



Supplementary Figure 1 PCA analysis of plasma and vitreous metabolites

A) 2D score plot of PCA model for plasma metabolites B) 3D score plot of PCA mode for plasma metabolites C) 2D score plot of PCA model for vitreous metabolites D) 3D score plot of PCA mode for vitreous metabolites

Supplementary Table 1 Differential metabolites from vitreous in PDR

KEGG ID	Metabolite Name	HMDB ID	FC	VIP	p.adjusted (1)	p.adjusted (2)
C00037	Glycine	HMDB0000123	0.164	1.656	0.000	0.000
C00082	L-Tyrosine	HMDB0000158	0.430	1.295	0.043	0.045
C00106	Uracil	HMDB0000300	0.169	1.590	0.001	0.000
C00109	2-Ketobutyric acid	HMDB0000005	0.190	1.596	0.001	0.001
C00120	Biotin	HMDB0000030	6.332	1.344	0.009	0.015
C00147	Adenine	HMDB0000034	0.265	1.146	0.011	0.008
C00157	PC (22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:1(9Z))	HMDB0008729	0.249	1.048	0.026	0.023
C00164	Acetoacetic acid	HMDB0000060	0.187	1.534	0.002	0.002
C00166	Phenylpyruvic acid	HMDB0000205	0.427	1.253	0.046	0.053
C00178	Thymine	HMDB0000262	0.084	1.868	0.000	0.000
C00183	L-Valine	HMDB0000883	0.246	1.073	0.048	0.047
C00246	Butyric acid	HMDB0000039	0.197	1.551	0.004	0.006
C00299	Uridine	HMDB0000296	0.217	1.506	0.001	0.001
C00328	L-Kynurenine	HMDB0000684	15.455	1.399	0.007	0.006
C00341	Geranyl 2-methylbutyrate	HMDB0032291	0.215	1.655	0.001	0.000
C00366	Uric acid	HMDB0000289	13.692	1.344	0.012	0.011
C00380	Cytosine	HMDB0000630	0.117	1.815	0.000	0.000
C00408	Pipecolic acid	HMDB0000070	0.036	1.538	0.000	0.000
C00429	Dihydrouracil	HMDB0000076	0.232	1.450	0.007	0.007
C00475	Cytidine	HMDB0000089	0.083	1.909	0.000	0.000
C00487	Malonyl-Carnitin	HMDB0062496	3.206	1.424	0.015	0.006
C00500_01	Biliverdin IX	HMDB0304275	24.819	1.026	0.003	0.004
C00500_02	Biliverdin	HMDB0001008	16.937	1.242	0.002	0.002
C00535	Testosterone	HMDB0000234	27.863	1.656	0.001	0.000
C00539	Benzoic acid	HMDB0001870	0.215	1.668	0.001	0.001
C00576	Betaine aldehyde	HMDB0001252	0.280	1.387	0.011	0.018
C00741	Diacetyl	HMDB0003407	0.253	1.303	0.028	0.046
C00762	Cortisone	HMDB0002802	0.232	1.654	0.001	0.000
C00777	All-trans-retinoic acid	HMDB0001852	128.810	1.287	0.014	0.018

C00831	Pantetheine	HMDB0003426	13.888	1.341	0.004	0.004
C00931	Porphobilinogen	HMDB0000245	5.508	1.072	0.043	0.079
C00942	Cyclic GMP	HMDB0001314	0.127	1.361	0.001	0.000
C00964	(-)-trans-Carveol	HMDB0003450	0.355	1.318	0.014	0.023
C01041	Ascorbic acid	HMDB0000044	0.063	1.975	0.000	0.000
C01042	N-Acetyl-L-aspartic acid	HMDB0000812	0.039	1.789	0.000	0.000
C01045	N-Formyl-L-glutamic acid	HMDB0003470	0.041	1.745	0.000	0.000
C01545	Octanal	HMDB0001140	0.251	1.255	0.014	0.019
C01770	Gamma-Butyrolactone	HMDB0000549	0.190	1.783	0.000	0.000
C01771	But-2-enoic acid	HMDB0010720	0.283	1.241	0.030	0.033
C01879	Pyroglutamic acid	HMDB0000267	0.272	1.377	0.003	0.005
C01909	Dethiobiotin	HMDB0003581	4.931	1.247	0.033	0.079
C02043	Indolelactic acid	HMDB0000671	2.847	1.146	0.030	0.001
C02067	Pseudouridine	HMDB0000767	0.292	1.263	0.002	0.000
C02442	N-Methyltyramine	HMDB0003633	0.321	1.237	0.007	0.013
C02494	1-Methyladenosine	HMDB0003331	0.169	1.264	0.003	0.002
C02505	2-Phenylacetamide	HMDB0010715	0.396	1.353	0.016	0.020
C02678	Dodecanedioic acid	HMDB0000623	0.268	1.506	0.006	0.008
C02710	N-Acetylleucine	HMDB0011756	0.207	1.109	0.007	0.009
C02838	L-Octanoylcarnitine	HMDB0000791	42.364	1.618	0.001	0.000
C02892	Thiamine acetic acid		0.159	1.695	0.001	0.000
C02896	Putrescine	HMDB0001414	0.249	1.234	0.006	0.004
C03089	5-Methylthioribose	HMDB0001087	8.824	1.291	0.004	0.012
C03205	Deoxycorticosterone	HMDB0000016	476.970	1.686	0.001	0.001
C03264	D-Leucic acid	HMDB0000624	0.255	1.431	0.002	0.001
C03299	O-decanoyl-L-carnitine	HMDB0062631	29.058	1.521	0.000	0.000
C04148	Alpha-N-Phenylacetyl-L-glutamine	HMDB0006344	16.652	1.343	0.007	0.009
C04217	Geranylarnesyl diphosphate	HMDB0012231	0.232	1.622	0.002	0.002
C04221	trans-1,2-Dihydrobenzene-1,2-diol	HMDB0001164	0.219	1.535	0.002	0.002
C04230_01	LysoPC (20:4(8Z,11Z,14Z,17Z))	HMDB0010396	2.776	1.278	0.044	0.013
C04230_02	Oleoyl lysophosphatidylcholine	HMDB0002815	3.170	1.191	0.048	0.016
C05127	1-Methylhistamine	HMDB0000898	0.280	1.097	0.039	0.037

C05131	(1-Ribosylimidazole)-4-acetate	HMDB0002331	0.085	1.773	0.000	0.000
C05380	Nicotinuric acid	HMDB0003269	17.518	1.231	0.015	0.014
C05464	Deoxycholic acid glycine conjugate	HMDB0000631	2.246	1.109	0.044	0.012
C05578	5,6-Dihydroxyindole	HMDB0004058	0.176	1.799	0.000	0.000
C05607	D-Phenyllactic acid	HMDB0000563	0.225	1.307	0.022	0.018
C05635	5-Hydroxyindoleacetic acid	HMDB0000763	16.965	1.416	0.006	0.005
C05793	L-Urobilin	HMDB0004159	0.242	1.746	0.001	0.001
C05853	2-Phenylethanol	HMDB0033944	0.262	1.251	0.003	0.001
C05956	Prostaglandin G2	HMDB0003235	0.234	1.686	0.001	0.000
C06199	Hordenine	HMDB0004366	0.218	1.006	0.013	0.013
C06423	Caprylic acid	HMDB0000482	0.195	1.698	0.001	0.001
C07086	Phenylacetic acid	HMDB0000209	0.226	1.640	0.001	0.001
C07215	2-Methylbenzoic acid	HMDB0002340	0.225	1.636	0.001	0.001
C10490	Safrole	HMDB0033591	0.219	1.676	0.002	0.002
C11489	N-Methylformamide	HMDB0001122	0.208	1.056	0.018	0.014
C15497	(24R)-Cholest-5-ene-3-beta,24-diol	HMDB0011643	12.992	1.303	0.016	0.036
C15604	3-Methyl-2-butenal	HMDB0012157	0.210	1.313	0.006	0.009
C17714	Heptanoic acid	HMDB0000666	0.273	1.209	0.043	0.049

Note: “p.adjusted (1)” was the p-value obtained after adjusting for age. “p.adjusted (2)” was the p-value obtained after adjusting for biochemical parameters, including FBG and urea.

Supplementary Table 2 Differential metabolites from plasma in PDR

KEGG ID	Metabolite Name	HMDB ID	FC	VIP	p.adjusted (1)	p.adjusted (2)
C00078	L-Tryptophan	HMDB0000929	0.472	2.571	0.006	0.008
C00408	Pipecolic acid	HMDB0000070	0.172	1.736	0.001	0.002
C00637	Indoleacetaldehyde	HMDB0001190	0.466	2.538	0.006	0.009
C00643	5-Hydroxy-L-tryptophan	HMDB0000472	0.557	2.538	0.019	0.018
C00831	Pantetheine	HMDB0003426	1.938	1.349	0.021	0.019
C01077	Acetylhomoserine	HMDB0029423	6.391	2.392	0.002	0.001
C01879	Pyroglutamic acid	HMDB0000267	7.487	2.281	0.000	0.001
C02291	L-Cystathionine	HMDB0000099	3.661	1.888	0.011	0.031
C02528	Chenodeoxycholic acid	HMDB0000518	0.707	1.852	0.033	0.037
C03089	5-Methylthioribose	HMDB0001087	9.001	2.466	0.030	0.084
C03594	7 α -Hydroxycholesterol	HMDB0001496	0.253	1.165	0.038	0.047
C04148	Alpha-N-Phenylacetyl-L-glutamine	HMDB0006344	10.11	2.324	0.000	0.001
C04230_01	LysoPC (14:1(9Z))	HMDB0010380	0.287	1.389	0.038	0.010
C04230_02	LysoPC (16:1(9Z))	HMDB0010383	0.398	1.681	0.038	0.085
C04230_03	LysoPC (18:4(6Z,9Z,12Z,15Z))	HMDB0010389	0.428	1.753	0.039	0.115
C04230_04	LysoPC (20:3(5Z,8Z,11Z))	HMDB0010393	0.412	1.945	0.019	0.065
C04230_05	LysoPC (20:3(8Z,11Z,14Z))	HMDB0010394	0.352	1.835	0.030	0.096
C04424	S-(2-Methylpropionyl)-dihydrolipoamide-E	HMDB0006868	4.537	1.573	0.041	0.111
C04483	Deoxycholic acid	HMDB0000626	0.622	1.705	0.021	0.016
C05598	Phenylacetyl glycine	HMDB0000821	2.595	2.051	0.038	0.094
C08313	3-Methylindole	HMDB0000466	0.503	2.534	0.009	0.012
C15497	(24R)-Cholest-5-ene-3-beta,24-diol	HMDB0011643	6.172	2.338	0.038	0.029

Note: “p.adjusted (1)” was the p-value obtained after adjusting for age. “p.adjusted (2)” was the p-value obtained after adjusting for biochemical parameters, including FBG and urea.

Supplementary Table 3 The correlation (P-value) between biochemical parameters and discriminatory metabolites from vitreous

Biochemical parameter	C00408	C00831	C01879	C04148	C15497
Albumin	0.630	0.087	0.005	0.029	0.338
Albumin/ Globulin	0.933	0.091	0.552	0.233	0.879
Aspartate transaminase (AST)	0.231	0.143	0.022	0.203	0.477
AST/ ALT	0.630	0.603	0.111	0.643	0.331
Glucose	0.012	0.480	0.321	0.800	0.724
Chlorine	0.091	0.737	0.089	0.667	0.970
Creatinine	0.548	0.149	0.024	0.095	0.179
Globulin	0.585	0.400	0.395	0.888	0.533
Lactate dehydrogenase	0.937	0.637	0.990	0.932	0.017
Mitochondrial AST	0.836	0.743	0.424	0.670	0.976
Potassium	0.381	0.229	0.953	0.249	0.374
Retinol binding protein	0.321	0.660	0.481	0.357	0.062
Alanine aminotransferase	0.223	0.066	0.001	0.079	0.282
Alkaline phosphatase	0.486	0.174	0.955	0.127	0.095
Bilirubin direct	0.401	0.047	0.839	0.023	0.039
Bilirubin indirect	0.548	0.464	0.734	0.332	0.176
Prealbumin	0.696	0.586	0.121	0.856	0.441
Total bile acids	0.955	0.768	0.418	0.724	0.385
Bilirubin total	0.884	0.215	0.858	0.129	0.083
Total cholesterol determination	0.582	0.578	0.680	0.709	0.541
Triglycerides	0.134	0.311	0.003	0.328	0.068

Uric acid	0.949	0.825	0.047	0.725	0.560
γ -glutamine acylase	0.200	0.189	0.188	0.398	0.127
Sodium	0.174	0.260	0.581	0.219	0.233
Total protein	0.492	0.497	0.011	0.147	0.282
Urea	0.168	0.009	0.010	0.004	0.011

Supplementary Table 4 The correlation (P-value) between biochemical parameters and discriminatory metabolites from plasma

	C00408	C00831	C01879	C04148	C15497
Albumin	0.267	0.048	0.003	0.002	0.001
Albumin/ Globulin	0.085	0.015	0.090	0.090	0.302
Aspartate transaminase (AST)	0.588	0.712	0.934	0.915	0.384
AST/ ALT	0.633	0.163	0.690	0.630	0.839
Glucose	0.008	0.196	0.170	0.143	0.368
Chlorine	0.958	0.680	0.634	0.566	0.267
Creatinine	0.040	0.509	0.000	0.000	0.000
Globulin	0.264	0.439	0.888	0.885	0.374
Lactate dehydrogenase	0.611	0.424	0.416	0.449	0.008
Mitochondrial AST	0.622	0.255	0.254	0.318	0.845
Potassium	0.419	0.130	0.024	0.014	0.225
Retinol binding protein	0.129	0.625	0.010	0.003	0.005
Alanine aminotransferase	0.446	0.512	0.880	0.911	0.240
Alkaline phosphatase	0.403	0.699	0.438	0.694	0.266
Bilirubin direct	0.040	0.059	0.103	0.064	0.046
Bilirubin indirect	0.092	0.044	0.462	0.396	0.040
Prealbumin	0.068	0.898	0.032	0.020	0.091
Total Bile Acids	0.272	0.050	0.724	0.662	0.075
Bilirubin total	0.047	0.029	0.260	0.198	0.025
Total Cholesterol determination	0.536	0.710	0.522	0.524	0.805
Triglycerides	0.919	0.009	0.999	0.714	0.724

Uric acid	0.258	0.347	0.123	0.116	0.000
γ -glutamine acylase	0.913	0.217	0.325	0.313	0.502
Sodium	0.804	0.639	0.922	0.855	0.570
Total protein	0.913	0.381	0.040	0.033	0.007
Urea	0.026	0.104	0.000	0.000	0.000
