.29E+05
Uracil	5.07E+08	9.04E+07	9.13E+07	5.12E+08	5.78E+08
Creatinine	1.35E+05	5.12E+04	1.12E+04	7.40E+04	1.11E+05
Proline	8.65E+08	1.04E+08	1.27E+08	1.60E+09	1.68E+09
Fumarate	1.53E+07	4.31E+06	1.08E+07	3.34E+07	1.94E+07
2-Oxoisovalerate	7.29E+07	1.29E+07	6.35E+07	9.24E+07	1.42E+07
Indole	7.83E+05	3.89E+05	6.66E+05	1.33E+06	1.35E+06
Valine	3.29E+08	1.00E+08	6.35E+08	6.30E+08	2.76E+08
3-Hydroxyisovaleric acid	4.00E+08	1.70E+08	3.68E+08	3.47E+08	6.24E+07
Homoserine/Threonine	1.71E+08	1.06E+08	2.28E+08	3.06E+08	1.13E+08
3-Methylthiopropionate	1.69E+06	9.13E+06	2.33E+06	5.68E+05	2.84E+05
Cysteine	3.72E+05	2.45E+06	2.39E+06	3.45E+06	5.01E+05
Nicotinate	1.04E+08	2.77E+08	1.12E+08	2.87E+08	2.20E+07
Taurine	1.08E+04	2.20E+06	1.04E+04	0.00E+00	9.73E+04
Thymine	1.25E+09	5.23E+08	9.38E+08	1.95E+09	1.09E+09
Hydroxyproline	1.41E+07	7.30E+06	3.93E+06	1.60E+07	4.49E+06

Table 24. Continued.

Metabolite	4 Days-1	4 Days-2	4 Days-3	4 Days-4	4 Days-5
N-Acetyl-beta-alanine	5.83E+07	5.97E+07	1.53E+08	5.97E+07	2.28E+07
Leucine/Isoleucine	1.06E+09	5.47E+08	1.85E+09	2.02E+09	1.56E+09
Glutaric acid	3.66E+08	2.78E+08	2.10E+08	5.52E+08	1.95E+08
Asparagine	4.28E+07	2.74E+07	2.15E+07	4.20E+07	1.34E+08
Hydroxyisocaproic acid	1.83E+09	2.63E+08	1.09E+09	4.46E+08	1.62E+08
Ornithine	5.49E+07	2.28E+07	2.57E+07	3.86E+07	3.66E+07
Salicylate	5.90E+07	1.79E+08	3.32E+09	2.41E+08	4.27E+07
Hydroxybenzoate	3.93E+07	7.29E+06	3.55E+06	2.42E+07	1.59E+07
Histidinol	1.81E+07	3.12E+07	1.97E+07	1.15E+07	1.11E+07
2-Oxoglutaric acid	1.78E+08	1.46E+07	2.60E+07	7.64E+07	5.07E+07
Glutamine	1.28E+08	1.75E+08	2.77E+07	3.03E+08	2.49E+08
2-hydroxyglutarate	2.30E+08	3.92E+08	2.94E+08	3.18E+08	1.87E+08
2-Hydroxy-2-methylsuccinate	2.30E+08	3.92E+08	2.93E+08	3.18E+08	1.86E+08
L-Methionine	3.59E+07	2.09E+07	1.00E+08	1.03E+08	3.70E+07
Guanine	2.49E+06	2.72E+06	1.68E+06	2.69E+06	5.60E+07
3-Methylphenylacetic acid	2.20E+07	1.59E+06	1.99E+06	1.28E+06	1.15E+06
Hydroxyphenylacetate	4.69E+07	1.79E+08	1.48E+08	3.65E+08	2.73E+08
Xylitol	5.77E+07	3.84E+07	1.41E+08	8.83E+07	2.34E+07
Dopamine	2.61E+06	5.64E+06	2.70E+06	1.74E+06	3.03E+06
2_3-Dihydroxybenzoate	1.93E+08	6.62E+07	6.73E+07	2.03E+06	9.51E+05
Histidine	6.28E+07	1.93E+07	2.23E+07	8.14E+07	3.23E+07
Orotate	4.36E+08	1.08E+07	6.59E+07	2.87E+08	7.64E+07
Dihydroorotate	1.63E+07	9.63E+05	6.21E+06	6.23E+06	6.01E+05
Allantoin	2.08E+07	1.24E+07	6.69E+06	5.49E+07	1.11E+08

Table 24. Continued.

Metabolite	4 Days-1	4 Days-2	4 Days-3	4 Days-4	4 Days-5
Indole-3-carboxylate	4.01E+07	3.12E+07	1.52E+07	1.45E+07	8.55E+06
Phenylpyruvate	1.48E+07	4.90E+06	4.62E+07	1.34E+07	6.98E+06
Phenylalanine	4.99E+08	2.40E+08	4.06E+08	8.47E+08	5.21E+08
Phenyllactic acid	8.51E+08	8.67E+08	1.67E+09	4.52E+09	1.55E+09
Quinolinate	4.69E+06	6.99E+05	2.02E+06	1.89E+07	9.08E+06
Phosphoenolpyruvate	3.76E+07	5.97E+04	3.89E+06	3.33E+07	1.09E+07
Uric acid	2.43E+08	4.24E+08	5.50E+08	4.60E+08	3.62E+08
3_4-Dihydroxyphenylacetate (DOPAC)	2.52E+07	1.04E+07	1.09E+07	2.46E+07	1.35E+07
Sulfolactate	1.40E+06	2.05E+06	4.97E+05	3.01E+06	3.27E+06
Glycerone phosphate	7.45E+04	4.05E+05	4.22E+06	1.81E+07	2.07E+05
Arginine	2.05E+07	1.37E+07	7.69E+06	4.63E+07	5.39E+07
Citrulline	1.90E+08	8.62E+07	7.69E+07	1.49E+08	1.08E+08
Ascorbate	8.34E+05	3.27E+05	1.36E+05	4.73E+05	1.52E+05
N-Carbamoyl-L-aspartate	5.92E+07	6.34E+06	2.84E+06	2.10E+07	8.73E+06
Allantoate	3.99E+08	4.63E+07	3.00E+06	2.22E+08	4.83E+08
2-Isopropylmalate	2.14E+09	1.30E+09	3.64E+08	2.81E+09	6.69E+08
Glucosamine	3.72E+06	3.91E+06	1.74E+06	1.12E+07	6.72E+06
myo-Inositol	1.83E+07	1.30E+07	2.87E+07	1.86E+07	8.05E+06
Tyrosine	2.32E+08	2.21E+08	4.42E+08	4.70E+08	1.45E+08
Homovanillic acid (HVA)	5.64E+07	4.43E+07	9.66E+07	4.77E+07	2.02E+07
Homocysteic acid	6.66E+05	7.87E+06	5.57E+05	9.31E+06	2.18E+06
4-Pyridoxate	1.11E+08	5.39E+07	4.51E+07	2.12E+08	1.00E+08
N-Acetylglutamine	1.86E+07	1.10E+07	8.24E+06	1.42E+07	9.18E+06
Citrate/isocitrate	5.36E+09	4.02E+09	2.79E+09	5.90E+09	7.48E+09

Table 24. Continued.

Metabolite	4 Days-1	4 Days-2	4 Days-3	4 Days-4	4 Days-5
D-Gluconate	3.18E+08	4.11E+08	4.81E+08	5.90E+08	1.46E+08
N-N Dimethylarginine	2.73E+06	1.07E+06	1.72E+06	2.88E+06	2.14E+06
Tryptophan	2.74E+08	1.46E+08	2.43E+08	4.61E+08	4.28E+08
Xanthurenic acid	6.70E+07	2.34E+08	9.38E+07	8.59E+07	2.69E+07
D-Glucarate	5.27E+07	1.64E+07	1.67E+09	4.58E+09	1.05E+09
Pantothenate	3.11E+09	1.59E+09	1.10E+09	2.62E+09	9.75E+08
Cystathionine	9.60E+06	8.79E+06	1.35E+07	1.32E+07	7.28E+06
Cystine	3.10E+05	6.74E+06	6.44E+06	5.98E+06	7.01E+05
Uridine	1.46E+08	5.77E+07	1.23E+08	3.81E+07	8.88E+06
Biotin	1.87E+06	2.62E+06	7.56E+05	8.60E+05	4.33E+05
Deoxyinosine	1.65E+06	6.87E+05	1.16E+06	6.20E+06	1.09E+06
Glucose 6-phosphate	3.01E+07	1.09E+07	1.60E+07	1.59E+07	1.88E+07
S-Ribosyl-L-homocysteine	3.72E+04	6.51E+04	4.52E+06	8.01E+05	4.64E+03
6-Phospho-D-gluconate	2.18E+07	3.35E+06	2.98E+06	2.17E+07	6.24E+06
Guanosine	1.51E+07	2.37E+07	5.05E+06	3.91E+07	1.05E+07
Xanthosine	1.53E+07	3.61E+06	1.45E+06	2.62E+07	9.55E+06
Glycinamide ribotide (GAR)	7.83E+03	0.00E+00	0.00E+00	9.82E+03	6.12E+04
Ophthalmate	3.71E+07	9.61E+06	4.62E+06	1.92E+07	9.70E+06
Glutathione	2.04E+07	2.18E+07	4.37E+07	4.85E+07	2.31E+07
UMP	1.37E+08	6.54E+07	4.26E+07	1.35E+08	1.28E+08
AICAR	3.06E+05	4.25E+05	1.32E+04	2.00E+06	6.08E+05
Trehalose/Sucrose/Cellobiose	5.68E+06	1.04E+07	5.05E+06	8.94E+06	1.12E+07
AMP/dGMP	5.75E+08	3.11E+08	2.03E+08	6.70E+08	5.32E+08
IMP	8.28E+06	9.39E+06	6.30E+06	2.68E+07	8.43E+06

Table 24. Continued.

Metabolite	4 Days-1	4 Days-2	4 Days-3	4 Days-4	4 Days-5
GMP	1.47E+08	6.79E+07	3.26E+07	2.49E+08	1.49E+08
Xanthosine 5--phosphate	1.05E+07	4.35E+04	4.76E+05	1.70E+05	1.05E+04
Riboflavin	4.56E+06	2.18E+06	6.77E+06	2.02E+06	9.30E+05
S-Adenosyl-L-homocysteine	1.11E+06	2.15E+05	2.94E+05	4.62E+05	1.67E+05
ADP	1.11E+08	2.97E+06	2.81E+07	1.00E+08	3.85E+07
Folate	6.26E+05	2.67E+05	6.09E+05	7.69E+05	6.04E+05
CDP-ethanolamine	1.05E+06	4.95E+05	2.78E+05	2.82E+06	1.22E+06
FMN	1.99E+07	9.91E+06	1.68E+07	1.31E+07	4.25E+06
UDP-glucose	9.60E+07	2.39E+07	2.27E+07	8.04E+07	5.32E+07
NAD+	1.43E+07	1.79E+07	6.75E+06	2.67E+07	6.85E+06
NADH	1.78E+05	2.02E+05	1.49E+05	3.29E+04	1.18E+04
Dephospho-CoA	9.15E+05	1.23E+05	2.15E+06	1.20E+06	7.00E+05
NADP+	1.54E+07	8.64E+06	4.37E+06	2.43E+07	6.26E+06
FAD	5.09E+06	1.99E+06	3.06E+06	9.09E+06	1.49E+06
N-Acetylglutamate	8.96E+08	1.23E+09	5.82E+08	4.56E+08	6.88E+08
Kynurenic acid	1.43E+08	9.01E+07	6.41E+07	1.26E+08	1.95E+08

Table 25. Intensities of *G. mellonella* replicates in 6 days post infection group.

Metabolite	6 Days-1	6 Days-2	6 Days-3	6 Days-4	6 Days-5
Glyoxylate	2.64E+04	0.00E+00	2.78E+03	9.74E+03	0.00E+00
Glycine	1.53E+05	1.63E+05	4.65E+04	0.00E+00	9.76E+04
Pyruvate	5.80E+07	7.76E+07	1.15E+08	1.11E+08	1.78E+08
Alanine/Sarcosine	6.94E+09	2.27E+09	3.96E+08	3.62E+08	6.60E+08
Lactate	1.59E+09	1.30E+09	4.26E+08	6.41E+08	1.04E+09
Dimethylglycine	5.49E+08	1.56E+08	3.73E+07	7.55E+07	8.13E+07
Serine	1.04E+07	6.23E+07	5.58E+07	8.50E+07	1.25E+08
Histamine	4.35E+04	3.10E+06	2.26E+06	1.93E+06	3.62E+06
Uracil	9.43E+08	2.00E+09	1.24E+09	1.22E+09	2.17E+09
Creatinine	5.00E+04	8.58E+04	6.33E+04	8.57E+05	2.56E+04
Proline	2.20E+09	7.19E+09	3.63E+09	3.20E+09	7.44E+09
Fumarate	2.14E+06	4.33E+07	4.20E+07	6.35E+07	8.61E+07
2-Oxoisovalerate	8.80E+07	1.20E+09	4.32E+07	2.67E+07	1.39E+08
Indole	4.15E+06	4.52E+05	8.80E+05	6.36E+05	1.58E+06
Valine	7.43E+09	2.94E+09	3.59E+08	3.53E+08	9.64E+08
3-Hydroxyisovaleric acid	2.71E+09	3.56E+09	1.99E+08	1.33E+08	6.02E+08
Homoserine/Threonine	4.19E+08	5.15E+08	1.82E+08	1.84E+08	4.41E+08
3-Methylthiopropionate	5.89E+07	9.25E+07	1.93E+05	7.22E+05	1.74E+05
Cysteine	6.12E+05	6.63E+05	1.22E+06	1.02E+06	1.57E+06
Nicotinate	2.43E+08	8.36E+07	9.11E+07	2.60E+08	2.41E+08
Taurine	1.76E+06	1.98E+06	2.07E+05	7.52E+05	7.24E+04
Thymine	5.24E+08	1.47E+09	1.59E+09	3.50E+09	3.47E+09
Hydroxyproline	5.15E+06	8.24E+06	9.46E+06	8.53E+06	1.02E+07

Table 25. Continued.

Metabolite	6 Days-1	6 Days-2	6 Days-3	6 Days-4	6 Days-5
N-Acetyl-beta-alanine	1.27E+09	2.78E+08	5.05E+08	6.82E+07	3.64E+08
Leucine/Isoleucine	1.20E+10	6.40E+09	1.34E+09	1.24E+09	3.60E+09
Glutaric acid	2.23E+08	3.27E+08	1.08E+09	5.55E+08	1.88E+09
Asparagine	7.13E+06	6.02E+08	3.97E+08	4.93E+08	2.57E+08
Hydroxyisocaproic acid	1.44E+10	2.63E+10	5.81E+08	3.88E+08	3.21E+09
Ornithine	1.48E+08	3.00E+08	2.37E+07	5.52E+07	4.78E+07
Salicylate	2.15E+07	4.14E+07	5.80E+08	7.28E+07	4.44E+08
Hydroxybenzoate	2.80E+07	1.16E+08	3.95E+07	1.12E+08	3.41E+07
Histidinol	7.65E+04	3.15E+06	2.16E+05	1.65E+07	6.58E+05
2-Oxoglutaric acid	1.45E+07	9.55E+07	2.02E+08	1.31E+08	8.06E+08
Glutamine	1.11E+08	6.62E+08	4.43E+08	5.09E+08	5.54E+08
2-hydroxyglutarate	4.15E+08	2.32E+09	6.23E+08	1.26E+09	8.72E+08
2-Hydroxy-2-methylsuccinate	4.15E+08	2.31E+09	6.23E+08	1.27E+09	8.74E+08
L-Methionine	2.50E+07	1.85E+08	4.76E+07	4.46E+07	9.09E+07
Guanine	1.75E+08	5.25E+06	1.87E+06	6.62E+07	2.57E+06
3-Methylphenylacetic acid	2.56E+09	2.31E+09	1.87E+06	2.58E+06	1.93E+06
Hydroxyphenylacetate	2.27E+07	1.59E+08	6.02E+08	1.08E+09	1.74E+08
Xylitol	3.09E+08	7.53E+07	1.10E+08	8.88E+07	1.15E+08
Dopamine	1.02E+08	8.29E+07	3.56E+06	4.25E+06	5.08E+06
2_3-Dihydroxybenzoate	4.55E+06	6.17E+06	8.20E+05	2.12E+07	1.50E+08
Histidine	1.74E+08	1.60E+08	5.81E+07	6.28E+07	1.16E+08
Orotate	1.12E+08	6.71E+08	2.52E+08	4.79E+07	6.13E+08
Dihydroorotate	8.96E+05	6.29E+06	4.64E+06	4.54E+05	1.23E+07
Allantoin	2.66E+07	4.15E+08	2.34E+08	6.86E+08	2.85E+08

Table 25. Continued.

Metabolite	6 Days-1	6 Days-2	6 Days-3	6 Days-4	6 Days-5
Indole-3-carboxylate	5.56E+07	1.38E+07	2.98E+07	4.07E+07	2.86E+07
Phenylpyruvate	2.08E+08	1.88E+09	5.89E+07	5.38E+07	8.81E+07
Phenylalanine	8.35E+09	2.38E+09	1.16E+09	4.60E+08	1.97E+09
Phenyllactic acid	6.97E+09	1.86E+09	1.44E+09	3.36E+09	2.30E+09
Quinolinate	3.13E+06	7.95E+07	3.16E+07	5.90E+07	5.48E+07
Phosphoenolpyruvate	1.07E+08	8.08E+07	3.03E+07	7.17E+07	1.10E+08
Uric acid	2.94E+08	2.14E+08	5.17E+08	7.19E+08	6.19E+08
3_4-Dihydroxyphenylacetate (DOPAC)	5.36E+07	8.09E+07	5.29E+07	9.40E+07	6.47E+07
Sulfolactate	2.43E+07	2.81E+07	1.57E+06	1.01E+08	3.13E+06
Glycerone phosphate	5.92E+06	1.95E+06	4.98E+06	1.28E+07	5.29E+06
Arginine	6.83E+07	3.51E+07	4.26E+07	4.27E+07	6.21E+07
Citrulline	1.70E+09	3.12E+08	2.97E+07	7.82E+07	1.26E+08
Ascorbate	8.22E+04	2.56E+06	3.16E+05	6.61E+05	4.75E+05
N-Carbamoyl-L-aspartate	9.89E+05	7.25E+07	5.17E+07	9.03E+06	1.35E+08
Allantoate	1.81E+07	7.93E+08	3.62E+08	1.55E+09	2.36E+08
2-Isopropylmalate	6.95E+08	1.84E+09	2.89E+09	2.29E+09	3.32E+09
Glucosamine	3.20E+06	7.28E+06	5.84E+06	2.62E+07	6.55E+06
myo-Inositol	2.02E+07	1.82E+07	2.58E+07	1.40E+07	3.33E+07
Tyrosine	1.34E+09	2.16E+08	2.07E+08	8.53E+07	4.18E+08
Homovanillic acid (HVA)	8.03E+08	2.03E+08	4.09E+07	2.90E+07	4.95E+07
Homocysteic acid	0.00E+00	5.94E+06	2.60E+05	8.81E+07	8.17E+04
4-Pyridoxate	1.00E+07	3.94E+07	2.49E+08	4.74E+08	2.94E+08
N-Acetylglutamine	1.01E+08	1.80E+08	4.97E+07	4.70E+07	7.60E+07
Citrate/isocitrate	5.86E+08	2.66E+09	2.00E+10	2.30E+10	1.73E+10

Table 25. Continued.

Metabolite	6 Days-1	6 Days-2	6 Days-3	6 Days-4	6 Days-5
D-Gluconate	7.35E+08	5.57E+08	5.70E+08	7.00E+08	6.78E+08
N-N Dimethylarginine	2.32E+05	4.40E+06	7.80E+05	2.67E+06	2.63E+06
Tryptophan	1.15E+09	1.90E+08	2.97E+08	2.39E+08	5.45E+08
Xanthurenic acid	2.24E+07	8.07E+06	8.91E+06	1.25E+07	1.14E+08
D-Glucarate	6.81E+09	2.62E+09	1.54E+09	4.92E+09	9.23E+08
Pantothenate	1.57E+09	1.98E+09	1.33E+09	2.89E+09	2.87E+09
Cystathionine	2.36E+04	1.06E+07	1.02E+07	1.80E+07	5.52E+06
Cystine	1.93E+04	5.72E+03	5.20E+05	1.93E+05	2.64E+05
Uridine	9.21E+07	1.84E+08	4.94E+07	6.76E+06	1.70E+08
Biotin	1.54E+06	6.90E+05	4.75E+05	2.25E+05	9.20E+05
Deoxyinosine	2.20E+05	3.72E+06	2.85E+06	8.03E+06	9.89E+06
Glucose 6-phosphate	9.01E+06	3.46E+07	2.87E+07	6.85E+07	3.15E+07
S-Ribosyl-L-homocysteine	1.75E+04	4.15E+06	3.01E+05	1.52E+05	1.12E+04
6-Phospho-D-gluconate	5.39E+06	2.44E+07	1.17E+07	1.86E+07	3.62E+07
Guanosine	3.18E+07	3.61E+06	1.53E+07	8.32E+06	2.47E+07
Xanthosine	4.15E+07	1.61E+06	3.03E+06	1.50E+07	4.37E+06
Glycinamide ribotide (GAR)	0.00E+00	6.28E+05	8.52E+05	4.35E+06	5.12E+04
Ophthalmate	2.24E+08	1.34E+07	4.56E+06	8.01E+07	2.16E+07
Glutathione	3.12E+07	9.78E+07	3.70E+07	1.64E+08	5.72E+07
UMP	1.21E+06	1.06E+08	2.09E+08	4.07E+08	3.07E+08
AICAR	1.30E+04	6.23E+05	7.80E+05	1.60E+06	7.51E+05
Trehalose/Sucrose/Cellobiose	5.28E+05	1.52E+07	1.52E+07	2.93E+07	1.68E+07
AMP/dGMP	1.60E+07	2.41E+08	5.19E+08	4.28E+08	7.29E+08
IMP	2.14E+04	4.43E+06	9.93E+06	9.71E+06	2.51E+07

Table 25. Continued.

Metabolite	6 Days-1	6 Days-2	6 Days-3	6 Days-4	6 Days-5
GMP	1.13E+06	4.34E+07	2.26E+08	1.55E+08	3.20E+08
Xanthosine 5--phosphate	4.55E+06	5.29E+06	1.10E+06	6.03E+05	7.18E+06
Riboflavin	5.32E+06	2.11E+06	7.88E+06	1.41E+06	6.91E+06
S-Adenosyl-L-homocysteine	0.00E+00	3.11E+05	2.95E+05	5.35E+05	2.91E+05
ADP	1.04E+07	2.29E+08	7.47E+07	3.24E+08	1.22E+08
Folate	4.52E+04	2.75E+04	1.49E+06	7.29E+05	1.81E+06
CDP-ethanolamine	0.00E+00	1.21E+06	1.79E+06	4.36E+06	3.23E+06
FMN	5.42E+06	4.79E+06	6.22E+06	8.51E+06	1.17E+07
UDP-glucose	8.64E+05	8.62E+07	8.69E+07	2.07E+08	2.04E+08
NAD+	1.54E+07	1.39E+07	3.57E+06	3.81E+07	1.12E+07
NADH	1.76E+05	1.50E+05	1.02E+04	1.36E+05	1.90E+05
Dephospho-CoA	2.75E+05	1.15E+06	2.46E+06	1.64E+06	3.31E+06
NADP+	3.18E+07	6.12E+06	2.41E+06	1.75E+07	8.77E+06
FAD	6.57E+06	2.24E+06	3.82E+06	3.57E+06	8.24E+06
N-Acetylglutamate	5.13E+08	1.30E+09	9.31E+08	5.71E+08	1.64E+09
Kynurenic acid	1.54E+08	3.76E+07	1.15E+08	7.92E+08	2.60E+08

Table 26. Intensities of *G. mellonella* replicates in 8 days post infection group.

Metabolite	8 Days-1	8 Days-2	8 Days-3	8 Days-4	8 Days-5
Glyoxylate	0.00E+00	1.14E+04	1.09E+07	0.00E+00	7.89E+07
Glycine	1.92E+05	3.69E+04	8.06E+08	0.00E+00	1.69E+08
Pyruvate	2.59E+07	1.38E+08	1.01E+08	2.41E+08	5.80E+07
Alanine/Sarcosine	9.66E+09	5.99E+08	8.88E+08	5.95E+08	5.14E+08
Lactate	7.62E+08	4.86E+08	6.34E+08	4.19E+08	1.05E+09
Dimethylglycine	4.92E+08	7.12E+07	1.50E+08	7.79E+07	7.07E+07
Serine	5.35E+06	5.34E+07	3.98E+07	7.18E+07	7.30E+07
Histamine	1.08E+06	1.64E+06	1.27E+06	1.79E+06	1.22E+05
Uracil	2.66E+09	9.49E+08	1.37E+09	2.09E+09	1.22E+09
Creatinine	7.04E+04	5.84E+05	2.10E+05	5.91E+05	2.25E+04
Proline	1.27E+10	4.28E+09	6.22E+09	6.31E+09	1.57E+09
Fumarate	2.10E+06	4.26E+07	3.36E+07	7.06E+07	2.35E+07
2-Oxoisovalerate	1.28E+07	3.04E+07	7.89E+07	7.36E+07	1.51E+07
Indole	1.12E+07	5.68E+05	6.54E+05	1.07E+06	3.94E+05
Valine	8.80E+09	2.01E+08	3.89E+08	5.13E+08	1.62E+08
3-Hydroxyisovaleric acid	3.52E+08	7.41E+07	9.64E+07	1.46E+08	1.71E+07
Homoserine/Threonine	2.45E+09	1.89E+08	1.88E+08	4.03E+08	1.58E+08
3-Methylthiopropionate	1.10E+07	2.82E+05	5.23E+05	1.15E+06	2.23E+05
Cysteine	1.34E+05	1.51E+06	7.13E+05	3.82E+06	3.77E+05
Nicotinate	1.27E+08	1.80E+08	2.00E+08	2.90E+08	3.17E+07
Taurine	4.20E+06	4.33E+05	2.32E+05	4.61E+05	3.38E+05
Thymine	7.35E+08	1.92E+09	1.60E+09	4.56E+09	2.19E+09
Hydroxyproline	7.28E+06	9.16E+06	6.42E+06	1.75E+07	6.35E+06

Table 26. Continued.

Metabolite	8 Days-1	8 Days-2	8 Days-3	8 Days-4	8 Days-5
N-Acetyl-beta-alanine	1.92E+09	9.08E+07	6.63E+07	3.95E+08	3.82E+07
Leucine/Isoleucine	2.99E+10	7.90E+08	1.41E+09	2.03E+09	5.05E+08
Glutaric acid	1.34E+08	4.48E+08	4.39E+08	4.20E+08	3.81E+08
Asparagine	1.50E+07	1.55E+08	3.42E+08	1.04E+08	1.95E+08
Hydroxyisocaproic acid	3.76E+09	2.58E+08	3.25E+08	6.67E+08	7.97E+07
Ornithine	1.31E+09	5.04E+07	6.94E+07	2.77E+07	1.68E+07
Salicylate	2.60E+07	3.29E+07	1.04E+07	6.43E+08	2.56E+07
Hydroxybenzoate	7.38E+06	3.08E+07	8.76E+07	9.91E+07	8.14E+06
Histidinol	1.71E+05	4.21E+06	2.00E+06	8.28E+06	3.51E+05
2-Oxoglutaric acid	7.61E+06	1.56E+08	1.31E+08	4.03E+08	1.20E+08
Glutamine	1.19E+09	4.81E+08	5.93E+08	5.38E+08	3.64E+08
2-hydroxyglutarate	1.35E+10	8.76E+08	4.02E+08	1.55E+09	3.49E+08
2-Hydroxy-2-methylsuccinate	1.35E+10	8.78E+08	4.02E+08	1.55E+09	3.49E+08
L-Methionine	5.94E+08	3.53E+07	3.30E+07	6.49E+07	2.15E+07
Guanine	1.21E+08	3.11E+06	3.24E+06	8.01E+06	7.03E+06
3-Methylphenylacetic acid	7.98E+08	1.34E+06	1.28E+06	3.94E+06	8.10E+06
Hydroxyphenylacetate	2.48E+06	6.42E+08	2.71E+08	1.70E+09	2.18E+07
Xylitol	3.55E+08	3.14E+07	5.06E+07	1.56E+08	6.18E+07
Dopamine	4.44E+08	1.19E+06	2.55E+06	1.41E+06	1.73E+06
2_3-Dihydroxybenzoate	9.49E+05	2.89E+06	3.75E+06	3.97E+08	6.16E+07
Histidine	1.51E+09	4.39E+07	5.48E+07	7.54E+07	3.31E+07
Orotate	6.04E+07	1.03E+08	6.05E+08	2.44E+08	2.74E+08
Dihydroorotate	1.82E+06	1.65E+06	5.52E+06	6.49E+06	3.58E+07
Allantoin	9.41E+06	3.51E+08	5.51E+08	4.07E+08	7.14E+07

Table 26. Continued.

Metabolite	8 Days-1	8 Days-2	8 Days-3	8 Days-4	8 Days-5
Indole-3-carboxylate	4.83E+06	6.05E+07	3.30E+07	8.36E+07	9.92E+06
Phenylpyruvate	5.75E+06	6.15E+07	1.08E+08	7.79E+07	4.94E+06
Phenylalanine	1.65E+10	6.26E+08	5.70E+08	1.30E+09	4.59E+08
Phenyllactic acid	3.07E+08	9.10E+08	7.48E+08	1.84E+09	1.46E+07
Quinolinate	9.88E+05	1.29E+08	5.80E+07	5.20E+08	5.22E+07
Phosphoenolpyruvate	5.36E+06	3.48E+07	3.44E+07	1.54E+08	5.30E+07
Uric acid	3.56E+07	1.31E+08	6.04E+08	1.11E+08	1.64E+08
3_4-Dihydroxyphenylacetate (DOPAC)	6.71E+06	1.96E+07	6.92E+07	3.75E+07	6.05E+06
Sulfolactate	1.04E+07	3.38E+06	2.49E+07	1.92E+07	8.88E+06
Glycerone phosphate	2.51E+06	8.17E+06	5.39E+05	2.33E+07	1.44E+05
Arginine	9.87E+06	5.13E+07	4.43E+07	5.35E+07	3.40E+07
Citrulline	1.00E+09	9.13E+07	1.00E+08	3.28E+07	4.13E+07
Ascorbate	9.12E+04	1.93E+05	5.31E+05	6.39E+05	2.95E+05
N-Carbamoyl-L-aspartate	3.72E+05	3.08E+07	1.17E+08	4.52E+07	2.02E+08
Allantoate	2.40E+06	7.66E+07	1.37E+09	1.38E+08	1.03E+07
2-Isopropylmalate	2.20E+08	3.09E+09	2.53E+09	4.72E+09	1.32E+08
Glucosamine	2.86E+06	1.93E+07	9.45E+06	1.65E+07	5.22E+07
myo-Inositol	1.93E+07	1.47E+07	1.80E+07	4.08E+07	2.92E+07
Tyrosine	2.21E+08	2.72E+08	1.41E+08	4.92E+08	1.57E+08
Homovanillic acid (HVA)	4.73E+07	3.27E+07	9.99E+07	6.74E+07	3.09E+06
Homocysteic acid	5.51E+03	3.87E+05	2.82E+06	8.64E+05	1.91E+05
4-Pyridoxate	1.36E+07	2.96E+08	1.76E+08	8.47E+08	3.75E+08
N-Acetylglutamine	1.21E+09	4.34E+07	3.81E+07	4.27E+07	4.34E+07
Citrate/isocitrate	1.62E+09	2.62E+09	5.38E+09	5.97E+09	4.29E+09

Table 26. Continued.

Metabolite	8 Days-1	8 Days-2	8 Days-3	8 Days-4	8 Days-5
D-Gluconate	4.86E+08	4.97E+08	4.54E+08	1.35E+09	4.74E+08
N-N Dimethylarginine	2.64E+06	5.68E+05	2.87E+06	4.25E+05	4.47E+05
Tryptophan	2.56E+09	1.89E+08	2.36E+08	3.52E+08	1.44E+08
Xanthurenic acid	8.13E+05	4.38E+07	6.09E+07	2.78E+07	8.22E+07
D-Glucarate	2.24E+09	1.57E+09	1.29E+09	3.66E+09	7.07E+07
Pantothenate	4.49E+08	2.18E+09	1.85E+09	6.61E+08	3.82E+08
Cystathionine	2.65E+06	1.91E+07	1.44E+07	4.81E+06	7.67E+06
Cystine	8.24E+03	1.07E+06	2.85E+05	9.26E+05	2.09E+05
Uridine	3.65E+08	1.26E+07	1.99E+07	3.63E+07	1.50E+07
Biotin	3.63E+06	6.47E+05	9.07E+05	7.35E+05	5.06E+05
Deoxyinosine	8.30E+05	2.61E+06	1.78E+06	1.03E+07	3.08E+06
Glucose 6-phosphate	2.27E+07	1.28E+07	2.09E+07	4.99E+07	4.88E+07
S-Ribosyl-L-homocysteine	1.10E+06	6.54E+05	6.96E+04	8.22E+05	5.35E+03
6-Phospho-D-gluconate	1.06E+06	4.15E+06	1.44E+07	1.19E+07	2.82E+07
Guanosine	8.48E+06	9.72E+07	1.65E+07	1.44E+08	1.27E+07
Xanthosine	2.32E+07	2.43E+06	3.70E+06	4.89E+06	6.91E+06
Glycinamide ribotide (GAR)	0.00E+00	9.38E+05	5.64E+06	1.78E+06	7.03E+04
Ophthalmate	1.03E+08	1.19E+07	1.29E+07	2.84E+07	1.82E+07
Glutathione	3.02E+07	2.55E+07	2.45E+07	7.57E+07	6.61E+06
UMP	3.29E+06	2.32E+08	2.58E+08	5.89E+08	1.36E+08
AICAR	0.00E+00	4.86E+05	1.06E+06	6.91E+05	1.20E+05
Trehalose/Sucrose/Cellobiose	2.94E+04	1.71E+07	1.65E+07	3.36E+07	1.36E+07
AMP/dGMP	6.36E+07	1.09E+09	8.68E+08	2.18E+09	3.01E+08
IMP	2.42E+05	9.33E+06	6.27E+06	2.38E+07	5.82E+06

Table 26. Continued.

Metabolite	8 Days-1	8 Days-2	8 Days-3	8 Days-4	8 Days-5
GMP	1.75E+06	4.51E+08	4.55E+08	1.42E+09	6.51E+07
Xanthosine 5--phosphate	5.28E+04	6.38E+05	7.91E+05	1.62E+06	1.83E+05
Riboflavin	4.62E+06	2.51E+06	3.66E+06	8.34E+06	2.66E+07
S-Adenosyl-L-homocysteine	0.00E+00	3.88E+05	3.74E+05	6.86E+05	4.90E+05
ADP	6.12E+07	1.23E+08	2.48E+08	2.70E+08	3.46E+07
Folate	2.09E+04	2.13E+06	1.12E+06	4.89E+06	5.72E+06
CDP-ethanolamine	0.00E+00	1.38E+06	1.50E+06	3.70E+06	1.71E+06
FMN	8.86E+06	6.73E+06	5.28E+06	1.12E+07	1.71E+07
UDP-glucose	1.38E+06	5.54E+07	7.17E+07	2.72E+08	1.17E+08
NAD+	1.47E+07	9.65E+06	1.00E+07	1.16E+07	1.01E+06
NADH	1.18E+06	1.85E+04	1.72E+04	2.19E+04	3.82E+04
Dephospho-CoA	3.15E+05	1.20E+06	1.13E+06	5.16E+06	1.15E+06
NADP+	5.62E+06	7.75E+06	5.04E+06	1.11E+07	5.08E+05
FAD	1.32E+06	2.45E+06	1.75E+06	7.64E+06	6.93E+06
N-Acetylglutamate	9.57E+08	7.96E+08	4.05E+08	1.06E+09	3.92E+08
Kynurenic acid	8.88E+05	9.71E+08	3.20E+08	8.93E+08	3.51E+07

Table 27. Intensities of *G. mellonella* replicates in 10 days post infection group.

Metabolite	10 Days-1	10 Days-2	10 Days-3	10 Days-4	10 Days-5
Glyoxylate	1.35E+04	4.15E+03	9.16E+06	0.00E+00	0.00E+00
Glycine	2.74E+04	1.01E+05	1.47E+09	1.84E+04	1.30E+06
Pyruvate	9.47E+07	7.35E+07	1.12E+08	1.78E+08	2.20E+08
Alanine/Sarcosine	3.85E+08	5.45E+08	1.10E+09	3.33E+08	4.14E+09
Lactate	1.42E+09	4.82E+08	5.45E+08	4.27E+08	1.83E+09
Dimethylglycine	1.03E+08	7.98E+07	7.63E+08	4.10E+07	2.14E+08
Serine	6.34E+07	8.00E+07	5.31E+07	8.67E+07	5.05E+07
Histamine	4.22E+06	1.37E+06	3.35E+06	1.33E+06	4.24E+06
Uracil	2.54E+09	1.77E+09	2.33E+09	8.49E+08	2.24E+09
Creatinine	6.47E+04	6.78E+05	3.66E+05	1.92E+06	1.10E+05
Proline	3.50E+09	9.81E+09	8.90E+09	5.16E+09	1.32E+10
Fumarate	1.70E+07	2.84E+07	1.49E+07	5.47E+07	5.99E+07
2-Oxoisovalerate	5.01E+07	2.08E+08	5.95E+08	3.03E+07	2.51E+08
Indole	2.24E+05	3.57E+05	3.59E+05	1.16E+06	3.65E+06
Valine	2.30E+08	2.98E+08	5.27E+08	2.42E+08	5.07E+09
3-Hydroxyisovaleric acid	7.00E+08	1.10E+08	4.04E+08	8.35E+07	7.35E+08
Homoserine/Threonine	1.88E+08	2.28E+08	1.80E+08	2.40E+08	6.96E+08
3-Methylthiopropionate	9.58E+05	5.78E+06	5.61E+06	2.55E+05	1.51E+08
Cysteine	8.61E+05	1.42E+06	2.09E+05	1.76E+06	2.58E+05
Nicotinate	1.29E+07	2.51E+07	1.51E+08	1.58E+08	1.03E+08
Taurine	3.41E+05	9.01E+05	2.54E+05	6.94E+05	3.79E+06
Thymine	2.98E+09	1.52E+09	2.29E+09	1.49E+09	1.27E+09
Hydroxyproline	3.89E+07	3.04E+07	1.30E+07	7.78E+07	2.11E+07

Table 27. Continued.

Metabolite	10 Days-1	10 Days-2	10 Days-3	10 Days-4	10 Days-5
N-Acetyl-beta-alanine	3.82E+08	2.12E+08	2.33E+08	1.29E+08	2.63E+08
Leucine/Isoleucine	5.41E+08	9.59E+08	1.14E+09	1.17E+09	1.59E+10
Glutaric acid	2.82E+09	7.96E+08	1.26E+09	8.31E+07	5.57E+08
Asparagine	4.24E+08	7.09E+08	2.98E+08	1.53E+08	1.19E+08
Hydroxyisocaproic acid	3.14E+09	5.25E+08	1.15E+09	5.60E+08	3.07E+09
Ornithine	1.13E+07	2.86E+07	4.15E+07	4.15E+07	5.49E+08
Salicylate	3.51E+08	5.80E+07	5.14E+07	3.57E+07	2.09E+07
Hydroxybenzoate	5.40E+08	5.10E+08	4.57E+08	4.75E+07	1.27E+08
Histidinol	5.27E+05	9.61E+05	3.06E+05	1.33E+07	7.00E+05
2-Oxoglutaric acid	7.30E+07	4.20E+07	5.72E+07	1.71E+08	1.16E+08
Glutamine	5.19E+08	7.62E+08	4.35E+08	4.26E+08	3.03E+08
2-hydroxyglutarate	1.57E+09	1.83E+09	6.51E+08	7.68E+08	1.03E+09
2-Hydroxy-2-methylsuccinate	1.58E+09	1.83E+09	6.50E+08	7.71E+08	1.03E+09
L-Methionine	1.85E+07	3.15E+07	2.88E+07	3.68E+07	4.12E+08
Guanine	5.83E+06	5.27E+06	4.99E+06	2.99E+06	3.40E+06
3-Methylphenylacetic acid	1.37E+09	3.11E+06	9.68E+05	1.56E+06	1.10E+07
Hydroxyphenylacetate	6.43E+08	1.01E+09	3.97E+08	1.16E+09	1.66E+07
Xylitol	6.62E+07	9.00E+07	7.76E+07	1.13E+08	8.66E+07
Dopamine	5.22E+06	7.09E+05	1.25E+06	7.83E+05	9.59E+06
2_3-Dihydroxybenzoate	5.26E+07	3.33E+07	3.55E+06	6.87E+07	7.21E+06
Histidine	3.45E+07	8.19E+07	6.06E+07	7.79E+07	2.62E+08
Orotate	6.64E+08	5.92E+08	1.31E+09	1.97E+07	1.48E+09
Dihydroorotate	3.83E+06	3.91E+06	1.51E+07	1.64E+06	9.90E+06
Allantoin	3.68E+08	4.72E+08	4.76E+08	1.36E+08	7.05E+08

Table 27. Continued.

Metabolite	10 Days-1	10 Days-2	10 Days-3	10 Days-4	10 Days-5
Indole-3-carboxylate	1.13E+08	1.47E+08	1.28E+08	7.30E+07	1.03E+08
Phenylpyruvate	8.62E+08	4.53E+08	1.57E+09	9.09E+07	2.76E+08
Phenylalanine	2.74E+08	4.52E+08	6.77E+08	7.17E+08	6.57E+09
Phenyllactic acid	3.91E+08	4.07E+08	2.38E+08	1.27E+09	8.77E+08
Quinolate	2.42E+08	1.30E+09	4.88E+08	6.06E+08	8.96E+07
Phosphoenolpyruvate	1.47E+08	3.51E+07	7.96E+07	5.37E+07	4.14E+08
Uric acid	4.95E+08	7.71E+08	6.18E+08	1.06E+07	1.34E+08
3_4-Dihydroxyphenylacetate (DOPAC)	1.97E+08	1.85E+08	1.90E+08	4.07E+07	2.94E+08
Sulfolactate	2.89E+07	1.28E+08	6.58E+07	2.72E+06	5.86E+07
Glycerone phosphate	6.31E+06	8.11E+06	7.16E+06	9.15E+06	6.71E+05
Arginine	1.80E+07	4.53E+07	3.55E+07	5.27E+07	3.55E+07
Citrulline	7.90E+07	3.83E+07	3.34E+07	3.37E+07	8.86E+08
Ascorbate	1.09E+06	2.76E+05	1.74E+06	7.69E+05	3.96E+05
N-Carbamoyl-L-aspartate	3.39E+07	4.53E+07	2.99E+08	1.01E+07	8.99E+08
Allantoate	3.13E+08	1.40E+09	1.05E+09	4.98E+07	8.16E+07
2-Isopropylmalate	1.03E+10	1.15E+10	9.14E+09	3.17E+09	5.00E+08
Glucosamine	1.45E+07	1.56E+07	6.82E+06	2.62E+07	6.54E+06
myo-Inositol	5.00E+07	4.24E+07	2.80E+07	3.28E+07	2.52E+07
Tyrosine	9.70E+07	1.75E+08	9.48E+07	4.27E+08	2.41E+08
Homovanillic acid (HVA)	1.05E+08	3.74E+07	3.96E+07	1.35E+07	9.99E+07
Homocysteic acid	6.44E+05	1.00E+07	1.28E+06	2.38E+05	9.43E+06
4-Pyridoxate	5.32E+08	5.78E+08	1.65E+08	7.70E+08	5.41E+07
N-Acetylglutamine	8.53E+07	3.78E+07	6.97E+07	4.73E+07	1.40E+08
Citrate/isocitrate	6.30E+09	5.14E+09	3.54E+09	3.62E+09	3.06E+09

Table 27. Continued.

Metabolite	10 Days-1	10 Days-2	10 Days-3	10 Days-4	10 Days-5
D-Gluconate	6.62E+08	9.10E+08	6.44E+08	1.41E+09	5.57E+08
N-N Dimethylarginine	3.20E+05	8.07E+05	5.98E+05	5.52E+05	3.30E+06
Tryptophan	9.54E+07	1.53E+08	1.48E+08	3.84E+08	1.09E+09
Xanthurenic acid	6.05E+07	4.11E+07	1.96E+07	3.87E+07	1.70E+05
D-Glucarate	4.07E+09	1.75E+09	5.22E+09	2.36E+09	4.61E+09
Pantothenate	4.06E+09	3.41E+09	3.94E+09	2.18E+08	1.39E+09
Cystathionine	6.94E+06	6.44E+06	4.64E+06	3.77E+06	9.00E+06
Cystine	0.00E+00	7.23E+04	1.85E+04	1.24E+06	1.36E+05
Uridine	4.96E+07	7.21E+06	8.75E+07	5.41E+06	1.02E+08
Biotin	1.70E+06	2.06E+06	1.61E+06	3.01E+05	1.56E+06
Deoxyinosine	6.90E+06	2.47E+06	2.23E+06	2.14E+06	1.45E+06
Glucose 6-phosphate	3.32E+07	1.72E+07	2.75E+07	1.48E+07	3.43E+07
S-Ribosyl-L-homocysteine	1.14E+05	8.73E+05	2.82E+06	1.30E+05	0.00E+00
6-Phospho-D-gluconate	2.93E+07	1.24E+07	2.15E+07	2.35E+06	3.51E+07
Guanosine	1.51E+07	6.16E+06	5.21E+07	5.57E+07	1.15E+07
Xanthosine	1.54E+07	1.20E+06	2.23E+06	2.93E+06	1.42E+07
Glycinamide ribotide (GAR)	1.34E+06	4.33E+05	8.40E+05	2.85E+05	4.09E+04
Ophthalmate	4.69E+07	2.68E+07	2.31E+07	2.11E+07	1.20E+07
Glutathione	1.08E+08	1.91E+08	4.06E+07	2.40E+07	7.23E+06
UMP	1.37E+08	2.65E+08	1.57E+08	3.51E+08	7.39E+07
AICAR	2.56E+05	7.40E+05	3.89E+05	1.05E+05	1.61E+05
Trehalose/Sucrose/Cellobiose	1.27E+07	2.81E+07	1.63E+07	3.18E+07	3.84E+06
AMP/dGMP	4.60E+08	7.65E+08	7.41E+08	1.80E+09	2.07E+08
IMP	3.43E+06	3.49E+06	2.92E+06	2.13E+07	3.23E+06

Table 27. Continued.

Metabolite	10 Days-1	10 Days-2	10 Days-3	10 Days-4	10 Days-5
GMP	1.38E+08	3.16E+08	3.11E+08	8.36E+08	8.49E+07
Xanthosine 5--phosphate	5.37E+06	1.64E+06	2.59E+06	7.38E+05	3.79E+07
Riboflavin	7.30E+06	8.50E+06	1.02E+07	3.57E+06	9.74E+05
S-Adenosyl-L-homocysteine	2.72E+04	1.67E+05	4.25E+05	2.80E+05	3.89E+04
ADP	3.31E+08	1.83E+08	3.16E+08	1.22E+08	6.66E+07
Folate	4.41E+05	1.19E+06	1.13E+06	1.95E+06	1.77E+04
CDP-ethanolamine	1.13E+06	9.43E+05	5.94E+05	1.33E+06	2.77E+05
FMN	6.07E+06	2.77E+06	6.21E+06	7.12E+06	3.24E+06
UDP-glucose	1.25E+08	9.57E+07	1.07E+08	1.97E+08	1.91E+07
NAD+	1.04E+07	1.03E+07	1.24E+07	1.22E+07	4.48E+06
NADH	4.89E+04	0.00E+00	6.69E+03	0.00E+00	0.00E+00
Dephospho-CoA	7.53E+05	9.77E+05	3.59E+05	2.36E+06	2.37E+05
NADP+	9.52E+06	3.19E+06	7.87E+06	1.41E+07	5.22E+06
FAD	3.92E+06	2.27E+06	3.40E+06	4.12E+06	1.59E+06
N-Acetylglutamate	1.61E+09	3.43E+08	1.48E+08	1.43E+09	1.66E+09
Kynurenic acid	7.01E+08	8.74E+08	5.15E+07	1.18E+09	4.40E+07

Table 28. Intensities of *G. mellonella* replicates in 12 days post infection group.

Metabolite	12 Day-3	12 Days-1	12 Days-2	12 Days-4	12 Days-5
Glyoxylate	5.87E+06	4.74E+07	1.58E+07	1.88E+04	7.46E+06
Glycine	2.21E+09	2.56E+08	4.03E+07	5.89E+05	1.42E+09
Pyruvate	6.83E+07	9.72E+07	6.38E+07	7.90E+07	5.37E+07
Alanine/Sarcosine	6.22E+09	6.52E+08	1.08E+08	8.56E+08	8.53E+08
Lactate	6.79E+10	4.68E+08	3.83E+08	9.20E+08	1.50E+09
Dimethylglycine	1.30E+08	1.09E+08	1.69E+07	2.27E+08	1.33E+09
Serine	1.65E+06	5.00E+06	3.72E+07	2.68E+07	7.52E+07
Histamine	8.64E+05	1.63E+05	1.99E+06	4.63E+06	6.49E+06
Uracil	4.74E+08	9.47E+08	4.14E+08	2.93E+09	1.79E+09
Creatinine	0.00E+00	1.77E+04	5.35E+05	6.19E+04	4.42E+05
Proline	1.08E+10	5.08E+08	1.22E+09	2.73E+09	2.42E+09
Fumarate	8.69E+05	1.37E+07	1.93E+07	1.74E+07	8.56E+06
2-Oxoisovalerate	6.87E+06	2.16E+07	1.73E+07	5.25E+07	8.34E+08
Indole	6.19E+06	7.68E+05	4.20E+05	1.75E+06	1.61E+05
Valine	5.69E+09	1.39E+09	1.01E+08	1.00E+09	6.36E+08
3-Hydroxyisovaleric acid	2.06E+08	5.82E+08	4.53E+07	1.13E+09	2.76E+09
Homoserine/Threonine	1.66E+09	2.49E+08	6.67E+07	2.47E+08	1.60E+08
3-Methylthiopropionate	5.15E+06	5.97E+06	1.12E+06	3.41E+07	1.19E+08
Cysteine	6.99E+04	5.95E+04	1.16E+06	7.43E+05	2.12E+05
Nicotinate	1.37E+08	4.26E+07	6.51E+06	5.36E+08	1.03E+08
Taurine	1.22E+06	0.00E+00	3.00E+05	6.79E+03	2.54E+06
Thymine	2.96E+08	9.80E+08	1.69E+08	3.58E+09	1.08E+09
Hydroxyproline	5.19E+06	3.24E+06	6.95E+06	8.69E+06	1.95E+07

Table 28. Continued.

Metabolite	12 Day-3	12 Days-1	12 Days-2	12 Days-4	12 Days-5
N-Acetyl-beta-alanine	9.15E+08	4.27E+07	8.19E+07	2.32E+08	9.74E+07
Leucine/Isoleucine	2.05E+10	5.96E+09	3.71E+08	1.93E+09	8.97E+08
Glutaric acid	6.76E+07	2.24E+08	2.83E+08	1.74E+09	3.24E+08
Asparagine	8.52E+08	1.56E+06	2.88E+08	2.86E+07	1.29E+08
Hydroxyisocaproic acid	3.32E+09	2.19E+09	1.17E+08	2.34E+09	1.28E+10
Ornithine	4.84E+08	2.99E+08	2.02E+07	4.41E+08	4.67E+07
Salicylate	1.00E+08	7.27E+06	7.21E+06	1.67E+08	2.51E+07
Hydroxybenzoate	4.97E+06	1.83E+07	1.18E+08	2.54E+07	5.47E+08
Histidinol	7.23E+04	1.51E+06	1.76E+06	3.79E+06	3.97E+05
2-Oxoglutaric acid	9.64E+06	2.53E+07	3.82E+07	6.80E+07	4.52E+07
Glutamine	2.22E+09	4.96E+06	2.18E+08	1.03E+08	3.04E+08
2-hydroxyglutarate	1.16E+10	1.73E+08	5.17E+08	7.63E+08	4.72E+08
2-Hydroxy-2-methylsuccinate	1.16E+10	1.73E+08	5.17E+08	7.64E+08	4.71E+08
L-Methionine	9.17E+08	1.33E+08	1.20E+07	1.81E+08	1.40E+07
Guanine	4.87E+04	1.52E+06	1.24E+06	8.92E+05	1.37E+07
3-Methylphenylacetic acid	1.51E+06	2.18E+09	7.03E+05	2.44E+06	1.39E+06
Hydroxyphenylacetate	2.81E+06	9.85E+07	1.52E+08	6.50E+08	3.46E+08
Xylitol	1.92E+08	5.41E+07	1.61E+07	4.17E+07	4.46E+07
Dopamine	8.65E+08	9.91E+06	5.91E+05	7.17E+06	1.51E+06
2_3-Dihydroxybenzoate	2.21E+06	8.26E+07	2.84E+06	1.11E+08	2.16E+06
Histidine	7.73E+08	1.18E+08	5.66E+07	3.20E+07	3.98E+07
Orotate	1.72E+07	2.09E+06	3.33E+07	2.28E+09	9.31E+08
Dihydroorotate	1.91E+06	1.60E+06	1.76E+06	1.08E+08	2.99E+06
Allantoin	3.42E+07	1.14E+06	3.22E+08	2.94E+07	5.37E+08

Table 28. Continued.

Metabolite	12 Day-3	12 Days-1	12 Days-2	12 Days-4	12 Days-5
Indole-3-carboxylate	1.47E+06	5.06E+07	3.98E+07	1.42E+08	9.24E+07
Phenylpyruvate	4.51E+06	2.57E+07	7.53E+07	5.24E+07	1.27E+09
Phenylalanine	9.49E+09	3.75E+09	2.00E+08	1.48E+09	4.61E+08
Phenyllactic acid	4.49E+08	4.17E+08	3.51E+07	1.12E+09	1.39E+09
Quinolinate	2.40E+05	4.73E+06	3.91E+08	5.43E+07	3.41E+08
Phosphoenolpyruvate	1.04E+06	2.12E+07	3.68E+07	5.99E+07	3.09E+08
Uric acid	1.56E+06	1.90E+08	1.53E+08	4.37E+08	2.75E+08
3_4-Dihydroxyphenylacetate (DOPAC)	2.83E+06	3.22E+07	4.97E+07	6.06E+07	2.79E+08
Sulfolactate	2.77E+06	7.45E+07	8.00E+07	2.51E+07	7.97E+07
Glycerone phosphate	2.13E+06	6.01E+04	5.63E+06	2.76E+06	3.42E+04
Arginine	7.48E+05	9.23E+05	3.56E+07	1.35E+07	2.53E+07
Citrulline	1.55E+08	5.35E+08	3.53E+06	1.53E+09	3.68E+07
Ascorbate	2.45E+05	1.28E+05	9.96E+05	9.48E+05	2.43E+06
N-Carbamoyl-L-aspartate	4.51E+06	1.60E+06	2.17E+07	9.01E+08	4.04E+07
Allantoate	2.00E+06	4.11E+05	7.90E+08	7.66E+06	1.46E+09
2-Isopropylmalate	1.78E+07	1.02E+09	6.53E+09	2.59E+09	3.62E+09
Glucosamine	4.28E+05	2.08E+07	7.23E+06	8.31E+06	6.37E+06
myo-Inositol	8.12E+08	4.39E+07	4.39E+07	5.52E+07	2.02E+07
Tyrosine	4.02E+07	1.24E+09	1.58E+08	5.99E+08	5.73E+07
Homovanillic acid (HVA)	4.26E+07	7.72E+08	3.13E+07	5.89E+07	8.76E+07
Homocysteic acid	0.00E+00	1.51E+05	9.48E+05	1.05E+07	1.30E+06
4-Pyridoxate	1.22E+07	3.85E+07	2.85E+08	1.55E+08	4.63E+07
N-Acetylglutamine	1.46E+09	2.23E+07	1.99E+07	2.28E+07	5.73E+07
Citrate/isocitrate	6.22E+07	4.78E+08	1.15E+09	1.80E+09	1.34E+09

Table 28. Continued.

Metabolite	12 Day-3	12 Days-1	12 Days-2	12 Days-4	12 Days-5
D-Gluconate	2.29E+08	1.37E+08	6.65E+08	4.73E+08	6.26E+08
N-N Dimethylarginine	1.47E+06	1.29E+06	5.83E+05	2.04E+06	1.02E+06
Tryptophan	1.94E+09	2.66E+08	1.56E+08	5.84E+08	7.18E+07
Xanthurenic acid	3.69E+05	1.24E+07	8.46E+06	4.49E+06	4.82E+05
D-Glucarate	2.88E+09	2.47E+07	1.10E+09	1.83E+08	4.04E+09
Pantothenate	1.15E+09	1.01E+09	1.75E+09	2.28E+09	4.48E+09
Cystathionine	6.44E+06	3.69E+05	6.30E+06	2.50E+06	8.49E+06
Cystine	0.00E+00	1.07E+05	1.21E+06	1.28E+05	8.94E+04
Uridine	3.43E+07	2.44E+08	1.16E+06	5.48E+07	1.21E+08
Biotin	2.45E+06	1.84E+06	6.10E+05	2.52E+06	1.01E+06
Deoxyinosine	1.10E+05	1.05E+06	2.96E+04	5.10E+06	7.87E+05
Glucose 6-phosphate	2.43E+07	2.20E+06	1.01E+07	3.68E+07	2.27E+07
S-Ribosyl-L-homocysteine	1.62E+06	1.50E+06	4.31E+05	2.03E+06	8.63E+04
6-Phospho-D-gluconate	1.73E+05	1.73E+06	3.33E+06	3.26E+07	1.83E+07
Guanosine	2.05E+06	2.17E+06	6.48E+06	1.02E+06	1.76E+07
Xanthosine	4.24E+06	7.80E+06	3.58E+05	2.81E+06	2.83E+06
Glycinamide ribotide (GAR)	0.00E+00	0.00E+00	2.71E+04	0.00E+00	1.49E+04
Ophthalmate	8.67E+05	1.04E+07	3.60E+06	5.78E+06	7.99E+06
Glutathione	2.87E+06	1.68E+06	3.69E+07	8.44E+06	1.64E+07
UMP	2.25E+06	1.03E+06	1.64E+08	9.76E+07	3.33E+07
AICAR	0.00E+00	0.00E+00	6.72E+03	4.21E+04	3.63E+04
Trehalose/Sucrose/Cellobiose	3.90E+05	8.91E+05	2.78E+07	6.20E+06	9.60E+06
AMP/dGMP	1.21E+07	8.60E+06	1.11E+09	2.94E+08	1.51E+08
IMP	1.29E+05	3.05E+04	1.06E+07	5.81E+06	1.26E+06

Table 28. Continued.

Metabolite	12 Day-3	12 Days-1	12 Days-2	12 Days-4	12 Days-5
GMP	8.53E+05	3.58E+05	3.36E+08	8.00E+07	2.71E+07
Xanthosine 5--phosphate	1.00E+04	1.21E+05	1.64E+06	1.36E+07	1.09E+07
Riboflavin	1.76E+06	1.30E+07	5.71E+06	1.15E+07	4.95E+06
S-Adenosyl-L-homocysteine	0.00E+00	0.00E+00	7.71E+04	1.69E+05	4.39E+04
ADP	1.38E+06	7.80E+06	7.71E+07	7.37E+07	4.89E+07
Folate	3.07E+04	2.47E+06	9.46E+05	2.45E+06	1.65E+05
CDP-ethanolamine	2.13E+04	0.00E+00	4.68E+05	3.95E+05	1.06E+05
FMN	5.28E+06	2.26E+07	2.80E+06	1.22E+07	6.00E+06
UDP-glucose	7.32E+05	2.77E+06	8.90E+07	5.33E+07	4.75E+07
NAD+	2.55E+06	5.72E+06	2.93E+06	2.25E+06	7.09E+06
NADH	1.90E+05	3.13E+05	0.00E+00	2.43E+05	1.25E+04
Dephospho-CoA	7.72E+03	2.78E+05	1.13E+06	6.47E+05	2.08E+05
NADP+	2.54E+06	1.18E+07	3.68E+06	1.78E+06	7.60E+06
FAD	3.53E+06	2.41E+07	2.47E+06	6.85E+06	3.58E+06
N-Acetylglutamate	1.13E+09	4.31E+08	2.27E+08	4.47E+08	6.19E+07
Kynurenic acid	5.24E+05	6.51E+07	1.70E+08	7.11E+08	1.40E+06

Table 29. Intensities of *G. mellonella* replicates in 16 days post infection group.

Metabolite	16 Days-1	16 Days-2	16 Days-3	16 Days-4	16 Days-5
Glyoxylate	0.00E+00	0.00E+00	0.00E+00	5.55E+08	7.39E+06
Glycine	1.49E+04	1.02E+04	7.47E+04	2.27E+07	2.48E+08
Pyruvate	2.79E+07	1.42E+08	3.43E+08	4.33E+07	4.77E+07
Alanine/Sarcosine	4.36E+07	2.69E+08	1.88E+09	3.54E+07	4.21E+08
Lactate	3.44E+08	7.95E+08	4.92E+08	2.10E+08	8.65E+08
Dimethylglycine	8.86E+06	3.23E+08	3.09E+08	7.70E+06	4.56E+08
Serine	1.93E+07	7.62E+07	1.14E+08	1.59E+07	4.89E+07
Histamine	2.76E+04	2.17E+06	4.78E+06	0.00E+00	1.82E+06
Uracil	7.69E+06	6.72E+08	2.85E+09	7.02E+07	6.62E+08
Creatinine	3.24E+05	5.76E+05	9.70E+04	5.27E+04	7.04E+05
Proline	2.60E+08	3.36E+09	5.64E+09	1.45E+08	7.57E+09
Fumarate	6.86E+06	3.64E+07	3.90E+07	3.53E+06	8.20E+06
2-Oxoisovalerate	1.10E+07	1.76E+07	1.47E+08	1.11E+07	1.11E+07
Indole	2.09E+05	4.40E+05	1.24E+06	2.21E+04	3.66E+05
Valine	2.18E+07	1.78E+08	2.06E+09	8.45E+07	1.43E+08
3-Hydroxyisovaleric acid	1.79E+07	1.21E+08	1.01E+09	1.40E+07	9.53E+07
Homoserine/Threonine	1.81E+07	1.26E+08	7.79E+08	4.63E+07	1.07E+08
3-Methylthiopropionate	1.69E+07	1.04E+06	8.89E+07	4.01E+07	1.44E+06
Cysteine	3.68E+05	1.38E+06	1.43E+06	2.51E+05	5.36E+05
Nicotinate	1.28E+07	2.53E+08	8.67E+07	3.81E+07	3.15E+08
Taurine	1.35E+06	2.61E+06	1.09E+06	1.47E+05	1.99E+06
Thymine	1.20E+07	2.52E+08	1.73E+09	3.21E+07	4.17E+08
Hydroxyproline	2.86E+06	1.23E+07	2.25E+07	2.57E+06	2.84E+07

Table 29. Continued.

Metabolite	16 Days-1	16 Days-2	16 Days-3	16 Days-4	16 Days-5
N-Acetyl-beta-alanine	7.54E+06	2.73E+08	2.15E+08	1.69E+07	3.38E+08
Leucine/Isoleucine	1.02E+08	6.13E+08	7.08E+09	3.23E+08	3.94E+08
Glutaric acid	1.88E+07	7.91E+08	8.70E+08	4.36E+07	4.82E+08
Asparagine	4.54E+08	3.73E+08	1.35E+08	8.03E+06	2.48E+08
Hydroxyisocaproic acid	3.96E+07	3.00E+08	3.40E+09	8.90E+07	3.13E+08
Ornithine	6.47E+06	2.48E+07	1.09E+08	2.33E+07	4.17E+07
Salicylate	3.63E+06	6.82E+07	3.56E+07	5.25E+07	3.23E+07
Hydroxybenzoate	6.93E+06	5.75E+08	3.34E+08	1.50E+07	3.14E+08
Histidinol	1.85E+05	1.10E+06	1.54E+06	9.53E+04	2.25E+06
2-Oxoglutaric acid	1.34E+07	5.71E+07	1.11E+08	2.91E+07	1.97E+07
Glutamine	2.13E+08	3.45E+08	5.00E+08	2.31E+07	4.24E+08
2-hydroxyglutarate	5.53E+07	1.65E+09	7.22E+08	1.68E+08	1.09E+09
2-Hydroxy-2-methylsuccinate	5.51E+07	1.66E+09	7.27E+08	1.68E+08	1.09E+09
L-Methionine	1.09E+07	1.89E+07	2.29E+08	1.49E+07	1.99E+07
Guanine	3.18E+06	1.08E+07	1.21E+06	3.03E+05	2.89E+06
3-Methylphenylacetic acid	1.41E+06	1.98E+06	2.18E+06	3.66E+06	1.77E+06
Hydroxyphenylacetate	4.42E+07	6.22E+08	6.49E+08	1.91E+07	6.17E+08
Xylitol	1.91E+08	6.75E+07	1.86E+08	6.65E+07	1.08E+08
Dopamine	4.51E+05	6.14E+05	6.50E+06	7.27E+05	1.48E+06
2_3-Dihydroxybenzoate	2.41E+07	1.45E+06	6.80E+06	1.36E+08	2.11E+07
Histidine	5.91E+07	7.43E+07	3.52E+07	3.74E+06	5.15E+07
Orotate	9.58E+06	8.34E+07	2.44E+09	6.52E+07	5.08E+08
Dihydroorotate	5.40E+06	3.04E+06	1.27E+07	3.39E+07	2.27E+06
Allantoin	3.96E+06	6.86E+08	1.67E+08	4.05E+06	5.73E+08

Table 29. Continued.

Metabolite	16 Days-1	16 Days-2	16 Days-3	16 Days-4	16 Days-5
Indole-3-carboxylate	1.76E+07	6.05E+07	8.96E+07	1.46E+07	4.99E+07
Phenylpyruvate	1.32E+07	1.57E+08	1.98E+08	4.61E+07	1.04E+08
Phenylalanine	6.51E+07	2.97E+08	3.84E+09	2.52E+08	3.16E+08
Phenyllactic acid	1.07E+07	2.50E+07	4.66E+08	8.55E+07	3.07E+07
Quinolate	4.72E+08	1.65E+09	2.01E+08	5.50E+07	9.53E+08
Phosphoenolpyruvate	7.43E+06	9.33E+07	8.54E+07	5.21E+07	5.71E+07
Uric acid	7.58E+06	3.61E+08	5.59E+08	2.95E+07	3.81E+08
3_4-Dihydroxyphenylacetate (DOPAC)	1.42E+07	2.19E+08	1.13E+08	3.86E+06	1.35E+08
Sulfolactate	4.42E+07	1.63E+08	4.82E+07	1.01E+08	1.04E+08
Glycerone phosphate	5.52E+06	1.17E+07	1.11E+07	6.19E+04	1.96E+05
Arginine	2.72E+07	3.02E+07	5.70E+07	2.10E+06	2.69E+07
Citrulline	8.46E+05	1.27E+07	3.61E+08	8.96E+07	4.34E+07
Ascorbate	2.34E+05	3.31E+05	5.32E+05	5.05E+05	7.22E+05
N-Carbamoyl-L-aspartate	7.00E+06	9.42E+07	1.21E+09	9.77E+07	2.88E+07
Allantoate	2.01E+06	1.57E+09	4.46E+08	3.99E+06	9.79E+08
2-Isopropylmalate	4.36E+08	1.16E+10	4.35E+09	2.88E+08	5.85E+09
Glucosamine	1.07E+07	1.63E+07	1.12E+07	4.59E+07	1.67E+07
myo-Inositol	5.89E+07	1.26E+08	4.83E+07	1.34E+08	5.28E+07
Tyrosine	1.21E+08	8.75E+07	1.12E+09	1.93E+08	8.70E+07
Homovanillic acid (HVA)	1.22E+06	2.63E+07	8.73E+07	2.40E+07	3.24E+07
Homocysteic acid	4.17E+06	1.42E+06	2.49E+07	4.42E+04	4.99E+06
4-Pyridoxate	6.93E+07	5.83E+08	1.38E+08	3.32E+08	4.07E+08
N-Acetylglutamine	6.61E+06	5.33E+07	1.03E+08	1.64E+07	4.23E+07
Citrate/isocitrate	1.78E+09	2.11E+09	3.10E+09	9.71E+08	1.71E+09

Table 29. Continued.

Metabolite	16 Days-1	16 Days-2	16 Days-3	16 Days-4	16 Days-5
D-Gluconate	2.18E+08	1.14E+09	7.00E+08	2.95E+08	8.78E+08
N-N Dimethylarginine	3.18E+05	1.29E+06	3.30E+06	2.02E+05	7.20E+05
Tryptophan	9.45E+07	1.70E+08	4.24E+08	2.71E+07	1.44E+08
Xanthurenic acid	3.18E+07	1.50E+07	2.63E+06	3.27E+06	1.35E+07
D-Glucarate	1.44E+08	4.02E+09	4.13E+09	1.10E+08	2.25E+09
Pantothenate	1.99E+08	3.28E+09	3.05E+09	5.93E+07	1.27E+09
Cystathionine	1.55E+06	3.22E+06	7.09E+06	9.10E+05	5.11E+06
Cystine	2.23E+05	7.24E+05	2.20E+06	2.42E+05	4.01E+05
Uridine	2.83E+05	1.13E+07	1.39E+07	4.82E+06	1.17E+07
Biotin	7.35E+05	1.48E+06	2.22E+06	1.56E+06	1.57E+06
Deoxyinosine	3.77E+03	2.67E+05	3.29E+06	1.80E+03	6.54E+04
Glucose 6-phosphate	8.20E+06	2.17E+07	8.73E+06	1.20E+07	1.55E+07
S-Ribosyl-L-homocysteine	2.36E+05	1.15E+06	5.10E+06	5.65E+05	3.33E+05
6-Phospho-D-gluconate	3.66E+06	1.42E+07	1.48E+07	1.04E+07	2.00E+07
Guanosine	2.46E+06	1.43E+07	4.59E+06	2.07E+06	2.22E+07
Xanthosine	1.41E+05	5.53E+05	1.03E+07	1.09E+06	7.23E+05
Glycinamide ribotide (GAR)	7.33E+03	5.27E+03	1.19E+05	1.24E+04	2.28E+04
Ophthalmate	1.34E+06	1.59E+07	5.84E+06	1.89E+06	1.56E+07
Glutathione	5.36E+07	1.68E+07	4.65E+06	5.42E+05	3.28E+07
UMP	8.02E+07	1.50E+08	3.15E+07	2.92E+07	1.80E+08
AICAR	0.00E+00	3.92E+04	1.41E+04	8.22E+03	2.33E+05
Trehalose/Sucrose/Cellobiose	3.18E+07	2.33E+07	5.59E+06	4.73E+06	2.50E+07
AMP/dGMP	5.28E+08	9.04E+08	1.53E+08	8.60E+07	1.05E+09
IMP	5.25E+05	1.56E+07	1.42E+06	1.91E+05	4.51E+06

Table 29. Continued.

Metabolite	16 Days-1	16 Days-2	16 Days-3	16 Days-4	16 Days-5
GMP	8.12E+07	3.26E+08	3.70E+07	8.79E+06	4.46E+08
Xanthosine 5--phosphate	0.00E+00	1.18E+07	3.45E+06	2.41E+05	1.03E+07
Riboflavin	2.62E+06	9.31E+06	2.80E+06	2.82E+07	8.37E+06
S-Adenosyl-L-homocysteine	6.67E+03	6.12E+04	1.07E+05	2.51E+04	2.50E+05
ADP	2.64E+08	1.40E+08	2.97E+07	1.97E+06	2.54E+08
Folate	8.18E+05	1.79E+06	2.38E+05	6.81E+06	1.81E+06
CDP-ethanolamine	5.15E+05	3.67E+05	1.75E+05	4.06E+04	5.58E+05
FMN	1.95E+06	3.99E+06	1.42E+06	2.57E+07	2.82E+06
UDP-glucose	3.83E+07	6.72E+07	1.42E+07	3.36E+07	9.74E+07
NAD+	7.00E+06	4.88E+06	2.16E+06	2.05E+06	6.63E+06
NADH	1.04E+05	0.00E+00	7.34E+03	2.72E+04	1.27E+04
Dephospho-CoA	5.49E+05	5.18E+05	5.80E+04	5.27E+03	5.62E+05
NADP+	1.63E+06	6.46E+06	1.15E+06	8.76E+05	5.53E+06
FAD	1.46E+06	2.73E+06	1.47E+06	1.09E+07	2.47E+06
N-Acetylglutamate	1.34E+07	1.59E+08	3.18E+08	5.04E+08	1.66E+08
Kynurenic acid	9.52E+06	7.09E+05	1.67E+08	2.18E+06	8.58E+05

Table 30. Intensities of nematode replicates in infection model.

Metabolite	Nematode-1	Nematode-2	Nematode-3	Nematode-4
Glyoxylate	0.00E+00	0.00E+00	0.00E+00	2.11E+03
Glycine	8.45E+03	2.63E+03	1.10E+03	1.14E+04
Pyruvate	2.55E+07	2.56E+07	2.19E+07	1.89E+07
Alanine/Sarcosine	7.59E+07	6.14E+07	4.80E+07	3.78E+07
Lactate	4.29E+08	4.07E+08	3.92E+08	2.57E+08
Dimethylglycine	8.66E+06	8.29E+06	8.21E+06	8.08E+06
Serine	1.08E+07	9.06E+06	5.14E+06	3.26E+06
Histamine	1.07E+04	6.28E+03	0.00E+00	1.00E+03
Uracil	4.45E+06	2.73E+06	2.12E+06	1.82E+06
Creatinine	3.69E+04	6.33E+04	1.49E+05	6.89E+04
Proline	7.86E+07	5.58E+07	6.75E+07	5.13E+07
Fumarate	4.11E+06	3.07E+06	1.28E+06	8.10E+05
2-Oxoisovalerate	8.37E+06	8.25E+06	8.41E+06	7.05E+06
Indole	3.56E+03	0.00E+00	0.00E+00	0.00E+00
Valine	7.27E+06	4.09E+06	3.63E+06	3.83E+06
3-Hydroxyisovaleric acid	1.75E+07	1.56E+07	1.56E+07	1.34E+07
Homoserine/Threonine	1.76E+07	7.70E+06	6.16E+06	4.36E+06
3-Methylthiopropionate	2.62E+05	1.80E+05	1.33E+05	9.13E+04
Cysteine	6.34E+04	7.01E+04	1.37E+03	3.75E+03
Nicotinate	1.88E+06	1.44E+06	1.23E+06	1.06E+06
Taurine	1.05E+05	8.81E+04	3.29E+04	1.11E+04
Thymine	9.08E+06	8.12E+06	8.36E+06	7.85E+06
Hydroxyproline	2.65E+06	2.13E+06	1.04E+06	5.32E+05

Table 30. Continued.

Metabolite	Nematode-1	Nematode-2	Nematode-3	Nematode-4
N-Acetyl-beta-alanine	6.90E+06	5.88E+06	5.56E+06	4.97E+06
Leucine/Isoleucine	1.54E+07	8.44E+06	5.67E+06	8.35E+06
Glutaric acid	5.37E+06	5.70E+06	5.07E+06	3.24E+06
Asparagine	2.07E+08	1.71E+08	5.80E+07	2.08E+07
Hydroxyisocaproic acid	4.23E+07	2.79E+07	2.71E+07	2.10E+07
Ornithine	1.46E+07	1.31E+07	5.06E+06	3.36E+06
Salicylate	2.05E+06	2.14E+06	2.08E+06	1.39E+06
Hydroxybenzoate	8.72E+05	1.19E+06	7.96E+05	6.48E+05
Histidinol	1.53E+04	3.64E+04	2.02E+04	2.30E+04
2-Oxoglutaric acid	1.04E+06	8.01E+05	5.68E+05	5.00E+05
Glutamine	5.13E+07	4.19E+07	1.79E+07	1.34E+07
2-hydroxyglutarate	4.91E+06	2.55E+06	1.70E+06	1.29E+06
2-Hydroxy-2-methylsuccinate	4.86E+06	2.53E+06	1.69E+06	1.30E+06
L-Methionine	2.49E+06	1.49E+06	8.75E+05	5.53E+05
Guanine	1.54E+06	1.10E+06	2.11E+05	1.14E+04
3-Methylphenylacetic acid	3.88E+06	2.41E+06	2.09E+06	1.69E+06
Hydroxyphenylacetate	7.79E+05	6.93E+05	7.17E+05	6.28E+05
Xylitol	4.24E+06	3.92E+06	4.76E+06	4.27E+06
Dopamine	8.77E+05	4.93E+05	3.52E+05	3.66E+05
2_3-Dihydroxybenzoate	1.06E+05	8.83E+04	7.05E+04	6.37E+04
Histidine	5.03E+07	3.60E+07	8.34E+06	4.36E+06
Orotate	7.56E+04	1.03E+04	2.40E+04	0.00E+00
Dihydroorotate	3.79E+04	4.01E+04	2.30E+04	9.02E+04
Allantoin	8.15E+05	5.67E+05	3.62E+05	2.30E+05

Table 30. Continued.

Metabolite	Nematode-1	Nematode-2	Nematode-3	Nematode-4
Indole-3-carboxylate	5.49E+05	3.30E+05	3.30E+05	3.39E+05
Phenylpyruvate	8.86E+05	5.77E+05	5.16E+05	4.90E+05
Phenylalanine	1.01E+08	5.17E+07	4.16E+07	3.42E+07
Phenyllactic acid	1.28E+06	8.29E+05	1.20E+06	9.12E+05
Quinolinolate	6.34E+05	4.31E+05	3.91E+05	2.95E+05
Phosphoenolpyruvate	2.54E+05	1.74E+05	3.02E+04	9.17E+03
Uric acid	3.93E+07	3.14E+07	6.08E+06	1.01E+06
3_4-Dihydroxyphenylacetate (DOPAC)	1.38E+05	1.36E+05	8.90E+04	9.02E+04
Sulfolactate	4.60E+05	3.64E+05	1.64E+05	7.11E+04
Glycerone phosphate	8.32E+04	1.17E+05	3.03E+04	1.48E+04
Arginine	3.02E+07	2.37E+07	6.67E+06	3.65E+06
Citrulline	3.00E+05	2.06E+05	5.86E+05	2.90E+05
Ascorbate	3.75E+06	2.64E+06	6.34E+03	3.68E+04
N-Carbamoyl-L-aspartate	1.18E+05	7.93E+04	8.31E+04	6.62E+04
Allantoate	2.82E+05	5.74E+03	1.90E+05	7.14E+03
2-Isopropylmalate	2.60E+06	1.96E+06	1.85E+06	1.55E+06
Glucosamine	4.82E+05	4.52E+05	2.66E+05	2.03E+05
myo-Inositol	4.51E+06	3.98E+06	3.54E+06	2.18E+06
Tyrosine	1.41E+07	9.96E+06	3.15E+06	1.87E+06
Homovanillic acid (HVA)	3.70E+05	3.01E+05	3.06E+05	2.46E+05
Homocysteic acid	1.92E+03	5.80E+03	0.00E+00	0.00E+00
4-Pyridoxate	4.06E+06	3.80E+06	3.49E+06	3.17E+06
N-Acetylglutamine	1.02E+06	8.92E+05	8.54E+05	5.14E+05
Citrate/isocitrate	4.75E+08	3.11E+08	2.22E+08	1.34E+08

Table 30. Continued.

Metabolite	Nematode-1	Nematode-2	Nematode-3	Nematode-4
D-Gluconate	1.73E+07	1.25E+07	2.66E+06	1.00E+06
N-N Dimethylarginine	3.09E+05	3.02E+05	3.16E+05	2.80E+05
Tryptophan	1.71E+07	1.07E+07	5.95E+06	3.99E+06
Xanthurenic acid	1.24E+05	4.28E+04	1.45E+05	1.09E+05
D-Glucarate	4.27E+06	1.98E+06	1.93E+06	1.40E+06
Pantothenate	6.57E+07	5.67E+07	3.30E+07	3.22E+07
Cystathionine	9.74E+04	6.30E+04	1.12E+04	4.10E+03
Cystine	7.30E+03	9.91E+03	3.51E+04	6.41E+04
Uridine	3.91E+04	1.50E+04	3.23E+04	1.69E+04
Biotin	0.00E+00	0.00E+00	0.00E+00	1.84E+03
Deoxyinosine	2.07E+03	1.69E+03	5.00E+03	8.86E+03
Glucose 6-phosphate	4.12E+06	2.96E+06	5.01E+05	9.16E+04
S-Ribosyl-L-homocysteine	2.39E+04	1.40E+04	1.20E+03	0.00E+00
6-Phospho-D-gluconate	2.04E+05	1.03E+05	7.23E+04	0.00E+00
Guanosine	1.37E+05	9.38E+04	4.93E+04	9.59E+03
Xanthosine	1.43E+04	1.26E+04	0.00E+00	0.00E+00
Glycinamide ribotide (GAR)	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Ophthalmate	1.98E+04	1.35E+04	5.13E+03	0.00E+00
Glutathione	1.63E+07	1.17E+07	1.23E+05	6.59E+05
UMP	1.07E+06	7.84E+05	5.35E+05	1.41E+05
AICAR	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Trehalose/Sucrose/Cellobiose	6.70E+06	5.70E+06	2.33E+06	9.77E+05
AMP/dGMP	2.17E+07	1.60E+07	1.16E+07	3.29E+06
IMP	3.02E+05	1.37E+05	3.70E+04	9.25E+04

Table 30. Continued.

Metabolite	Nematode-1	Nematode-2	Nematode-3	Nematode-4
GMP	8.39E+05	5.33E+05	5.15E+05	4.29E+04
Xanthosine 5--phosphate	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Riboflavin	1.90E+05	7.92E+04	8.57E+03	0.00E+00
S-Adenosyl-L-homocysteine	3.39E+03	0.00E+00	0.00E+00	0.00E+00
ADP	3.84E+07	2.09E+07	1.61E+07	3.51E+06
Folate	2.24E+05	1.46E+05	3.93E+03	0.00E+00
CDP-ethanolamine	7.57E+04	5.68E+04	2.10E+03	0.00E+00
FMN	6.48E+05	2.33E+05	1.54E+04	0.00E+00
UDP-glucose	3.83E+06	2.74E+06	2.33E+06	1.47E+05
NAD+	1.29E+06	8.88E+05	2.72E+05	6.46E+04
NADH	3.44E+05	2.05E+05	0.00E+00	0.00E+00
Dephospho-CoA	7.96E+04	2.37E+04	1.10E+04	5.39E+03
NADP+	3.97E+04	1.99E+04	8.53E+04	0.00E+00
FAD	1.22E+05	6.00E+04	4.15E+04	0.00E+00
N-Acetylglutamate	4.01E+05	2.68E+05	2.50E+05	1.79E+05
Kynurenic acid	1.73E+05	1.51E+05	1.36E+05	8.42E+04

Table 31. Intensities of *X. nematophila* whole cell replicates.

Metabolite	1495-1	1495-2	1495-3	1496-1	1496-2	1496-3
Alanine/Sarcosine	1.97E+07	2.84E+07	3.79E+07	4.36E+07	2.93E+07	4.03E+07
Uracil	8.04E+07	1.08E+08	1.38E+08	1.45E+08	1.21E+08	1.60E+08
Valine	1.67E+08	2.78E+08	3.13E+08	3.24E+08	2.43E+08	2.69E+08
Succinate/Methylmalonate	3.97E+09	4.07E+09	2.65E+09	2.34E+09	2.18E+09	2.09E+09
Homoserine/Threonine	6.23E+06	8.68E+06	8.47E+06	8.81E+06	6.70E+06	8.82E+06
Thymine	7.33E+06	7.89E+06	1.02E+07	9.09E+06	7.28E+06	1.40E+07
Leucine/Isoleucine	5.56E+07	9.22E+07	8.82E+07	1.02E+08	8.80E+07	9.40E+07
Ornithine	5.42E+05	1.36E+06	1.28E+06	1.44E+06	1.11E+06	2.84E+06
Acetylphosphate	1.57E+08	1.47E+08	1.44E+08	6.83E+07	1.48E+08	9.82E+07
Histidinol	7.73E+05	1.30E+06	2.55E+06	3.93E+06	2.31E+06	3.11E+06
alpha-Ketoglutarate	1.04E+07	1.88E+07	1.29E+07	1.52E+07	8.75E+06	1.28E+07
Lysine	9.01E+05	1.43E+06	1.71E+06	2.38E+06	1.92E+06	1.78E+06
O-Acetyl-L-serine	1.77E+08	1.34E+08	1.07E+08	1.79E+08	9.48E+07	2.83E+08
2-Hydroxy-2-methylsuccinate	4.00E+08	3.71E+08	2.17E+08	1.83E+08	1.43E+08	2.19E+08
Methionine	3.40E+06	5.54E+06	5.74E+06	7.08E+06	6.32E+06	6.91E+06
Guanine	2.01E+07	2.17E+07	2.12E+07	2.89E+07	2.34E+07	2.55E+07
Histidine	2.34E+06	2.75E+06	2.79E+06	3.71E+06	3.18E+06	2.53E+06
Orotate	1.02E+05	1.44E+05	2.58E+05	7.59E+04	4.69E+05	1.53E+05
Allantoin	1.52E+05	2.46E+05	2.83E+05	2.66E+05	2.82E+05	3.92E+05
2-Aminoadipate	6.60E+06	1.21E+07	1.00E+07	1.01E+07	7.34E+06	1.16E+07
Phenylpyruvate	1.10E+07	2.51E+07	1.81E+07	1.64E+07	1.98E+07	1.30E+07
Phenylalanine	1.03E+08	1.37E+08	1.20E+08	1.46E+08	1.40E+08	1.47E+08
Phenyllactic acid	2.13E+08	2.40E+08	2.34E+08	2.19E+08	2.18E+08	1.88E+08

Table 31. Continued.

Metabolite	1495-1	1495-2	1495-3	1496-1	1496-2	1496-3
Aconitate	7.79E+07	5.26E+07	1.54E+08	1.22E+08	1.24E+08	1.98E+08
N-Acetylornithine	3.05E+05	6.51E+05	5.47E+05	3.96E+05	4.01E+05	9.74E+05
Citrulline	3.17E+06	5.12E+06	5.42E+06	6.36E+06	5.18E+06	1.05E+07
N-Carbamoyl-L-aspartate	7.84E+05	1.21E+06	1.26E+06	1.60E+06	1.72E+06	9.04E+05
2-Isopropylmalate	2.70E+09	4.03E+09	3.95E+09	4.88E+09	5.35E+09	3.08E+09
Tyrosine	1.81E+07	2.43E+07	2.32E+07	2.92E+07	2.44E+07	2.75E+07
3-Phosphoglycerate	1.04E+09	9.20E+08	9.19E+08	1.18E+09	9.13E+08	2.85E+09
N-Acetylglutamate	6.75E+07	8.11E+07	5.68E+07	5.66E+07	5.42E+07	9.34E+07
5-Hydroxyindoleacetic acid (5-HIAA)	1.43E+04	5.14E+03	1.22E+04	4.81E+03	4.81E+03	1.72E+04
2-Dehydro-D-gluconate	2.10E+07	4.14E+07	2.84E+07	2.57E+07	1.94E+07	3.34E+07
D-Gluconate	4.26E+08	4.77E+08	4.62E+08	5.58E+08	5.81E+08	3.97E+08
Tryptophan	2.54E+07	3.52E+07	4.41E+07	5.44E+07	4.82E+07	5.64E+07
Lipoate	8.48E+08	8.60E+08	6.01E+08	5.88E+08	5.56E+08	6.56E+08
Deoxyribose phosphate	7.98E+07	8.87E+07	9.50E+07	1.07E+08	9.42E+07	1.08E+08
Ribose phosphate	9.79E+08	1.16E+09	1.07E+09	1.09E+09	1.21E+09	1.30E+09
Xylitol 5-phosphate	1.65E+08	2.31E+08	2.05E+08	1.85E+08	2.21E+08	1.54E+08
Cystine	8.12E+06	8.36E+06	1.52E+07	1.34E+07	9.51E+06	2.58E+07
Uridine	1.10E+07	1.39E+07	1.55E+07	1.92E+07	1.40E+07	1.76E+07
Glucosamine phosphate	3.47E+06	5.46E+06	5.87E+06	9.18E+06	9.03E+06	8.42E+06
S-Ribosyl-L-homocysteine	8.86E+05	6.01E+05	1.20E+06	9.27E+05	8.56E+05	1.52E+06
Adenosine	9.61E+06	1.08E+07	1.39E+07	1.36E+07	1.28E+07	1.40E+07
Homocystine	1.60E+04	3.44E+04	2.07E+05	2.94E+05	2.25E+05	1.70E+05
Inosine	7.55E+07	8.94E+07	8.92E+07	9.43E+07	9.02E+07	7.39E+07
6-Phospho-D-gluconate	6.06E+08	5.97E+08	4.08E+08	6.76E+08	5.67E+08	3.61E+08

Table 31. Continued.

Metabolite	1495-1	1495-2	1495-3	1496-1	1496-2	1496-3
Guanosine	1.71E+07	1.83E+07	3.96E+07	5.64E+07	4.54E+07	4.81E+07
Xanthosine	1.12E+07	1.61E+07	1.83E+07	2.67E+07	2.58E+07	2.89E+07
Glycinamide ribotide (GAR)	2.01E+04	1.50E+05	2.66E+04	4.94E+04	6.97E+04	3.68E+04
Aminoimidazole ribotide (AIR)	1.25E+04	5.86E+04	1.23E+05	6.27E+04	1.73E+05	8.16E+05
N-Acetylglucosamine 1/6-phosphate	7.99E+06	9.86E+06	1.23E+07	1.50E+07	1.59E+07	1.79E+07
Octulose 8/1P	6.02E+06	7.76E+06	7.81E+06	6.98E+06	8.80E+06	7.50E+06
CMP	4.24E+06	4.09E+06	5.17E+06	6.28E+06	5.46E+06	7.61E+06
UMP	6.29E+06	3.72E+06	5.79E+06	9.09E+06	7.04E+06	9.95E+06
AICAR	3.73E+07	3.68E+07	4.33E+07	5.24E+07	4.83E+07	5.66E+07
Fructose 1_6-bisphosphate	1.93E+10	2.52E+10	2.29E+10	2.48E+10	2.41E+10	2.20E+10
Trehalose/Sucrose/Cellobiose	4.67E+06	4.92E+06	4.25E+06	4.39E+06	4.26E+06	5.61E+06
AMP/dGMP	1.91E+07	1.48E+07	1.54E+07	1.75E+07	1.32E+07	2.37E+07
IMP	1.01E+06	9.44E+05	8.07E+05	9.55E+05	7.28E+05	2.18E+06
S-Adenosyl-L-methioninamine	9.64E+05	1.41E+06	1.83E+06	2.21E+06	1.92E+06	4.60E+06
Sedoheptoluse bisphosphate	8.09E+08	1.06E+09	8.77E+08	1.03E+09	1.02E+09	9.20E+08
dTDP	3.14E+06	2.96E+06	2.12E+06	1.67E+06	1.43E+06	1.86E+06
UDP	1.51E+07	2.61E+08	3.51E+08	3.38E+08	3.29E+08	3.20E+08
FMN	4.96E+07	5.45E+07	4.30E+07	4.52E+07	4.20E+07	3.71E+07
UDP-glucose	4.25E+08	2.76E+08	3.15E+08	3.68E+08	2.37E+08	4.71E+08
UDP-glucuronate	1.12E+06	3.63E+07	3.68E+08	7.12E+08	5.76E+08	5.03E+08
UDP-N-acetylglucosamine	6.28E+07	4.37E+07	7.12E+07	8.12E+07	6.39E+07	1.07E+08
NAD+	4.91E+07	3.63E+07	3.71E+07	4.22E+07	3.12E+07	7.22E+07
NADH	1.15E+07	1.81E+07	9.03E+06	9.42E+06	7.38E+06	6.59E+06
Dephospho-CoA	5.69E+06	4.83E+06	5.16E+06	7.05E+06	5.27E+06	5.14E+06

Table 31. Continued.

Metabolite	1495-1	1495-2	1495-3	1496-1	1496-2	1496-3
NADP+	2.70E+08	1.70E+08	1.80E+08	1.56E+08	1.58E+08	2.18E+08
FAD	4.32E+07	4.14E+07	3.15E+07	2.98E+07	2.91E+07	2.80E+07
Pyruvate	2.29E+09	2.44E+09	2.96E+08	2.09E+09	3.30E+08	3.91E+08
Fumarate	4.82E+08	5.89E+08	5.98E+08	6.08E+08	5.40E+08	5.24E+08
Cysteine	7.67E+04	9.11E+04	2.03E+05	1.15E+05	9.48E+04	2.79E+05
Nicotinate	2.84E+09	3.24E+09	2.87E+09	2.87E+09	2.90E+09	3.11E+09
Malate	1.06E+10	1.16E+10	1.27E+10	1.25E+10	1.17E+10	1.14E+10
Hypoxanthine	7.14E+07	8.19E+07	8.21E+07	8.96E+07	7.43E+07	6.85E+07
Indole-3-carboxylate	2.30E+04	9.16E+03	5.59E+03	1.22E+04	3.40E+03	1.03E+04
Phosphoenolpyruvate	2.47E+08	3.74E+08	2.82E+08	3.60E+08	3.11E+08	1.29E+09
Glycerone phosphate	1.29E+09	1.46E+09	1.47E+09	1.54E+09	1.62E+09	1.43E+09
sn-Glycerol 3-phosphate	1.43E+08	1.33E+08	1.42E+08	1.46E+08	1.42E+08	2.34E+08
Citrate/isocitrate	3.86E+09	3.92E+09	9.28E+09	9.35E+09	9.70E+09	1.16E+10
Sedoheptulose 1/7-phosphate	4.55E+07	4.88E+07	4.59E+07	5.86E+07	6.19E+07	6.29E+07

Table 32. Intensities of *X. nematophila* supernatant replicates.

Metabolite	1495-1	1495-2	1495-3	1496-1	1496-2	1496-3
Alanine/Sarcosine	1.30E+06	1.66E+06	6.54E+05	4.31E+05	1.54E+05	1.11E+05
Uracil	4.26E+06	6.34E+06	9.93E+06	2.66E+07	2.50E+07	4.83E+07
Valine	3.45E+07	4.33E+07	3.58E+07	3.58E+07	3.95E+07	2.16E+07
Succinate/Methylmalonate	9.93E+05	1.21E+06	1.44E+06	1.10E+06	1.41E+06	8.50E+05
Homoserine/Threonine	9.61E+06	1.48E+07	1.23E+07	1.34E+07	1.18E+07	1.52E+07
Thymine	1.85E+06	2.16E+06	2.58E+06	6.19E+06	4.91E+06	9.83E+06
Leucine/Isoleucine	1.35E+05	1.45E+05	1.92E+05	1.69E+05	2.32E+05	2.28E+05
Ornithine	7.02E+05	5.56E+05	4.45E+05	5.58E+05	5.48E+05	7.90E+05
Acetylphosphate	5.95E+05	3.47E+05	4.22E+05	4.23E+05	2.93E+05	3.09E+05
Histidinol	8.14E+07	7.80E+07	6.84E+07	7.52E+07	6.10E+07	8.19E+07
alpha-Ketoglutarate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Lysine	7.86E+07	9.05E+07	8.80E+07	1.10E+08	1.04E+08	1.41E+08
O-Acetyl-L-serine	1.45E+08	1.53E+08	1.36E+08	1.46E+08	1.35E+08	1.56E+08
2-Hydroxy-2-methylsuccinate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Methionine	5.39E+05	1.02E+06	3.69E+05	4.80E+05	4.18E+05	3.79E+05
Guanine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	5.74E+03	0.00E+00
Histidine	1.10E+07	1.21E+07	8.73E+06	1.04E+07	1.01E+07	1.34E+07
Orotate	8.03E+04	9.05E+04	4.87E+04	1.09E+05	5.21E+04	1.09E+04
Allantoin	3.99E+07	4.45E+07	3.39E+07	4.11E+07	3.72E+07	4.88E+07
2-Amino adipate	4.17E+06	5.49E+06	4.00E+06	5.65E+06	4.83E+06	6.88E+06
Phenylpyruvate	1.96E+06	2.39E+06	2.11E+06	4.36E+06	3.02E+06	2.73E+06
Phenylalanine	5.66E+07	6.65E+07	4.75E+07	6.46E+07	5.78E+07	7.51E+07
Phenyllactic acid	7.16E+07	7.14E+07	5.56E+07	6.58E+07	5.74E+07	9.15E+07

Table 32. Continued.

Metabolite	1495-1	1495-2	1495-3	1496-1	1496-2	1496-3
Aconitate	2.12E+05	1.71E+05	2.62E+05	1.45E+05	2.27E+05	1.80E+05
N-Acetylornithine	1.91E+06	1.78E+06	2.16E+06	2.22E+06	2.35E+06	2.54E+06
Citrulline	8.22E+04	1.20E+05	8.08E+04	1.20E+05	7.92E+04	1.49E+05
N-Carbamoyl-L-aspartate	6.83E+08	8.10E+08	6.27E+08	7.77E+08	6.87E+08	1.00E+09
2-Isopropylmalate	1.33E+04	5.98E+04	6.41E+03	1.84E+04	0.00E+00	0.00E+00
Tyrosine	9.54E+07	3.50E+07	1.33E+07	1.39E+07	1.26E+07	1.53E+07
3-Phosphoglycerate	3.75E+06	2.85E+06	3.20E+06	2.58E+06	2.66E+06	2.05E+06
N-Acetylglutamate	4.61E+05	4.44E+05	3.16E+05	5.41E+05	2.83E+05	5.03E+05
5-Hydroxyindoleacetic acid (5-HIAA)	2.57E+07	2.95E+07	2.60E+07	3.31E+07	3.01E+07	3.88E+07
2-Dehydro-D-gluconate	1.26E+07	1.66E+07	1.45E+07	1.81E+07	1.66E+07	2.02E+07
D-Gluconate	6.38E+05	8.11E+05	6.17E+05	1.10E+06	9.44E+05	1.68E+06
Tryptophan	2.28E+08	2.51E+08	2.70E+08	2.92E+08	2.47E+08	2.51E+08
Lipoate	4.10E+06	5.18E+06	4.51E+06	5.86E+06	5.72E+06	6.79E+06
Deoxyribose phosphate	7.36E+07	8.75E+07	7.12E+07	9.09E+07	8.75E+07	1.27E+08
Ribose phosphate	1.22E+07	1.34E+07	1.06E+07	1.36E+07	1.30E+07	2.07E+07
Xylitol 5-phosphate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	5.92E+03	0.00E+00
Cystine	0.00E+00	3.01E+05	1.14E+06	3.63E+05	1.81E+05	5.82E+04
Uridine	4.64E+05	3.08E+05	3.56E+05	4.98E+05	3.11E+05	4.48E+05
Glucosamine phosphate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
S-Ribosyl-L-homocysteine	3.07E+05	1.56E+04	2.12E+04	0.00E+00	3.80E+03	4.86E+03
Adenosine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Homocystine	3.52E+06	4.52E+06	5.20E+06	5.77E+06	6.58E+06	6.42E+06
Inosine	9.00E+06	5.09E+06	3.05E+06	2.18E+06	1.21E+06	2.25E+06
6-Phospho-D-gluconate	9.45E+04	1.03E+05	1.58E+05	1.34E+05	2.10E+05	1.89E+05

Table 32. Continued.

Metabolite	1495-1	1495-2	1495-3	1496-1	1496-2	1496-3
Guanosine	2.50E+06	2.98E+06	1.84E+06	2.43E+06	2.36E+06	2.66E+06
Xanthosine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	6.78E+03	0.00E+00
Glycinamide ribotide (GAR)	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Aminoimidazole ribotide (AIR)	3.08E+04	2.66E+04	3.49E+04	3.34E+04	4.90E+04	2.45E+04
N-Acetylglucosamine 1/6-phosphate	1.65E+04	8.84E+04	4.05E+04	8.97E+04	1.14E+05	7.06E+04
Octulose 8/1P	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
CMP	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
UMP	0.00E+00	2.16E+03	1.62E+04	1.37E+04	9.20E+03	1.05E+04
AICAR	3.47E+09	4.00E+08	5.90E+07	1.57E+07	5.99E+06	3.57E+06
Fructose 1_6-bisphosphate	7.44E+06	8.84E+06	9.56E+06	1.03E+07	9.01E+06	8.39E+06
Trehalose/Sucrose/Cellobiose	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
AMP/dGMP	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
IMP	6.33E+05	4.09E+05	6.41E+05	6.52E+05	6.23E+05	9.51E+05
S-Adenosyl-L-methioninamine	1.37E+08	1.02E+07	1.55E+05	1.82E+04	1.31E+04	0.00E+00
Sedoheptoluse bisphosphate	0.00E+00	3.49E+03	0.00E+00	0.00E+00	0.00E+00	0.00E+00
dTDP	2.96E+08	1.68E+07	2.13E+06	1.27E+04	3.00E+03	3.50E+03
UDP	1.90E+06	5.55E+05	3.40E+05	3.02E+05	2.87E+05	4.93E+05
FMN	3.90E+05	3.85E+05	5.22E+03	0.00E+00	0.00E+00	0.00E+00
UDP-glucose	4.70E+08	2.82E+07	2.22E+07	5.03E+06	7.57E+05	7.64E+05
UDP-glucuronate	5.86E+03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
UDP-N-acetylglucosamine	0.00E+00	0.00E+00	0.00E+00	4.25E+03	0.00E+00	0.00E+00
NAD+	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
NADH	1.53E+05	4.86E+03	3.93E+03	9.68E+03	0.00E+00	0.00E+00
Dephospho-CoA	3.41E+06	0.00E+00	6.01E+03	7.64E+03	4.23E+03	0.00E+00

Table 32. Continued.

Metabolite	1495-1	1495-2	1495-3	1496-1	1496-2	1496-3
NADP+	1.50E+05	1.03E+05	5.29E+04	6.69E+04	5.69E+04	2.13E+05
FAD	3.38E+07	4.82E+07	4.44E+07	4.92E+07	5.08E+07	5.40E+07
Pyruvate	5.90E+06	4.37E+06	4.46E+06	3.35E+06	4.06E+06	2.23E+06
Fumarate	2.82E+03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Cysteine	4.85E+09	5.64E+09	4.65E+09	5.87E+09	5.80E+09	7.53E+09
Nicotinate	1.47E+08	9.05E+07	9.42E+07	7.50E+07	8.46E+07	5.76E+07
Malate	1.23E+05	4.20E+05	7.00E+05	7.30E+05	8.52E+05	7.52E+05
Hypoxanthine	4.48E+05	4.24E+05	3.48E+05	4.65E+05	3.58E+05	4.94E+05
Indole-3-carboxylate	7.53E+07	3.28E+07	2.75E+07	1.51E+07	8.62E+06	6.51E+06
Phosphoenolpyruvate	1.86E+07	1.45E+07	1.10E+07	1.32E+07	1.12E+07	1.57E+07
Glycerone phosphate	9.20E+06	1.09E+07	8.68E+06	1.03E+07	1.07E+07	1.05E+07
sn-Glycerol 3-phosphate	5.16E+09	2.56E+09	2.06E+09	1.65E+09	1.33E+09	1.28E+09
Citrate/isocitrate	8.53E+06	1.18E+07	7.87E+06	9.57E+06	7.29E+06	8.34E+06
Sedoheptulose 1/7-phosphate	1.41E+05	2.07E+04	5.75E+04	7.90E+04	6.06E+04	2.66E+04

VITA

Jordan Ashley Rogerson is the daughter of Chris and Jenny Ashley. She attended Ware Shoals High School then later graduated from Lander University in spring of 2014 with a Bachelor's Degree in Chemistry. After teaching middle and high school science for two years, she attended the University of Tennessee, Knoxville to pursue a Master's Degree in Analytical Chemistry.