Table S1 The main metabolites of HP were significantly different from those of crucian carp infected with *A. hydrophila.*

Class	Metabolite	VIP	FC	P_value	Regulate
Glycerophospholipids	LysoPE(0:0/20:2(11Z,14Z))	2.2878	0.8592	0.0179	down
	LysoPE(18:3(9Z,12Z,15Z)/0:0)	2.4251	0.8813	0.0004522	down
	PGP(i-12:0/i-14:0)	1.9956	0.8909	0.0177	down
	LysoPE(0:0/20:3(8Z,11Z,14Z))	2.0064	0.8913	0.007411	down
	PC(17:2(9Z,12Z)/0:0)	1.8634	0.9433	0.0006157	down
	LysoPE(20:3(5Z,8Z,11Z)/0:0)	1.9037	0.9115	0.004871	down
	PC(18:0/20:4(8Z,11Z,14Z,17Z))	1.9649	1.0976	0.01587	up
	1-Oleoylglycerophosphoserine	1.7908	0.9276	0.00241	down
	PS(20:4(8Z,11Z,14Z,17Z)/14:0)	1.6822	0.9355	0.003818	down
	1-eicosanoyl-glycero-3-phosphate	1.6031	0.9371	0.01139	down
	PS(15:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	1.6908	0.9281	0.00997	down
	PC(16:1(9E)/0:0)	1.5358	0.9413	0.007616	down
	1-Linoleoyl-sn-Glycero-3-Phosphocholine	1.5643	0.956	0.01267	down
	LysoPE(18:1(11Z)/0:0)	1.6138	0.9496	0.001356	down
	PS(18:1(9Z)/0:0)	1.5523	0.9426	0.01924	down
	LysoPA(20:2(11Z,14Z)/0:0)	1.6275	0.9358	0.01512	down
	LysoPE(22:2(13Z,16Z)/0:0)	1.4483	0.9419	0.01828	down
	LysoPE(18:2(9Z,12Z)/0:0)	1.6153	0.9452	0.003924	down
	LysoPC(18:3(9Z,12Z,15Z)/0:0)	1.4894	0.9504	0.02359	down
	PC(15:0/0:0)	1.5311	0.9563	0.00107	down
	LysoPC(20:3(8Z,11Z,14Z)/0:0)	1.5279	0.9543	0.03169	down
	PC(20:1(11Z)/14:0)	1.6106	1.0596	0.04311	up
	1-Stearoylglycerophosphoserine	1.481	0.946	0.00649	down
	(2R)-2-{[(9Z)-Hexadec-9-enoyl]oxy}-3-hydroxypropyl	1.2842	0.9647	0.01716	down

	2-(trimethylazaniumyl)ethyl phosphate				
	LysoPC(20:1(11Z)/0:0)	1.2919	0.9632	0.02415	down
	LysoPC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	1.4658	0.9583	0.04341	down
	1-O-Hexadecyl-sn-glycero-3-phosphocholine	1.8534	1.0476	0.00197	up
	LysoPE(0:0/18:1(11Z))	1.383	0.9543	0.02457	down
	LysoPC(0:0/18:2(9Z,12Z))	1.2124	0.9711	0.02623	down
	LysoPC(18:3(6Z,9Z,12Z)/0:0)	1.2716	0.97	0.008159	down
Fatty Acyls	(11E,13Z)-10-Hydroxyoctadeca-11,13-dienoylcarnitine	2.391	0.8768	7.76E-05	down
	N-(2-Hydroxyisobutyl)-2,4,8,10,12-tetradecapentaenamide	2.7827	1.4096	0.04586	up
	10-Hydroxy-E4-neuroprostane	2.1979	1.189	0.04084	up
	Linoleic Acid	1.7339	0.9347	0.005758	down
	7,10,13,16,19-Docosapentaenoic acid	1.7087	0.9389	0.00433	down
	Citronellyl formate	1.768	0.9089	0.01355	down
	Docosahexaenoic Acid	1.3136	0.9688	0.003588	down
	Prostaglandin D3	1.1141	1.0325	0.02274	up
	Tetranor-PGFM	1.7021	0.9205	0.03134	down
	Ethyl Myristate	1.1783	0.9686	0.01178	down
	13,14-Dihydro-15-keto-PGE2	1.0306	1.0259	0.02161	up
	Resolvin E2	1.0899	1.0338	0.04871	up
	(5Z)-(15S)-11alpha-Hydroxy-9,15-dioxoprostanoate	1.1357	1.0274	0.02923	up
Carboxylic acids and derivatives	Glycylserylprolylmethionylphenylalanylvalinamide	2.3206	0.8516	0.01542	down
	L-Pyroglutamyl-L-histidyl-3,3-dimethylprolinamide	2.0171	0.8764	0.04205	down
	Kinetensin 4-7	2.89	1.2627	0.01708	up
	Neuromedin N	1.5785	0.9166	0.03845	down
	L-2-Amino-3-oxobutanoic acid	1.7096	0.9006	0.01764	down
	Furylacryloylalanyllysine	1.513	0.9298	0.02901	down

	Deoxyspergualin	1.8455	0.9173	0.01701	down
	Argininic acid	1.5956	0.9508	0.002366	down
	Gamma-Glutamylglutamic acid	1.5505	0.9368	0.007838	down
	N-Acetyl-L-Histidine	1.5568	1.0511	0.009063	up
	Ipamorelin	1.2877	0.959	0.04788	down
	N-Linoleoyl Glutamine	1.2966	0.9469	0.02667	down
	Isodesmosine	1.5331	0.9402	0.03214	down
	Gamma-Glutamylglutamine	1.3051	0.9523	0.02491	down
	Glutamylisoleucine	1.1806	0.9629	0.03037	down
	Asparaginylisoleucine	1.1366	0.9653	0.01957	down
	Glucitol-lysine	1.4282	1.0548	0.01561	up
	Aspartyl-Isoleucine	1.0138	0.9723	0.03126	down
	Leucylproline	1.1583	0.96	0.03728	down
	L-Canaline	1.1084	1.0334	0.01682	up
	Beta-Hydroxy-gamma-trimethylaminobutyric acid	1.1962	1.0371	0.002287	up
	Succinic Acid	1.0558	0.972	0.03908	down
	N-Palmitoyl Histidine	1.005	0.9681	0.0387	down
	Isoleucylproline	1.1471	1.0483	0.04396	up
	Acivicin	0.9176	1.028	0.009234	up
	Prolyl-Valine	1.363	1.0463	0.01582	up
Benzene and substituted derivatives	((4-(3-(4-Fluoro-alpha-hydroxybenzyl)-4-hydroxyphenoxy)-3,5-dimethy lphenyl)amino)oxoacetate	2.9875	1.264	0.04067	up
	4-Methylbenzoic Acid	2.083	1.1625	0.03165	up
	Diamfenetide	1.6935	0.907	0.03724	down
	Lasinavir	1.3562	1.0557	0.02947	up
Indoles and derivatives	Alpha-(Dimethylaminomethyl)-2-(3-ethyl-5-methyl-4-isoxazolyl)-1H-in	1.6694	0.9266	0.01274	down

	dole-3-methanol				
	2-Amino-Alpha-Carboline	2.1905	0.8597	0.01987	down
	Indolelactic acid	1.5616	1.067	0.04687	up
Organooxygen compounds	(2S,3S,4S,5S)-2-(5-Amino-7-methyl-2,6,7,9,11-pentazatricyclo[6.3.1.04,12]dodeca-1(12),3,5,8,10-pentaen-2-yl)-5-(hydroxymethyl)oxolane-3,4-diol	2.1783	1.1531	0.01744	up
	Risbitin	1.3164	1.0564	0.01706	up
	Erythromycin C	1.3839	0.9516	0.008831	down
	2-Isopropoxyethanol	1.3863	1.0608	0.02147	up
	4,4alpha,5,6-Tetrahydro-7-methyl-2(3H)-naphthalenone	0.9301	1.0253	0.04272	up
Prenol lipids	Ret-P-man	2.9992	1.2517	0.01802	up
	Sambutoxin	2.1366	0.8989	0.001112	down
	Goshonoside F7	1.5612	0.943	0.01153	down
	Germacrone	1.6254	1.0735	0.02547	up
	Contignasterol	1.3667	0.9572	0.01363	down
	4,5-Dihydrovomifoliol	1.9352	0.8974	0.04412	down
	(R)-Carvone	0.8222	1.0211	0.02724	up
Steroids and steroid derivatives	18-Hydroxycorticosterone	1.8289	1.0858	0.04794	up
	Asparagoside B	1.6871	1.0895	0.02149	up
	Uzarigenin 3-[xylosyl-(1->2)-rhamnoside]	1.8011	0.9189	0.02182	down
	Cucurbitacin A	1.4064	0.9514	0.04237	down
	Taurochenodesoxycholic acid	1.3595	0.9546	0.01721	down
	Rocuronium	1.3497	0.9688	0.01272	down
	Norethindrone	1.2516	1.038	0.007272	up
	Drostanolone	1.2875	0.9647	0.006007	down
Purine nucleosides	2,6-Diaminopurine 2',3'-dideoxyriboside	1.825	1.0971	0.03659	up

	ADP	1.0293	1.0346	0.04737	up
Pyridines and derivatives	Nicoboxil	2.5274	1.2395	0.03732	up
	Gymnodimine	1.7938	0.9284	0.000753	down
	Y-27632 Dihydrochloride	1.6422	0.9052	0.044	down
	N-Cyano-N'-(1,1-dimethylpropyl)-N''-(3-pyridinyl)guanidine	1.5409	0.9405	0.01054	down
Azoles	Aminophenazone	1.6059	0.9492	0.001009	down
Benzimidazole ribonucleosides and ribonucleotides	N1-(5-Phospho-a-D-ribosyl)-5,6-dimethylbenzimidazole	1.2789	1.0519	0.006049	up
Benzothiazines	Promazine	1.7167	1.0694	0.001513	up
Cinnamic acids and derivatives	Neogitogenin 3-[glucosyl-(1->2)-glucosyl-(1->4)-galactoside]	1.2218	1.0584	0.04113	up
Flavonoids	Pelargonidin 3-sophoroside	1.7936	0.9241	0.02801	down
Glycerolipids	DG(14:1(9Z)/14:1(9Z)/0:0)	2.349	1.1585	0.007417	up
Homoisoflavonoids	1-(3-(4-Phenylbenzyl)-4-hydroxychroman-7-yl)cyclopentane-1-carboxylic acid	2.2151	0.8307	0.03441	down
Imidazopyrimidines	Caffeine	1.8101	0.89	0.04837	down
Indanes	Metabolite M6	1.2644	1.0389	0.01708	up
Macrolides and analogues	Pectenotoxin 2	1.7801	1.102	0.01227	up
Naphthalenes	2,6-Dimethylnaphthalene	1.0278	1.0306	0.01588	up
Naphthopyrans	Penitrem A	1.4342	0.9312	0.03899	down
Organic sulfonic acids and derivatives	2-Hydroxyethanesulfonate	1.1036	1.0322	0.03914	up
Peptidomimetics	Destruxin E	1.463	0.9301	0.04935	down
Phenanthrenes and derivatives	7-Benzylidenenaltrexone	1.7394	0.9123	0.03713	down
Phenols	Eugenol	0.8319	1.023	0.03011	up
Piperidines	Fagomine	1.0774	1.0489	0.04719	up
Polypeptides	Solnatide	1.9477	1.1324	0.04719	up
Quinolines and derivatives	Mefloquine	1.3807	1.0957	0.04093	up

Stilbenes	Dibenzo-P-dioxin	1.8851	1.1378	0.0343	up
Strychnos alkaloids	19-Epischolaricine	2.2066	1.1945	0.03658	up
other	Phe Asp Thr Gly Leu	2.7386	1.3935	0.03119	up
	4-Piperidinone, 1-hydroxy-2,2,6,6-tetramethyl-	2.2865	1.2574	0.02895	up
	Arachidonoyl PAF C-16	2.1733	1.136	0.03401	up
	PE(18:2/0:0)	2.068	0.9326	0.0001197	down
	PE(20:3/0:0)	2.088	0.9344	0.0001665	down
	1-O-Hexadecyl-2-C-Methyl-3-Phosphatidylcholine	2.3444	1.1841	0.03334	up
	4-[[1-(3,4-difluorobenzoyl)piperidin-3-yl]methoxy]-N-propan-2-ylbenzamide	2.1742	1.1534	0.04243	up
	PE(16:1/0:0)	1.7366	0.923	0.01426	down
	Tyr Ala	1.824	1.129	0.008008	up
	PE(18:1(9Z)/0:0)	1.7078	0.9488	0.003163	down
	L-a-Lysophosphatidylserine	1.5601	0.947	0.009217	down
	N-Acetyl-DL-Aspartic Acid	1.1508	1.0543	0.03959	up
	2,3-Diaminopyridine	1.1211	1.0279	0.00552	up
	Val Ile Asp Lys	1.1644	0.9549	0.04217	down
	Leu Val Ala	1.233	1.0326	0.01535	up
	Val Ala Ala	1.2053	1.0327	0.03053	up
	PS(5-iso PGF2VI/14:0)	1.6967	0.9128	0.04455	down
	CDP-DG(TXB2/22:5(4Z,7Z,10Z,13Z,16Z))	2.1624	1.1973	0.02845	up
	CDP-DG(20:4(6Z,8E,10E,14Z)-2OH(5S,12R)/i-15:0)	1.7676	1.1177	0.03685	up
	DG(2:0/20:3(8Z,11Z,14Z)-2OH(5,6)/0:0)	1.6201	0.9344	0.01068	down
	CDP-DG(PGF1alpha/i-22:0)	1.9017	1.1051	0.001799	up
	PGP(LTE4/16:1(9Z))	1.7485	1.0949	0.03229	up
	Deoxycholyl-L-dopa	1.3556	0.9585	0.01166	down

Not Available	PC(20:4(8Z,11Z,14Z,17Z)-2OH(5S,6R)/2:0)	1.4279	0.9422	0.01681	down

VIP: VIP value of the metabolite in OPLS-DA model between the two groups; P-value: test result of the significance of the difference of the metabolite between the two samples, VIP > 1, P-value < 0.05 was the metabolic difference between the two groups; FC(HPAS/CG): differential expression ratio of this metabolite between the two groups; Adducts: Stable structures formed by covalent bonds between metabolites and cellular macromolecules.