Supporting information: Supplemental Table 1 and Supplemental Figures 1–5

Metabolomic Analysis Characterizes Tissue Specific Metabolic Perturbations of Rats Induced by Indomethacin

Running title: Tissue Metabolic Perturbations of rats treated Indomethacin

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The authors have no conflict of interest

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Supplemental Table 1. Original input data for the IPA analysis

Metabolites ID	C	D1	D2	D3	HUMB ID
(10E,12E)-9-hydroxyoctadeca-10,12-dienoic acid	652.53	326.30	656.94	904.36	HMDB10223
2-Methylcitric acid	1209.70	989.40	574.81	830.71	HMDB00379
Famotidine	195.31	56.21	429.87	203.06	HMDB01919
Putreanine	20.39	336.80	158.83	79.86	HMDB06078
Prostaglandin E2	318.76	114.30	170.01	190.93	HMDB01220
Docosanamide	26.04	16.35	223.59	61.90	HMDB00583
Creatinine	13.28	102.90	149.53	227.62	HMDB00562
Pregnenolone	1173.10	983.80	623.06	751.38	HMDB00253
Palmitoleic acid	25.84	149.40	90.72	116.06	HMDB03229
L-Carnitine	105.70	30.17	168.73	89.33	HMDB00062
Guanosine	105.14	6.83	2.70	2.44	HMDB00133
Thiamine monophosphate	20.60	17.40	54.46	25.32	HMDB02666
D-Ribulose 5-phosphate	15.42	10.20	29.95	15.54	HMDB00618
Nervonic acid	16.13	14.28	27.02	15.78	HMDB02368
Spermine	37.25	6.52	65.20	47.81	HMDB01256
5-Hydroxy-L-tryptophan	4.63	2.61	7.86	4.56	HMDB00472
3-Chlorotyrosine	5.54	3.85	8.87	5.26	HMDB01885
15-Keto-prostaglandin F2a	6.07	2.74	8.41	2.88	HMDB04240
N1-Acetylspermidine	16.59	1.00	0.62	10.27	HMDB01276
Proline betaine	2.39	1.28	0.64	0.10	HMDB04827

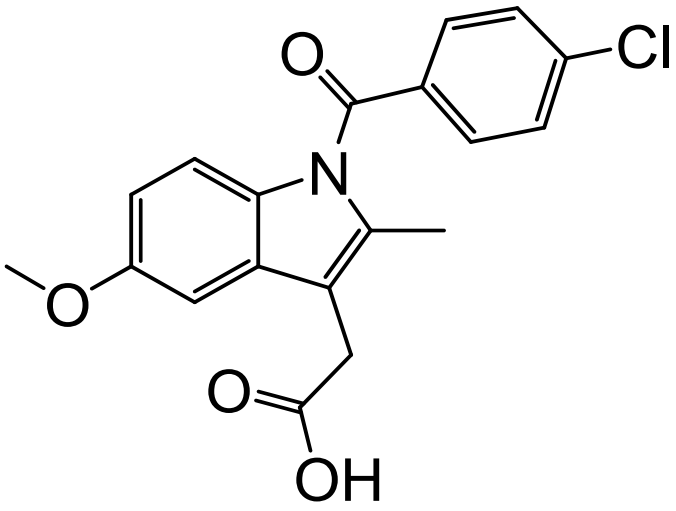
C: -24-0 h post-dosage of indomethacin

D1: 0-48 h post-dosage of indomethacin

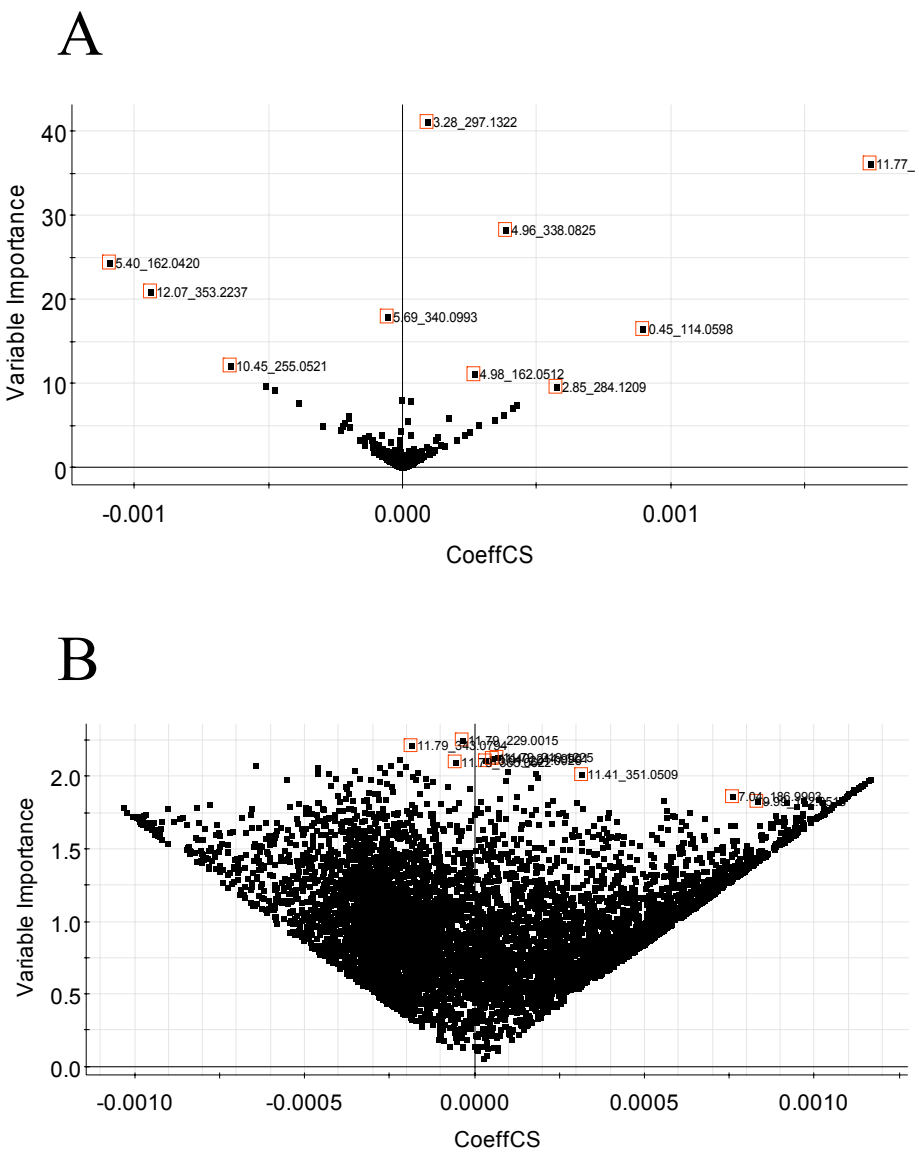
D2: 24-48 h post-dosage of indomethacin

D3: 48-72 h post-dosage of indomethacin

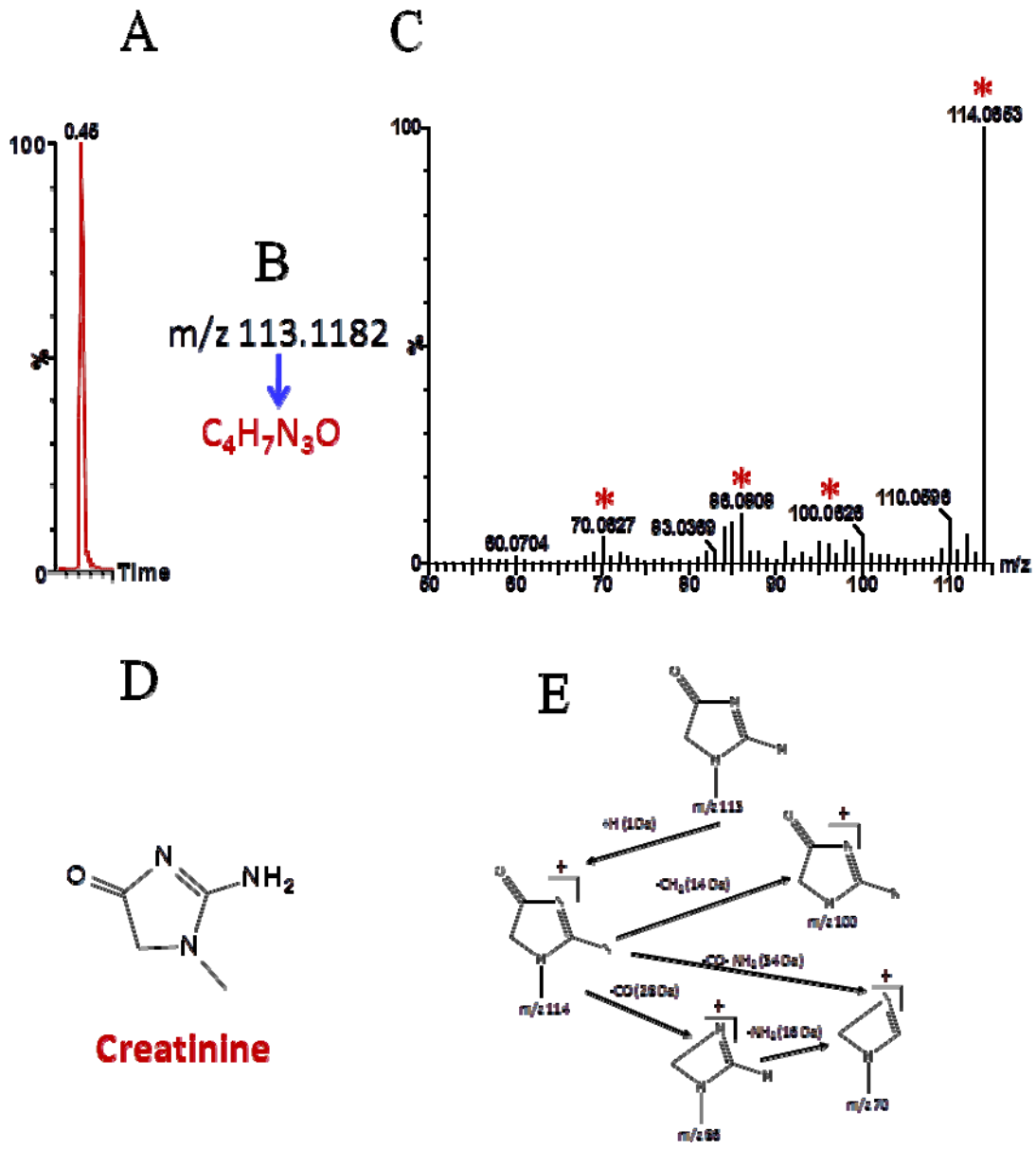
HUMB: Human Metabolome Database



Supplemental Figure 1. Chemical structure of indomethacin

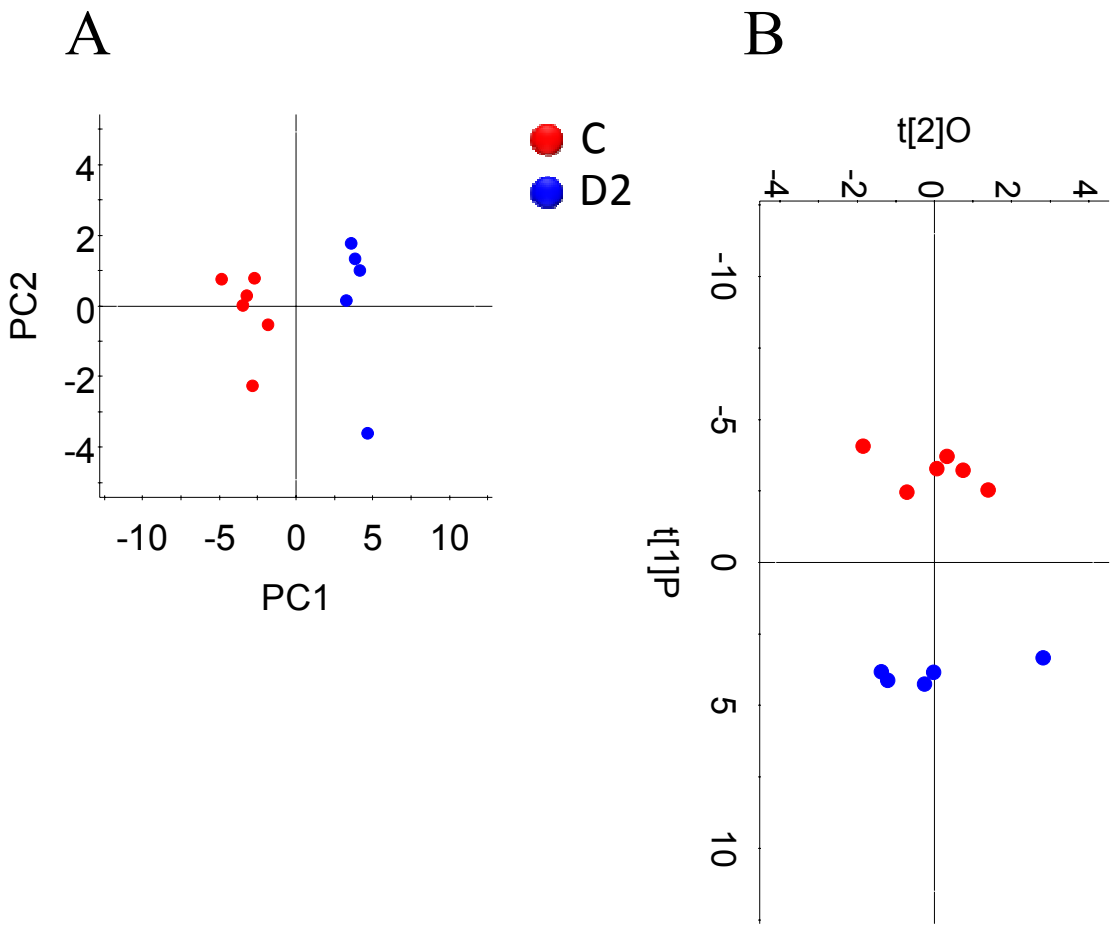


Supplemental Figure 2. Loading plots from the variable importance of PLS-DA analyses of urine metabolome in positive (A) and negative (B) ionization modes from urine samples of rats treated with indomethacin. The plots lead to identify the principal ions contributing to the differential inter-groups clustering. Subsequently, the data of the biomarkers was selectively collected: retention time and mass-to-charge ratio. The ID signatures of the ions allowed to identifying the metabolites differentially altered in the different groups of samples.

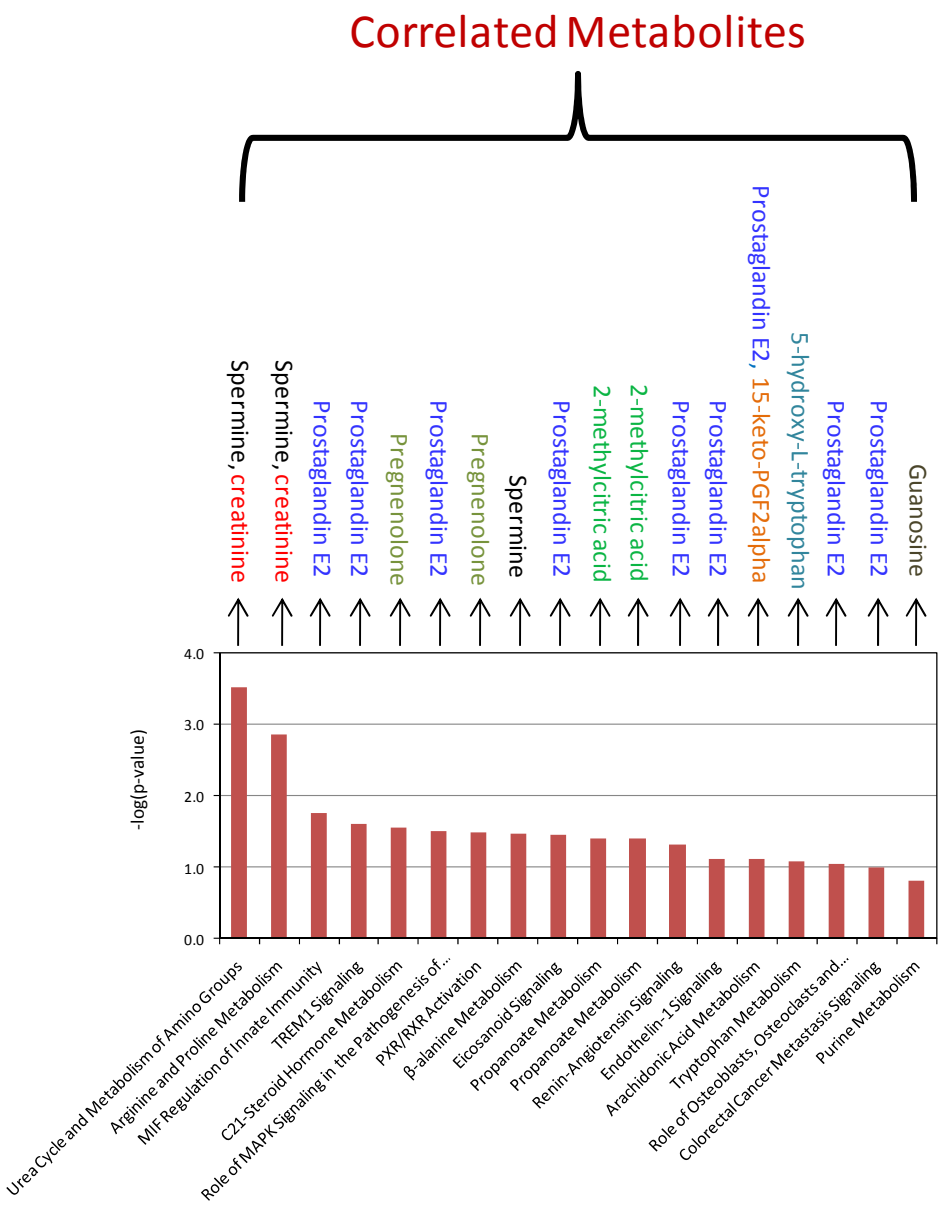


Supplemental Figure 3. The deduced identification of the creatinine.

A. extract mass spectra; B. The extract mass and formula; C. ms/ms spectra; D. The chemical structure of the creatinine; E. The pathway mechanism of collision induced dissection of the creatinine.



Supplemental Figure 4. Pattern recognition analyses of the metabolic perturbations induced by indomethacin using the data of 20 most significantly changing metabolites in the groups of samples from -24-0 h (C) and 24-48 h (D2). (A) PCA Score plot; R2Y (cum): 0.88; Q2(cum): 0.76; (B) OPLS-DA Score plot; R2Y (cum): 0.81; Q2(cum): 0.94.



Supplemental Figure 5. IPA graphical correlation of the 20 more significant biomarkers and the most probable metabolic pathways altered by the oral administration of indomethacin. Individual metabolites were distinctively labeled with different colors.