Supplementary materials and methods

16S rRNA sequencing

16S rRNA sequencing was performed using the fecal genomic DNA kit (Tiangen, China). Source DNA was extracted from colon contents by CTAB / SDS method. The V3-V4 variable region of 16S rRNA gene was amplified by PCR using specific primers. The product was purified by Vazyme VAHTSTM DNA Clean Beads and quantified by Quant-iT PicoGreen dsDNA Assay Kit. The TruSeg Nano DNA LT Library Prep Kit of Lumina company was used to prepare the sequencing library. Sequencing was performed using the ilumina NovaSeg platform and NovaSeg 6000 SP Reagent Kit.

High-resolution non-target metabolomics

After the feces samples were slowly thawed at 4°C, an appropriate amount of samples were added with pre-cooled methanol/acetonitrile/water solution (2:2:1, v/v), vortexed and mixed, and ultrasonicated at low temperature for 30 min, standing at -20 °C for 10 min, centrifuged at 14000 g 4 °C for 20 min, and the supernatant was vacuum dried. During mass spectrometry analysis, 100 μL acetonitrile aqueous solution (acetonitrile: water = 1: 1, v/v) was added for reconstitution, vortexed, centrifuged at 14000 g 4 °C for 15 min, and the supernatant was injected for analysis. The samples were separated by Agilent 1290 Infinity LC ultra-high performance liquid chromatography (UHPLC) HILIC column. The injection volume was 2 μL, and the column temperature was 25 °C. The flow rate was 0.5 mL/min. The chromatographic mobile phase A was water + 25 mM ammonium acetate + 25 mM ammonia, and B was acetonitrile. The gradient elution procedure was as follows: 0-0.5 min, 95 % B; 0.5-7min, B from 95 % linear change to 65 %; 7-8 min, B changed linearly from 65 % to 40 %; 8-9 min, B maintained at 40 %; 9--9.1 min, B from 40 % linearity Change to 95 %; 9.1-12 min, B maintained at 95 %; The samples were detected by electrospray ionization (ESI) in positive and negative ion modes. After UPLC separation, the samples were analyzed using an OE Plus mass spectrometer. MSDIAL 4.9 software was used to extract the peak of the data. The identification of metabolites was carried out by

accurate mass number matching and secondary spectrum matching. The structures of metabolites were identified by searching HMDB, MassBank, GNPS, other public databases, and the self-built metabolite standard library. Multidimensional statistical analysis of mass spectrometry data was performed using Python software.

Supplementary Table 1 Potential biomarkers screened out in rat fecal samples

ID	m/z	RT (s)	Name	Adduct	OVX *vs* Sham	XLGB-M *vs* OVX	VIP (O/S)	*P* value (O/S)	VIP (X/O)	*P* value (X/O)
M509T150	509.28185	150.1720	1-oleoyl-2-hydroxy-sn-glycero-3-phospho-(1′-rac-glycerol)	[M-H]-	↑	↓	4.546500178	0.014895433	4.567744903	0.008458047
M527T34_1	527.26091	34.0880	2-cis-4-trans-abscisic acid	[2M-H]-	↓	↑	1.583357459	0.048913908	2.143606413	0.003274839
M177T317	177.04010	317.3840	2-dehydro-3-deoxy-d-gluconate	[M-H]-	↑	↓	3.254864708	0.011026677	2.632453872	0.042151942
M115T71	115.04039	70.7140	Alpha-ketoisovaleric acid	[M-H]-	↑	↓	7.057349542	0.037390985	6.805732691	0.036880202
M101T97	101.02498	96.8160	D-arabitol	[M-H-CH6O2]-	↑	↓	4.099024245	0.020567519	4.049233849	0.008301153
M391T164_2	391.28356	163.5570	Deoxycholic acid	[M-H]-	↓	↑	16.08941013	0.02802987	30.94842577	0.010095025
M497T33	497.28757	32.6590	Ganoderic acid a	[M-H-H2O]-	↓	↑	3.219954423	0.049727503	3.042676897	0.048182209
M809T34	809.47510	34.4710	Pg(16:0/10-hdohe)	[M-H]-	↑	↓	1.766586197	0.031704392	1.725522753	0.026334912
M163T54	163.03951	54.2960	Phenylpyruvate	[M-H]-	↑	↓	2.20090066	0.008430385	1.927564994	0.019095041
M335T106	335.21923	106.2415	Prostaglandin b1	[M-H]-	↓	↑	1.224800518	0.008893563	1.257939937	0.003033768
M160T65	160.04015	65.2420	Quinoline-2,8-diol	[M-H]-	↑	↓	2.99711335	0.038699712	2.628304945	0.045404645
M124T299	124.00744	298.9150	Taurine	[M-H]-	↓	↑	1.952688583	0.02677415	4.193586693	0.017836225
M151T217	151.02679	216.5485	Xanthine	[M-H]-	↑	↓	6.438382221	0.041063412	6.39170024	0.031022479
M473T33	473.39560	33.0365	.alpha.-tocopheryl acetate	[M+H]+	↑	↓	3.726792985	0.034355734	3.758549045	0.020612677
M363T415	363.18787	415.0900	Asp-Thr-Lys	[M+H]+	↑	↓	1.016161155	0.047587967	1.000319772	0.018015682
M551T35	551.41946	35.0035	Celaxanthin	[M+H]+	↑	↓	4.050424209	0.006668467	3.989447291	0.000764127
M397T89	397.30646	89.1860	Diosgenin	[M+H-H2O]+	↓	↑	2.066560656	0.030143451	1.674487497	0.008132631
M231T344	231.14307	343.7730	DL-proline	[2M+H]+	↑	↓	1.888911412	0.006564528	1.658963268	0.011400344
M434T390_2	434.18627	390.0120	Fluvastatin	[M+Na]+	↑	↓	11.14704537	0.008940996	8.777138091	0.00676892
M405T380	405.16193	379.5400	Furathiocarb	[M+Na]+	↑	↓	1.088785632	0.044630995	1.114354671	0.013374768
M285T50	285.07331	49.9710	Glu-His	[M+H]+	↓	↑	1.84823615	0.049954138	2.587544055	0.023179753
M324T294	324.21399	293.9910	Lsd	[M+H]+	↑	↓	2.337235133	0.031342223	2.200303006	0.01870394
M492T36	492.47266	35.6670	N-(1,3-dihydroxyoctadec-4-en-2-yl)tetradecanamide	[M+H-H2O]-	↑	↓	1.438480825	0.0424974	1.395607428	0.005045224
M484T34	484.46790	34.3465	N-lauroyl-d-erythro-sphinganine	[M+H]+	↑	↓	1.161580612	0.004498021	1.226387111	0.002764276

M162T64	162.05329	63.9710	N-methyl-l-glutamic acid	[M+H]+	↑	↓	8.083416876	0.015390635	5.831527164	0.034010435
M124T218	124.03817	218.2550	Nicotinate	[M+H]+	↑	↓	3.514574116	0.028846337	3.096844125	0.024129163
M313T410	313.13675	410.2475	Olanzapine	[M+H]+	↑	↓	1.438001214	0.003668787	1.242778033	0.001051155
M461T298_1	461.16971	298.2790	Oxytetracycline	[M+H]+	↑	↓	2.162316982	0.025222811	1.633681474	0.026829659
M341T418	341.17792	417.6950	Pentamidine	[M+H]+	↑	↓	2.205583913	0.04224744	2.001199623	0.03192067
M202T88	202.10555	87.7930	Pro-Met-Arg	[M+2H]2+	↑	↓	1.375418002	0.0441646	1.512917768	0.005724115
M411T34	411.35862	34.3435	Stigmasta-4,22-dien-3-one	[M+H]+	↑	↓	2.559374993	0.042208814	3.271710335	0.005598789

'S' represents the Sham group; 'O' represents the OVX group; 'X' represents the XLGB-M group; ↑ means up, ↓ means down