

Supplementary material S3: Multivariate Statistical Analysis and Hierarchical Cluster Analysis parameters

Table S5. MANOVA (P = 0.05) method statistical significance *p*-values generated *post-hoc* pairwise multiple comparisons.

MANOVA, <i>p</i> -values	C50_T00	C50_T12	C50_T24	C50_T36	C50_T48	C50_T60	CTRL_T00	CTRL_T12	CTRL_T24	CTRL_T36	CTRL_T48	CTRL_T60	CTRL0_T00	CTRL0_T12	CTRL0_T24	CTRL0_T36	CTRL0_T48	CTRL0_T60
C50_T00		0.0000	0.0000	0.0000	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.9902	0.0000	0.0000	0.0000	0.0000	0.0000
C50_T12	0.0000		0.0000	0.0000	0.0000	0.0000	0.0000	0.0586	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0010	0.0000	0.0000	0.0000
C50_T24	0.0000	0.0000		0.0000	0.0000	0.0000	0.0000	0.0000	0.0105	0.0103	0.0313	0.0027	0.0000	0.0000	0.0000	0.0001	0.0037	0.0044
C50_T36	0.0000	0.0000	0.0000		0.8877	0.9770	0.0000	0.0000	0.0000	0.0020	0.0006	0.0066	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C50_T48	0.0000	0.0000	0.0000	0.8877		0.9817	0.0000	0.0000	0.0000	0.0007	0.0002	0.0021	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C50_T60	0.0000	0.0000	0.0000	0.9770	0.9817		0.0000	0.0000	0.0000	0.0012	0.0004	0.0040	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CTRL_T00	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000		0.0000	0.0000	0.0000	0.0000	0.0000	0.9902	0.0000	0.0000	0.0000	0.0000	0.0000
CTRL_T12	0.0000	0.0586	0.0000	0.0000	0.0000	0.0000	0.0000		0.0000	0.0000	0.0000	0.0000	0.0000	0.0001	0.0005	0.0000	0.0000	0.0000
CTRL_T24	0.0000	0.0000	0.0105	0.0000	0.0000	0.0000	0.0000	0.0000		0.0014	0.8549	0.8419	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CTRL_T36	0.0000	0.0000	0.0103	0.0020	0.0007	0.0012	0.0000	0.0000	0.0014		0.8549	0.8419	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CTRL_T48	0.0000	0.0000	0.0313	0.0006	0.0002	0.0004	0.0000	0.0000	0.0045	0.8549		0.4048	0.0000	0.0000	0.0000	0.0000	0.0001	0.0000
CTRL_T60	0.0000	0.0000	0.0027	0.0066	0.0021	0.0040	0.0000	0.0000	0.0004	0.8419	0.4048		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CTRL0_T00	0.9902	0.0000	0.0000	0.0000	0.0000	0.0000	0.9902	0.0000	0.0000	0.0000	0.0000	0.0000		0.0000	0.0000	0.0000	0.0000	0.0000
CTRL0_T12	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0001	0.0000	0.0000	0.0000	0.0000	0.0000		0.1100	0.0000	0.0000	0.0000
CTRL0_T24	0.0000	0.0010	0.0000	0.0000	0.0000	0.0000	0.0000	0.0005	0.0000	0.0000	0.0000	0.0000	0.0000	0.1100		0.0000	0.0000	0.0000
CTRL0_T36	0.0000	0.0000	0.0001	0.0000	0.0000	0.0000	0.0000	0.0000	0.0002	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000		0.0391	0.0127
CTRL0_T48	0.0000	0.0000	0.0037	0.0000	0.0000	0.0000	0.0000	0.0000	0.0029	0.0000	0.0001	0.0000	0.0000	0.0000	0.0000	0.0391		0.4757
CTRL0_T60	0.0000	0.0000	0.0044	0.0000	0.0000	0.0000	0.0000	0.0000	0.0006	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0127	0.4757	
Cluster_#1 Cluster_#2 Cluster_#3 Cluster_#4 Cluster_#4 Cluster_#4 Cluster_#1 Cluster_#2 Cluster_#5 Cluster_#6 Cluster_#6 Cluster_#6 Cluster_#6 Cluster_#1 Cluster_#7 Cluster_#7 Cluster_#8 Cluster_#9 Cluster_#9																		

Table S6. Agglomerative hierarchical cluster analysis (AHC) results on PC1÷PC3 principal coordinates as MANOVA's input.

Cluster_#1	Cluster_#2	Cluster_#3	Cluster_#4	Cluster_#5	Cluster_#6	Cluster_#7	Cluster_#8	Cluster_#9
C50_T2	CTRL_T	CTRL_T	CTRL0_T	CTRL0_T	C50_T1	CTRL0_T		C50_T3
4	36	24	T48	T36	2	T12	C50_T00	6
	CTRL_T		CTRL0_T		CTRL_T	CTRL0_T	CTRL_T	C50_T4
	48		T60		12	T24	00	8
	CTRL_T						CTRL0_T	C50_T6
	60						T00	0

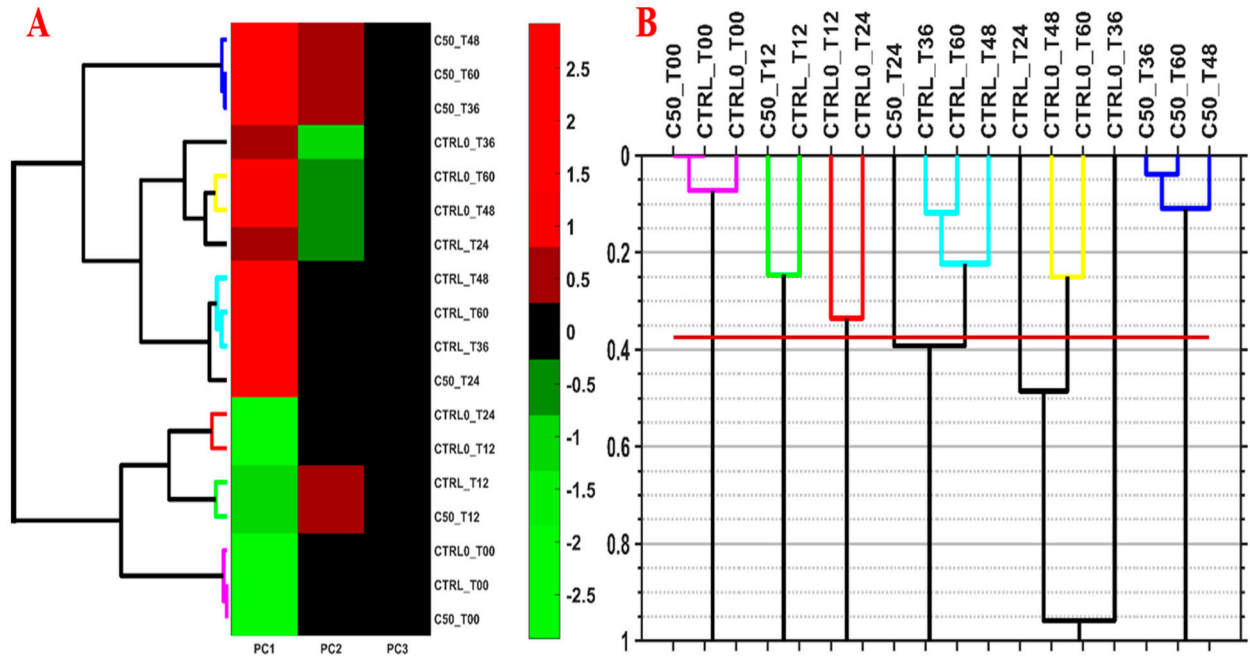


Figure S13. Cluster analysis of MANOVA ($P = 0.05$) results (A) Heatmap representation for Canon1 ÷ Canon4 canonical coordinates; (B) Dendrogram representation for Canon1 ÷ Canon4 canonical coordinates with the cut-off red line that generates the clusters.

The canonical coordinates are the ones that increase the variance-covariance level and perform the highest Euclidean distance between the sample groups. Furthermore, the AHC clustering method was used on the Canon1 to Canon3 coordinate values. In consequence, the proper number of the sample clusters was generated. The AHC results are presented as heat map with a dendrogram (**Figure S13a**) and a simple dendrogram with the cut-off similarity distance value (**Figure S13b**) used to obtain the proper number of clusters, based on MANOVA's p-values matrix.