

Metabolomic Profile Comparison of Osteoarthritic and Traumatically Injured Synovial Joints

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Results

Introduction

- The widespread prevalence of degenerative joint diseases, such as osteoarthritis, characterized as a leading cause of disability, affects thousands of people around the world.
- Post-traumatic arthritis is a joint condition following joint injuries such as fractures or dislocations.
- Recent studies have applied metabolomics to the study of Osteoarthritis and Post Traumatic arthritis, and several metabolism-related pathways, as well as specific metabolic markers, have been identified as contributing factors.
- Hypothesis:** It is hypothesized that there will be a significant difference between metabolites collected from healthy controls and those collected from injured or diseased test subjects, while the metabolites from affected patients will be similar.

Methods

Samples: This study utilizes 13 patient samples of synovial fluid.

1 Trauma Sample (3 Pseudo Samples)

7 Osteoarthritis Samples

5 Healthy Samples

Metabolite Extraction: The metabolites were extracted from the biofluid samples by way of mixing them with methanol.

Spectral Data Collection: The samples were processed via Liquid Chromatography - Mass Spectrometry (LC-MS) at MSU Bozeman.

Data Processing: Statistical analysis was performed on the data using the online program MetaboAnalyst. Both univariate and multivariate statistics were utilized.

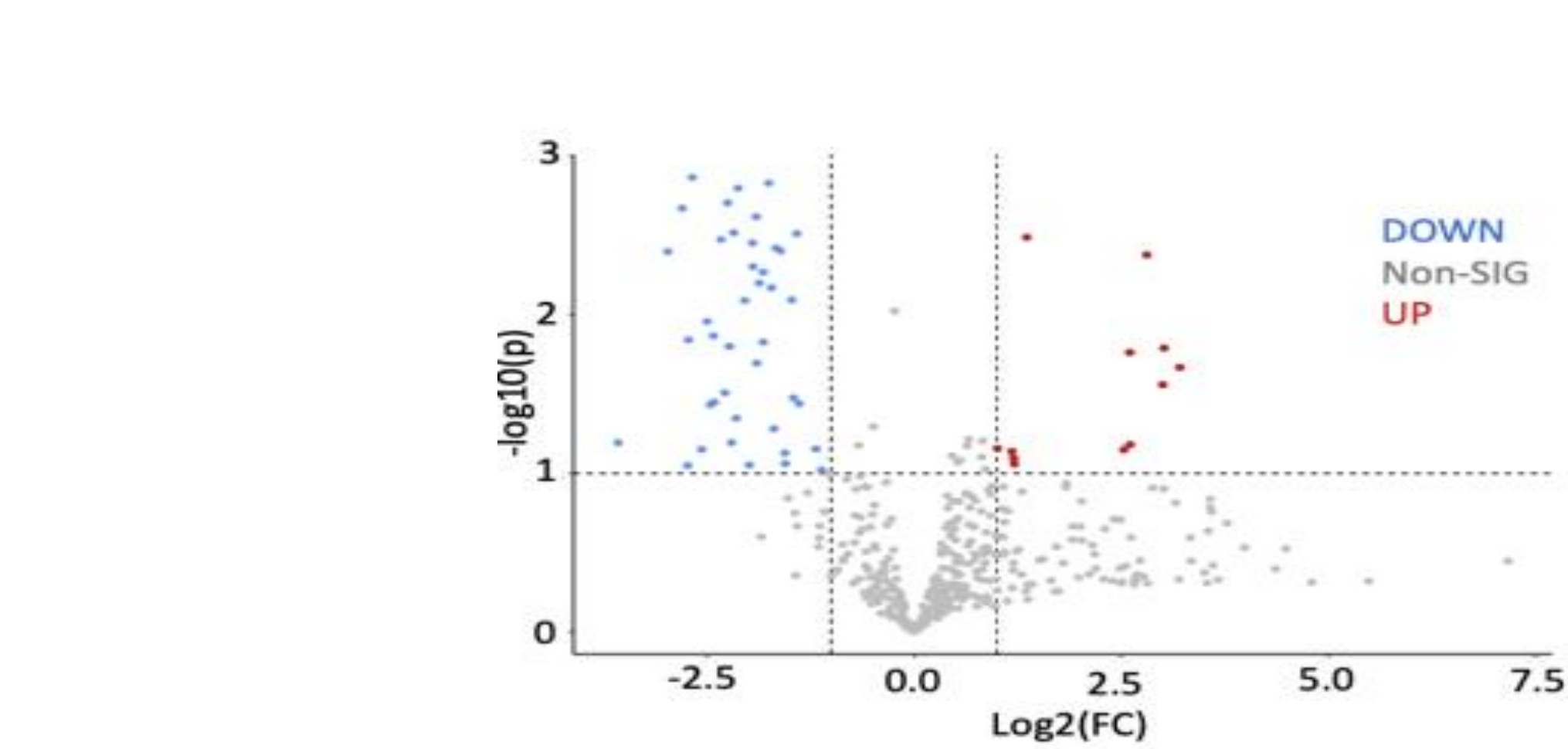


Figure 1 Volcano Plot of Healthy vs. Trauma - This figure displays the two-group comparison between healthy and trauma. The ratio is healthy to trauma with a p-value threshold of 0.1 and no FDR corrections were utilized. As shown in the graph, there is significant separation between the two groups.

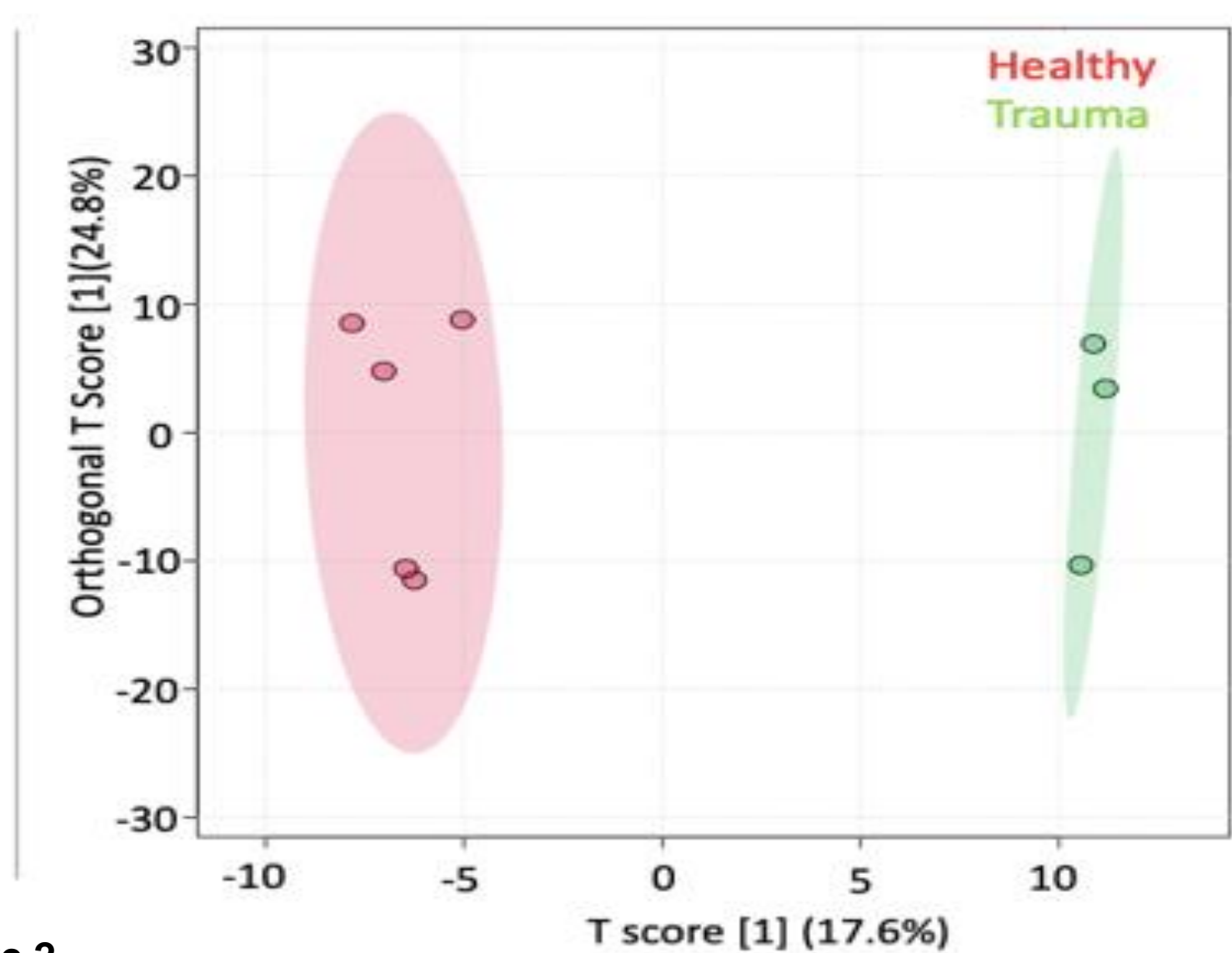


Figure 2 Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA) Healthy vs. Trauma - This figure displays the OPLS-DA of the Healthy and Trauma groups. The samples associated with Healthy are red, while those associated with Trauma are green. There is a very clear separation among the two groups, which shows that there are certain metabolites that present a clear difference when you take into account the different samples.

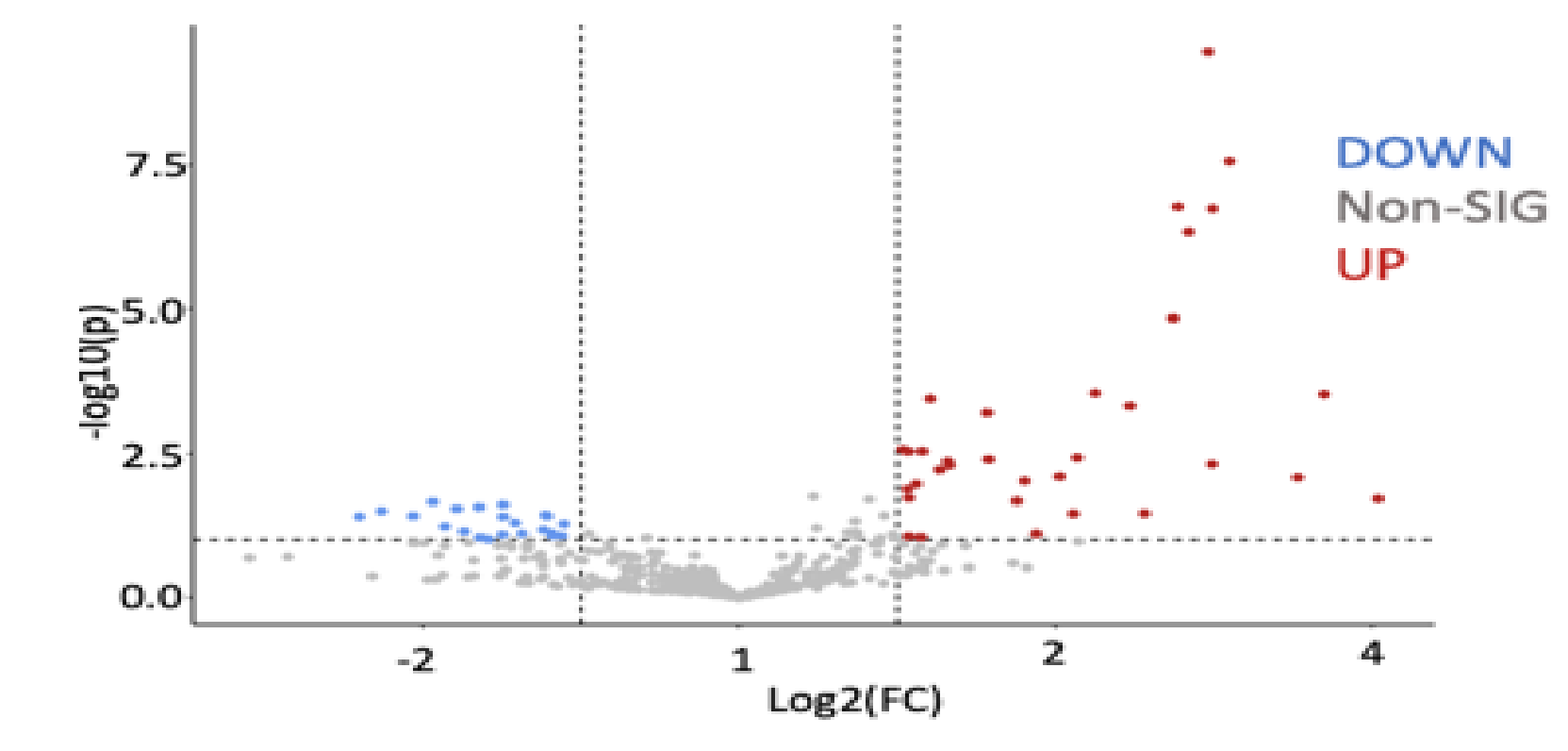


Figure 3 Volcano Plot of Healthy vs. OA - This figure shows the two-group comparison amongst the Osteoarthritis and Healthy groups. The ratio is healthy to osteoarthritis with a p-value threshold of 0.1 and no FDR corrections were utilized. This figure is intended to show that there is significant separation between the two groups.

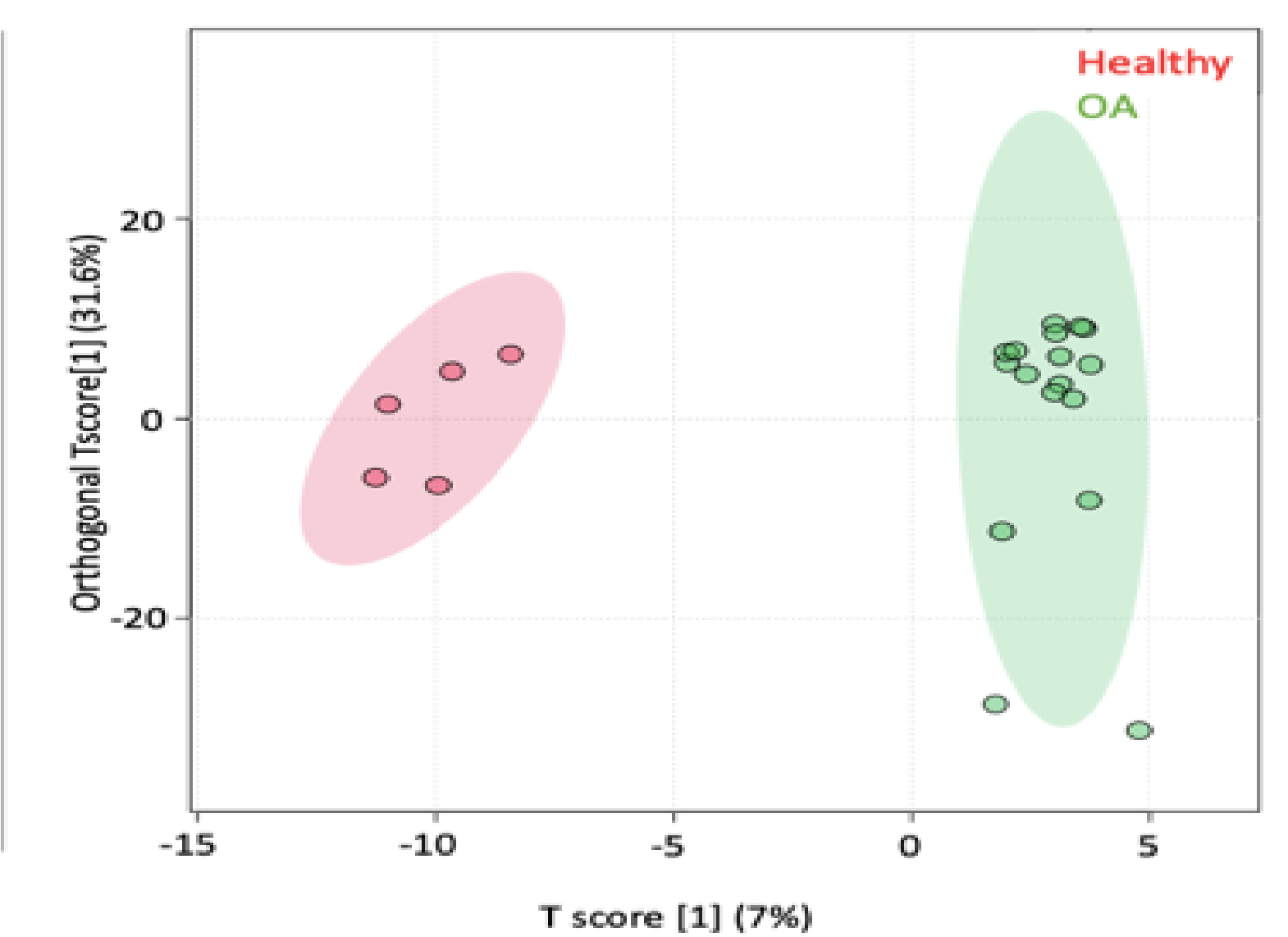


Figure 4 Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA) Healthy vs. OA - This is the OPLS-DA showing the comparison between the Osteoarthritis group and the Healthy group. The samples associated with Healthy are red, while those associated with OA are green. There is a very clear separation among the two groups, which shows that there are certain metabolites that present a clear difference when you take into account that the samples come from different groups.

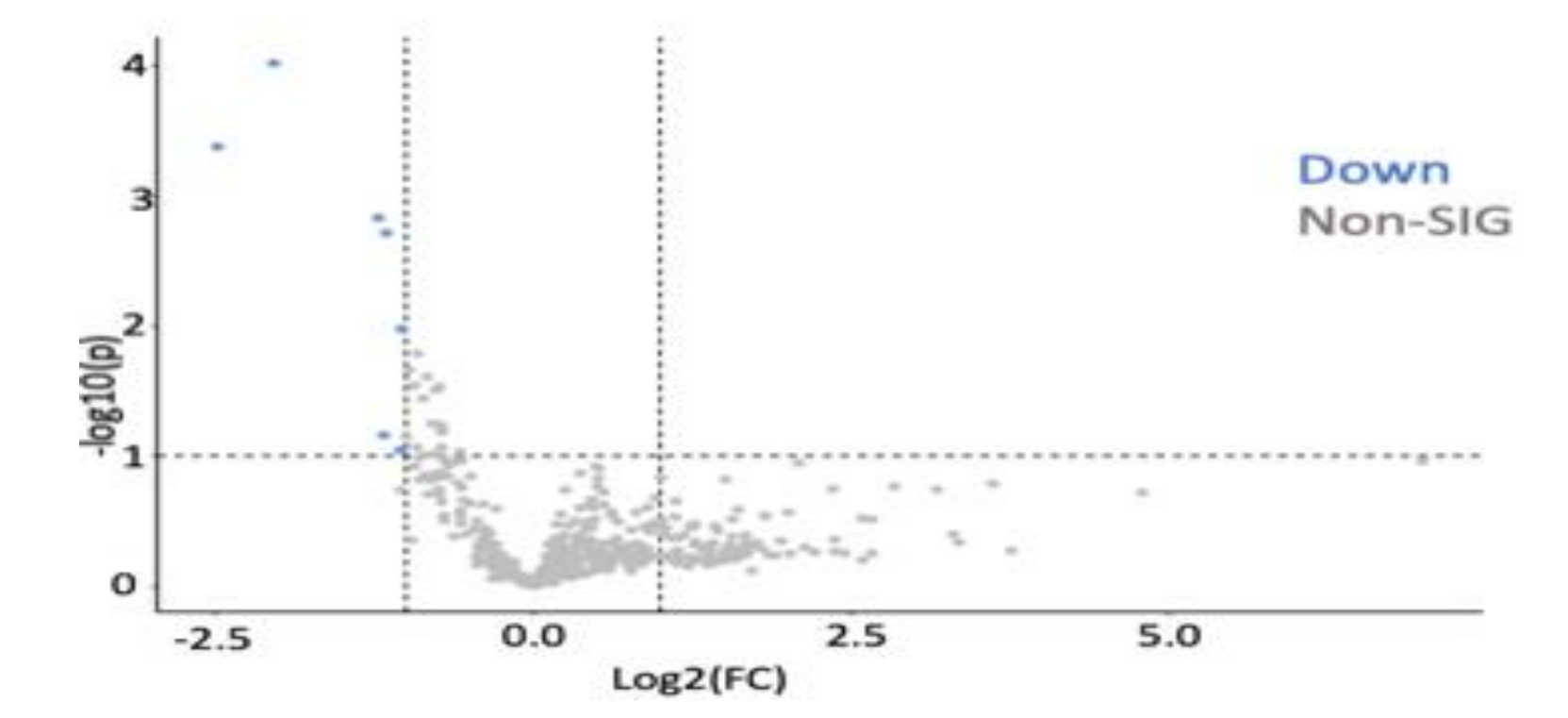


Figure 5 Volcano Plot of OA vs. Trauma - This figure shows the two group comparisons amongst the Osteoarthritis and Trauma groups. The ratio is osteoarthritis to trauma with a p-value threshold of 0.1 and no FDR corrections were utilized. This figure shows that there is significant separation between the two groups.

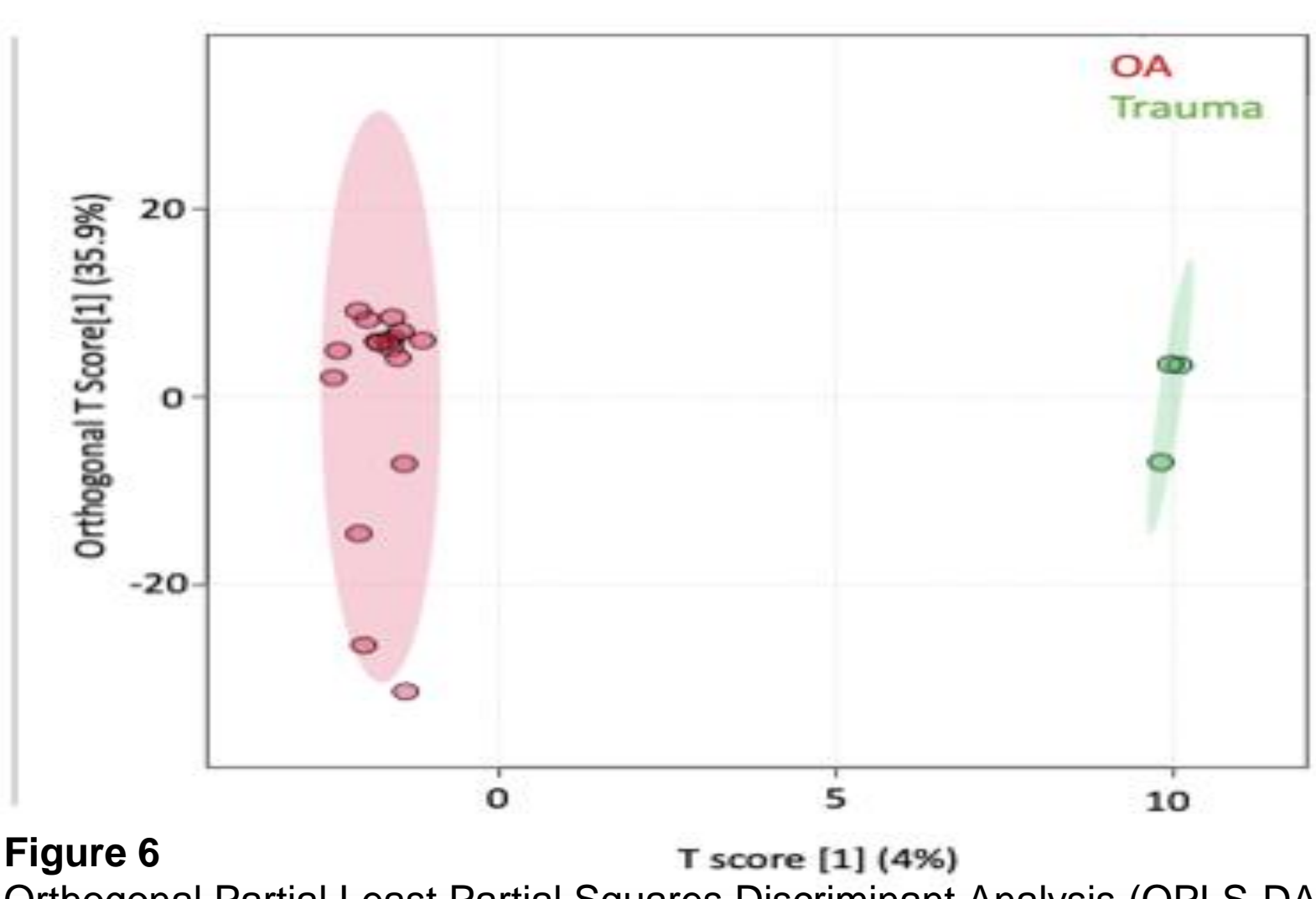


Figure 6 Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA) OA vs. Trauma - This is the OPLS-DA showing the comparison between the Osteoarthritis group and the Trauma group. The samples associated with Osteoarthritis are red, while those associated with Trauma are green. As the graph shows, there is a very clear separation among the two groups, which shows that there are certain metabolites that present a clear difference when you take into account that the samples come from different groups.

Healthy, Trauma, and Osteoarthritis VIP Scores PLS-DA				
	Total	Detected	Sig.	P- Value
Glycerophospholipid metabolism	156	3	3	0.19937
Lysine metabolism	52	4	3	0.21729
TCA cycle	31	2	2	0.2276
Urea cycle/amino group metabolism	85	5	3	0.23673
Vitamin E metabolism	54	3	2	0.25398
Tryptophan metabolism	94	9	4	0.26327
Purine metabolism	80	4	2	0.2798
Vitamin B6 (pyridoxine) metabolism	11	4	2	0.2798
Tyrosine metabolism	160	11	4	0.30108
Carnitine shuttle	72	12	4	0.32055

Table 1 The perturbed pathways in patients with OA, trauma, and in healthy individuals. Data collected through statistical analysis using PLS-DA. The pathways display the number of metabolites in the pathway, the number of metabolites detected in that pathway, and the number of significant metabolites in that pathway. (P>0.05)

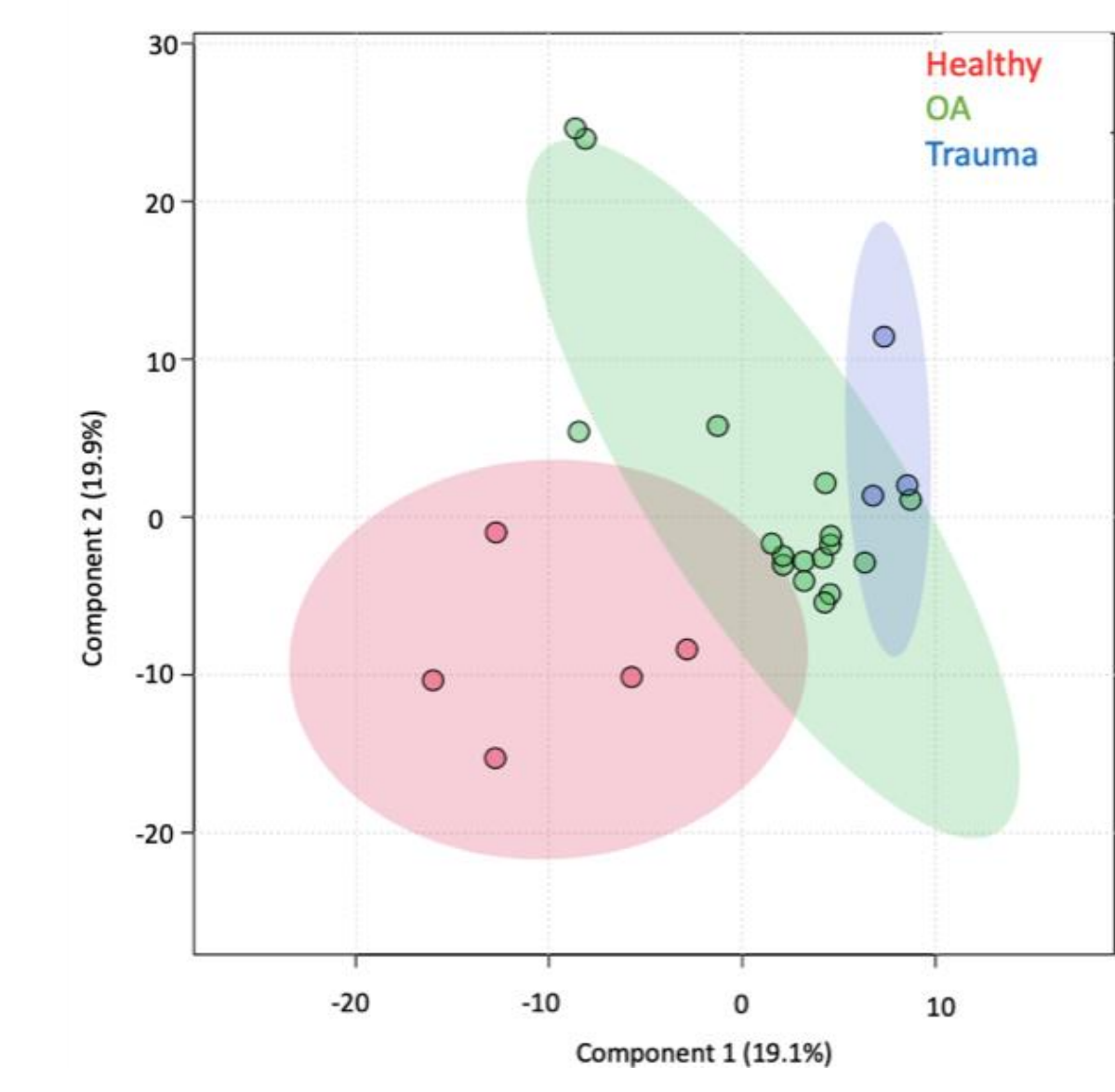


Figure 7 Partial Least Squares Derivative (PLS-DA) of Healthy vs. OA vs. Trauma - This figure shows the comparison of the three sample groups. The red labels correspond to Healthy samples, the blue labels correspond to Trauma samples, and the green labels correspond to OA samples. There is some clustering among the three groups, but each group does have several metabolites which are separated out from the other groups.

Conclusion

- The metabolic pathways that were impacted during this experiment for healthy, Osteoarthritis, and trauma were the following: Lysine, TCA cycle, Vitamin E and B6, Tryptophan metabolism.
- Studies indicate that these pathways may be involved in osteoarthritis.
- When comparing healthy to diseased and trauma subjects, there were differences in metabolite concentration, as shown in Fig. 2 and Fig. 3.
- This result contradicts our hypothesis showing that there are differences in metabolite populations between osteoarthritis and post-traumatic arthritis. Furthermore, this result shows differences between healthy individuals and patients with chronic disease or injury.

References

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