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Supplementary Information 3 (Additional Tables and Figures) for the paper **'Metabolomics reveals the physiological response of *Pseudomonas putida* KT2440 (UWC1) after pharmaceutical exposure.'**

Table SI3 1. Structures and modes of action of the pharmaceuticals used in this study.

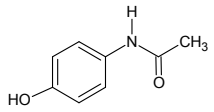
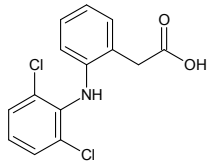
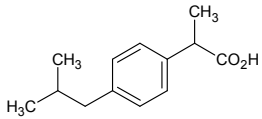
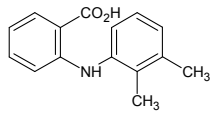
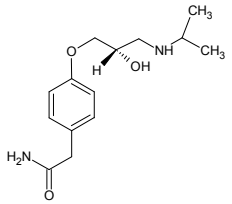
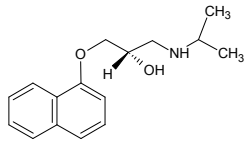
Pharmaceutical	Mode of Action	Chemical Structure
Acetaminophen	Analgesic: possible COX -isoform inhibitor but mechanism of action ill-defined	
Diclofenac	Non-steroidal anti-inflamatory drug: non-selective COX inhibitor	
Ibuprofen	Non-steroidal anti-inflamatory drug: non-selective COX inhibitor	
Mefenamic acid	Non-steroidal anti-inflamatory drug: non selective COX inhibitor	
Atenolol	β1-adrenergic blocker	
Propranolol	Non-selective β-adrenergic blocker	

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Table SI3 2. Alterations in the concentration of amino acids in *P. putida* exposed to propranolol identified from the ANOVA analysis. Amino acids and the related metabolite 3-oxyisovaleric acid were reduced in concentration on exposure to propranolol by 0.29 – 0.73 fold on exposure to propranolol. Alterations in phenylalanine, glutamine acid and beta-alanine were observed on exposure to ibuprofen, diclofenac and acetaminophen (see main text for detail).

Metabolite ID	Metabolite Name	Definitive ID	p-value ANOVA	AUROC	Fold Difference exposed/control
146	**glycine**	*	3.06×10^{-4}	0.93	0.5712
89	**alanine**	*	1.29×10^{-4}	0.96	0.4572
83	**alanine**		1.68×10^{-2}	0.88	0.2901
80	**valine**		2.12×10^{-3}	0.88	0.3565
87	**isoleucine**		1.45×10^{-2}	0.88	0.3243
20	**phenylalanine**		3.48×10^{-4}	0.94	0.7279
116	**lysine**		1.63×10^{-2}	0.88	0.5612
97	**glutamic acid**	*	3.46×10^{-4}	0.95	0.2066
12	**glutamic acid**	*	2.17×10^{-3}	0.92	0.7316
91	**beta-alanine**		1.32×10^{-2}	0.88	0.6645
17	**pyroglutamic acid**		5.38×10^{-3}	0.88	0.3986
84	**3-oxyisovaleric acid**		1.57×10^{-2}	0.88	0.4405

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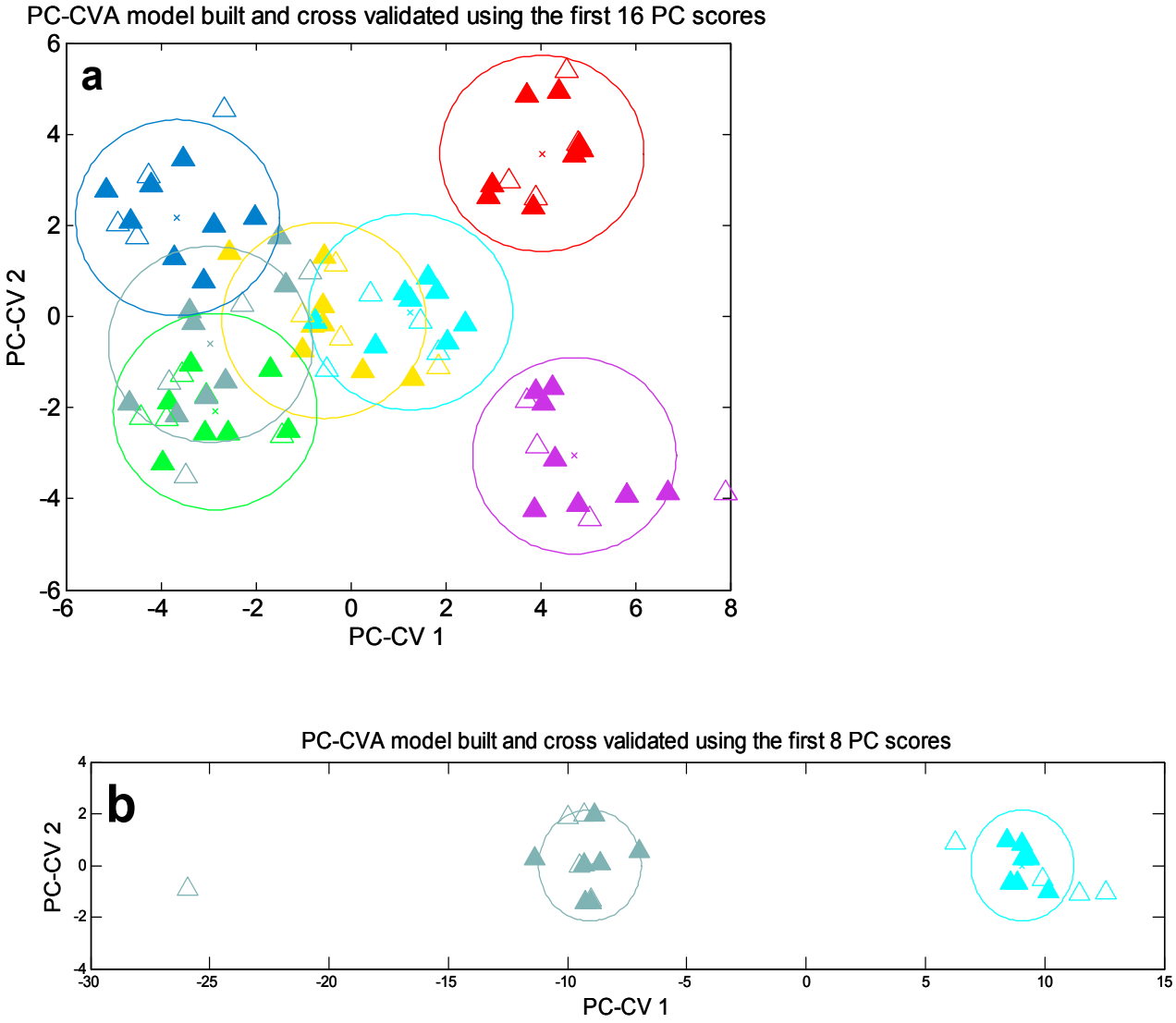

Figure SI3 1 a) Cross-validated PC-CVA models for the GC-MS data of *P. putida* exposed to the six pharmaceuticals. 16 PC scores (99.5% explained variance) were used in the analysis which was trained on 2 analytical replicates (filled triangles) and tested with a third unknown replicate (open triangles). Key: acetaminophen red, atenolol gold, diclofenac green, ibuprofen cyan, mefenamic acid blue, propranolol purple, control grey. Cells exposed to propranolol and acetaminophen are separated along CV1; Circles represent the 95% confidence limit from the group centres here constructed around each group mean by the χ^2 distribution on two degrees of freedom.

b) Models were generated which discriminate between *P. putida* exposed to individual pharmaceuticals and cell exposed to water, shown for cells exposed to ibuprofen using 8 PC scores (99.6% explained variance).

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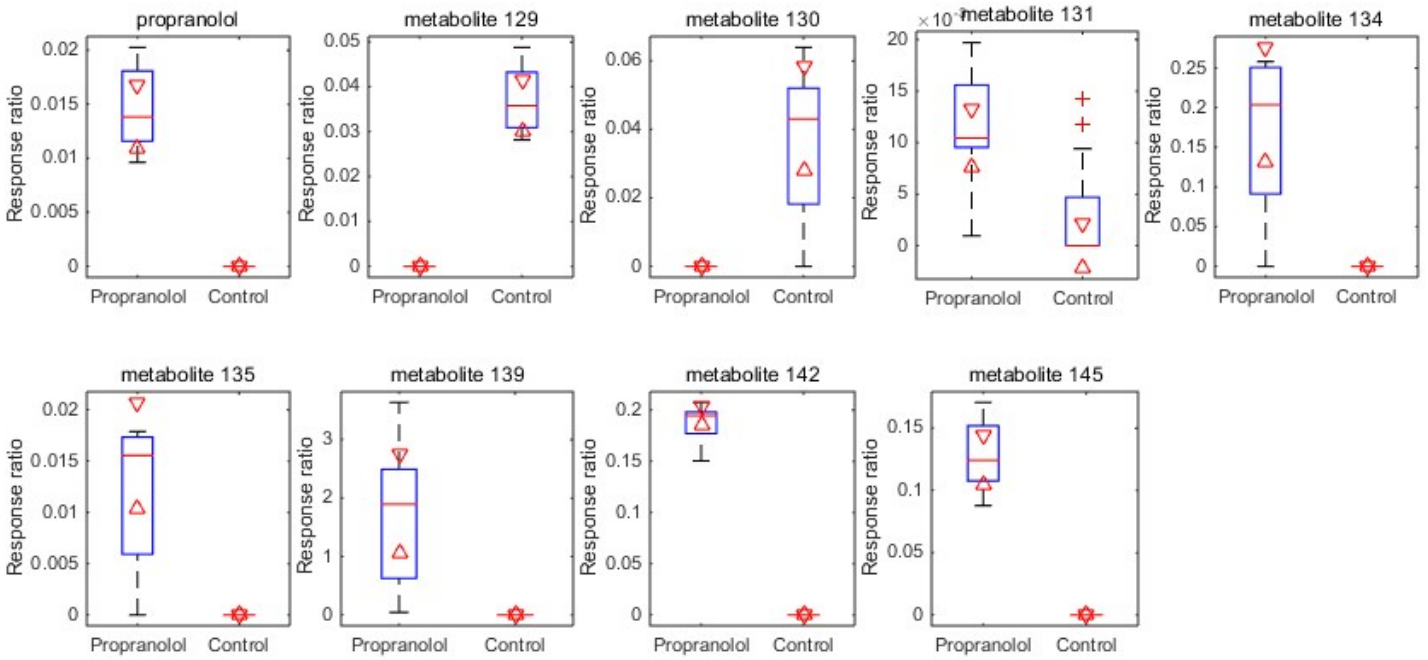

Figure SI3 2. Significant alterations in the concentration of 9 metabolites in *P. putida* exposed to propranolol identified from the ANOVA analysis. Propranolol itself was present in the extracts of exposed cells and absent in the control cells. The concentration of metabolites 129 and 130 (for which there was no definitive identification) fell below the limit of detection in exposed cells, while metabolites 131, 134, 135, 139, 142, and 145 were raised from below the limit of detection in exposed cells, and were not present in cells exposed to any other pharmaceutical in the study. Metabolites 142, 145 and 129 had the lowest p-values (below 10^{-12}) in the ANOVA analysis and all except metabolites 130 and 131 had an area under the ROC curve of 1, implying that these metabolites are entirely diagnostic of cells exposed to propranolol.