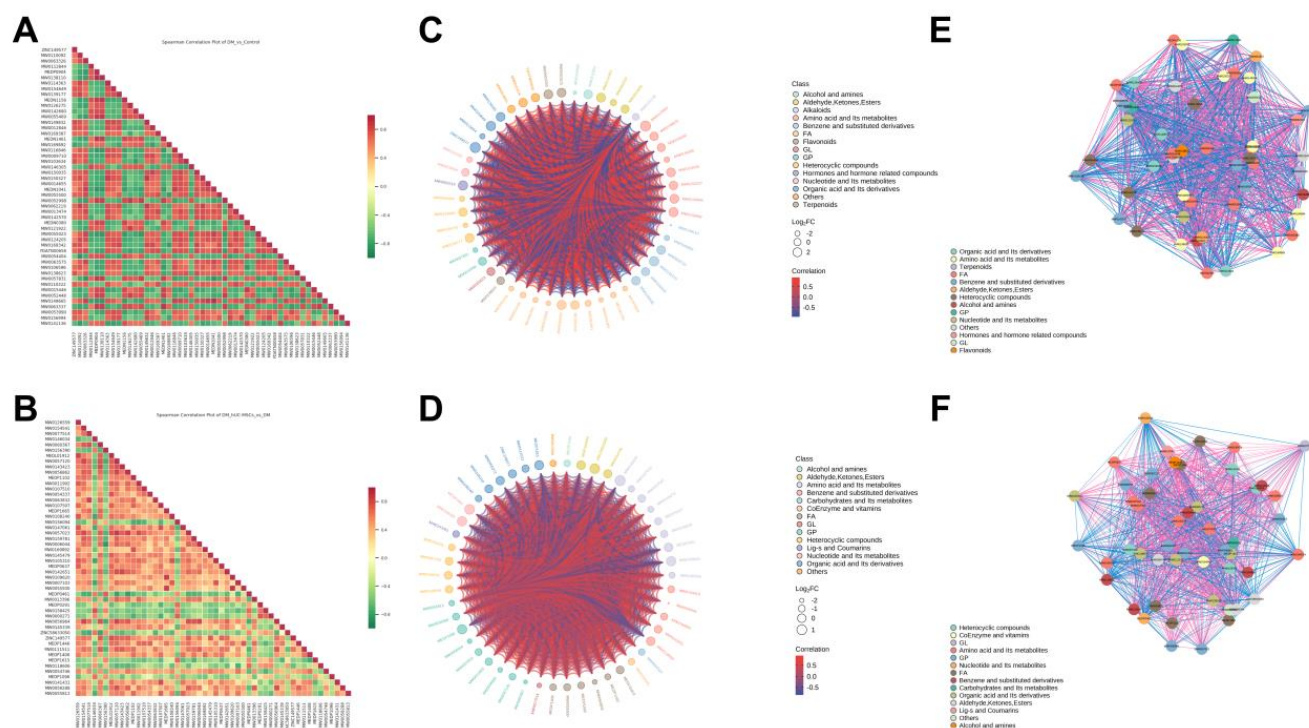


Supplementary material



Supplementary Figure 1 Correlation analysis of the differential metabolites in liver samples from each group. A and B: Correlation heatmaps of the differential metabolites between the DM group and the Control group (A) and between the DM + hUC-MSCs group and the DM group (B). Red represents a positive correlation and green represents a negative correlation; the color intensity is proportional to the absolute value of the correlation coefficient between the samples; C and D: Correlation chord diagrams for the differential metabolites between the DM group and the Control group (C) and between the DM + hUC-MSCs group and the DM group (D). The size of the dots reflects the log₂ fold-change (FC) values for the differential metabolites and the color of the dots corresponds to the different categories. Red lines represent positive correlations and blue lines represent negative correlations; E and F: Correlation network diagrams of the differential metabolites between the DM group and the Control group (E) and between the DM + hUC-MSCs group and the DM group (F). The nodes represent different metabolites while the size of each node is positively correlated with the degree value. Red lines represent positive correlations and blue lines represent negative correlations; the

thickness of the lines is proportional to the strength of the correlation. The correlation heatmap, chord diagram, and network diagram display the top 50 differential metabolites based on VIP-value ranking. Control group, $n = 8$; DM group, $n = 6$; DM + hUC-MSCs group, $n = 5$.

**Supplementary Table 1 Results of the KEGG pathway enrichment analysis
for intersecting differential metabolites**

Pathway	Classification level 1	Classification level 2	<i>P</i> value	Enrichment score
Olfactory transduction	Organismal Systems	Sensory system	0.012	80.500
Phototransduction	Organismal Systems	Sensory system	0.012	80.500
Circadian entrainment	Organismal Systems	Environmental adaptation	0.014	71.556
Long-term depression	Organismal Systems	Nervous system	0.014	71.556
cGMP-PKG signaling pathway	Environmental Information Processing	Signal transduction	0.015	64.400
Gap junction	Cellular Processes	Cellular community - eukaryotes	0.017	58.545
Oxytocin signaling pathway	Organismal Systems	Endocrine system	0.019	53.667
Vascular smooth muscle contraction	Organismal Systems	Circulatory system	0.020	49.538
Platelet activation	Organismal Systems	Immune system	0.022	46.000
Regulation of lipolysis in adipocytes	Organismal Systems	Endocrine system	0.022	46.000
Renin secretion	Organismal Systems	Endocrine system	0.026	37.882
Salivary secretion	Organismal Systems	Digestive system	0.071	37.882
Aldosterone synthesis and secretion	Organismal Systems	Endocrine system	0.032	30.667
Bile secretion	Organismal Systems	Digestive system	0.034	29.273
Thermogenesis	Organismal Systems	Environmental adaptation	0.035	28.000
Alanine, aspartate and glutamate metabolism	Metabolism	Amino acid metabolism	0.043	23.000
Vitamin B6 metabolism	Metabolism	Metabolism of cofactors and vitamins	0.056	22.207

Pentose phosphate pathway	Metabolism	Carbohydrate metabolism	0.044	17.405
Primary bile acid biosynthesis	Metabolism	Lipid metabolism	0.026	13.702
Purine metabolism	Metabolism	Nucleotide metabolism	0.009	12.752

Classification level 1 and Classification level 2 represent primary classification and secondary classification, respectively; A *P* value of < 0.05 indicates that the enrichment pathway is statistically significant.

Supplementary Table 2 Correlation analysis between differential metabolites and biochemical indexes in the diabetes mellitus group *versus* Control group comparison

Biochemical index	Differential metabolite ID	Correlation coefficient	<i>P</i> value
FBG	MW0129372	-0.876388232	< 0.001
FBG	ZINC149577	0.796917259	< 0.001
FBG	MEDP1665	0.874180705	< 0.001
FBG	MW0105310	0.81899253	< 0.001
FBG	MW0055500	0.889633395	< 0.001
FBG	MEDP1381	0.805747367	< 0.001
FBG	MW0109620	0.883010814	< 0.001
FBG	MW0115265	0.783672097	< 0.001
FBG	MW0053910	0.843275327	< 0.001
FBG	MW0111511	0.827822638	< 0.001
FBG	MW0008605	0.865350597	< 0.001
FBG	MW0056727	-0.801332313	< 0.001
FBG	MW0007103	0.790294678	< 0.001
FBG	MEDP1440	0.724068867	< 0.01
FBG	MW0106195	0.708616178	< 0.01
FBG	MW0002133	0.693163489	< 0.01
FBG	FDATN01012	0.774841989	< 0.01
FBG	MEDL01912	0.772634462	< 0.01
FBG	MW0050103	0.724068867	< 0.01
FBG	MW0138813	0.761596827	< 0.01
FBG	MW0077514	0.774841989	< 0.01
FBG	MW0063832	0.717446286	< 0.01
FBG	MW0006044	0.746144137	< 0.01
FBG	MW0106596	0.748351664	< 0.01
FBG	MEDL02562	0.69978607	< 0.01
FBG	MW0152475	0.679918326	< 0.01
FBG	MW0009714	0.673295745	< 0.01

FBG	MW0108240	0.719653813	< 0.01
FBG	MW0118606	-0.697578543	< 0.01
FBG	MW0124440	0.710823705	< 0.01
FBG	MEDP1434	0.713031232	< 0.01
FBG	MEDN1575	-0.735106502	< 0.01
FBG	MW0128125	0.697578543	< 0.01
FBG	MW0010041	0.739521556	< 0.01
FBG	MW0054746	0.567334448	< 0.05
FBG	MW0009539	0.560711867	< 0.05
FBG	MW0123852	0.538636596	< 0.05
FBG	MW0124143	0.593824772	< 0.05
FBG	MEDN1113	0.613692515	< 0.05
FBG	MW0159225	0.651220475	< 0.05
FBG	MEDN0161	0.624730151	< 0.05
FBG	MW0017091	0.626937678	< 0.05
FBG	MW0052323	0.657843056	< 0.05
FBG	MEDP2111	0.660050583	< 0.05
FBG	MW0014190	0.657843056	< 0.05
FBG	MEDP1524	0.60265488	< 0.05
FBG	MW0168835	0.593824772	< 0.05
FBG	MW0013853	0.615900042	< 0.05
FBG	MW0156774	0.560711867	< 0.05
FBG	MW0016971	0.644597894	< 0.05
FBG	MW0160275	-0.646805421	< 0.05
FBG	MW0063704	-0.653428002	< 0.05
FBG	MW0152568	0.615900042	< 0.05
FBG	MW0152097	0.651220475	< 0.05
FBG	MW0150760	0.591617245	< 0.05
FBG	MW0137976	-0.637975313	< 0.05
FBG	MW0107510	0.562919394	< 0.05
FBG	MW0144016	0.55850434	< 0.05

TG	ZINC149577	0.806593407	< 0.001
TG	MW0108240	0.850549451	< 0.001
TG	MEDP1434	0.810989011	< 0.001
TG	MW0128125	0.806593407	< 0.001
TG	MW0129372	-0.718681319	< 0.01
TG	MW0055500	0.679120879	< 0.01
TG	MEDP1381	0.687912088	< 0.01
TG	MEDP1440	0.762637363	< 0.01
TG	MW0052323	0.701098901	< 0.01
TG	MW0158316	-0.731868132	< 0.01
TG	MW0106195	0.696703297	< 0.01
TG	FDATN01012	0.714285714	< 0.01
TG	MW0050103	0.753846154	< 0.01
TG	MW0111511	0.727472527	< 0.01
TG	MW0063832	0.762637363	< 0.01
TG	MW0006044	0.784615385	< 0.01
TG	MW0008605	0.758241758	< 0.01
TG	MW0106596	0.705494505	< 0.01
TG	MW0152475	0.775824176	< 0.01
TG	MW0118606	-0.723076923	< 0.01
TG	MW0056727	-0.740659341	< 0.01
TG	MW0156686	0.749450549	< 0.01
TG	MW0110455	0.679120879	< 0.01
TG	MW0054746	0.674725275	< 0.05
TG	MEDP1665	0.621978022	< 0.05
TG	MW0009539	0.621978022	< 0.05
TG	MW0105310	0.551648352	< 0.05
TG	MW0123852	0.551648352	< 0.05
TG	MW0124143	0.630769231	< 0.05
TG	MEDN1113	0.586813187	< 0.05
TG	MW0159225	0.630769231	< 0.05

TG	MW0017091	0.578021978	< 0.05
TG	MEDP2111	0.591208791	< 0.05
TG	MW0014190	0.578021978	< 0.05
TG	MW0109620	0.617582418	< 0.05
TG	MW0115265	0.573626374	< 0.05
TG	MW0053910	0.657142857	< 0.05
TG	MEDP1524	0.578021978	< 0.05
TG	MW0168835	0.613186813	< 0.05
TG	MW0126559	0.613186813	< 0.05
TG	MW0013853	0.608791209	< 0.05
TG	MW0138813	0.665934066	< 0.05
TG	MW0156774	0.621978022	< 0.05
TG	MW0016971	0.595604396	< 0.05
TG	MW0160275	-0.665934066	< 0.05
TG	MW0063704	-0.657142857	< 0.05
TG	MEDL02562	0.67032967	< 0.05
TG	MW0009714	0.67032967	< 0.05
TG	MW0150760	0.582417582	< 0.05
TG	MW0137976	-0.630769231	< 0.05
TG	MW0107510	0.617582418	< 0.05
TG	MW0124440	0.652747253	< 0.05
TG	MEDN1575	-0.652747253	< 0.05
ALT	MW0129372	-0.785479023	< 0.001
ALT	MW0105310	0.783278802	< 0.001
ALT	MEDP1440	0.809681458	< 0.001
ALT	MW0106195	0.851485664	< 0.001
ALT	MW0126559	0.78107858	< 0.001
ALT	FDATN01012	0.840484557	< 0.001
ALT	MW0008605	0.787679245	< 0.001
ALT	MW0160275	-0.860286549	< 0.001
ALT	MW0063704	-0.816282122	< 0.001

ALT	MW0152475	0.794279909	< 0.001
ALT	MW0108240	0.906491198	< 0.001
ALT	MW0137976	-0.789879466	< 0.001
ALT	MW0056727	-0.783278802	< 0.001
ALT	MW0128125	0.853685885	< 0.001
ALT	ZINC149577	0.761276588	< 0.01
ALT	MW0009539	0.662266627	< 0.01
ALT	MW0055500	0.741474596	< 0.01
ALT	MEDP1381	0.662266627	< 0.01
ALT	MEDN0161	0.66666707	< 0.01
ALT	MW0052323	0.750275482	< 0.01
ALT	MEDP2111	0.671067513	< 0.01
ALT	MW0109620	0.695269948	< 0.01
ALT	MW0115265	0.745875039	< 0.01
ALT	MW0053910	0.756876146	< 0.01
ALT	MW0002133	0.772277695	< 0.01
ALT	MEDL01912	0.686469062	< 0.01
ALT	MW0138813	0.717272161	< 0.01
ALT	MW0111511	0.754675924	< 0.01
ALT	MW0106596	0.708471276	< 0.01
ALT	MEDL02562	0.71507194	< 0.01
ALT	MW0009714	0.719472383	< 0.01
ALT	MW0118606	-0.743674817	< 0.01
ALT	MW0124440	0.675467955	< 0.01
ALT	MEDP1434	0.752475703	< 0.01
ALT	MW0010041	0.726073047	< 0.01
ALT	MW0054746	0.572057552	< 0.05
ALT	MW0129025	-0.607261094	< 0.05
ALT	MEDP1665	0.640264414	< 0.05
ALT	MW0123852	0.640264414	< 0.05
ALT	MW0124143	0.554455781	< 0.05

ALT	MEDN1113	0.567657109	< 0.05
ALT	MW0159225	0.624862864	< 0.05
ALT	MW0017091	0.6182622	< 0.05
ALT	MW0158316	-0.572057552	< 0.05
ALT	MW0050103	0.631463528	< 0.05
ALT	MW0156774	0.578658216	< 0.05
ALT	MW0077514	0.576457995	< 0.05
ALT	MW0063832	0.640264414	< 0.05
ALT	MW0006044	0.660066406	< 0.05
ALT	MW0150760	0.587459101	< 0.05
ALT	MW0007103	0.556656002	< 0.05
ALT	MW0107510	0.638064192	< 0.05
ALT	MW0105468	0.598460208	< 0.05
ALT	MW0144016	0.55225556	< 0.05
ALT	MW0110455	0.629263307	< 0.05
AST	MW0129372	-0.846153846	< 0.001
AST	MW0158316	-0.850549451	< 0.001
AST	MW0006044	0.81978022	< 0.001
AST	MW0106596	0.837362637	< 0.001
AST	MW0108240	0.841758242	< 0.001
AST	MW0156686	0.828571429	< 0.001
AST	MW0128125	0.872527473	< 0.001
AST	ZINC149577	0.789010989	< 0.01
AST	MW0054746	0.753846154	< 0.01
AST	MEDP1665	0.727472527	< 0.01
AST	MW0055500	0.784615385	< 0.01
AST	MEDP1381	0.775824176	< 0.01
AST	MEDP1440	0.758241758	< 0.01
AST	MW0159225	0.714285714	< 0.01
AST	MW0052323	0.718681319	< 0.01
AST	MW0014190	0.740659341	< 0.01

AST	MW0109620	0.749450549	< 0.01
AST	MW0115265	0.740659341	< 0.01
AST	MW0053910	0.753846154	< 0.01
AST	MW0106195	0.740659341	< 0.01
AST	MEDP1524	0.687912088	< 0.01
AST	FDATN01012	0.714285714	< 0.01
AST	MW0050103	0.789010989	< 0.01
AST	MW0111511	0.758241758	< 0.01
AST	MW0063832	0.784615385	< 0.01
AST	MW0008605	0.771428571	< 0.01
AST	MW0160275	-0.758241758	< 0.01
AST	MW0063704	-0.771428571	< 0.01
AST	MEDL02562	0.70989011	< 0.01
AST	MW0152475	0.687912088	< 0.01
AST	MW0137976	-0.683516484	< 0.01
AST	MW0118606	-0.692307692	< 0.01
AST	MW0056727	-0.736263736	< 0.01
AST	MW0107510	0.78021978	< 0.01
AST	MW0124440	0.745054945	< 0.01
AST	MEDP1434	0.749450549	< 0.01
AST	MW0129025	-0.556043956	< 0.05
AST	MW0009539	0.617582418	< 0.05
AST	MW0105310	0.648351648	< 0.05
AST	MW0123852	0.56043956	< 0.05
AST	MW0124143	0.63956044	< 0.05
AST	MEDN1113	0.643956044	< 0.05
AST	MW0017091	0.657142857	< 0.05
AST	MEDP2111	0.608791209	< 0.05
AST	MW0126559	0.595604396	< 0.05
AST	MW0002133	0.626373626	< 0.05
AST	MEDL01912	0.586813187	< 0.05

AST	MW0013853	0.556043956	< 0.05
AST	MW0138813	0.643956044	< 0.05
AST	MW0156774	0.613186813	< 0.05
AST	MW0077514	0.582417582	< 0.05
AST	MW0016971	0.608791209	< 0.05
AST	MW0009714	0.6	< 0.05
AST	MW0150760	0.564835165	< 0.05
AST	MEDN1575	-0.648351648	< 0.05
AST	MW0110455	0.578021978	< 0.05
AST	MW0010041	0.621978022	< 0.05

FBG: Fasting blood glucose; TG: Triglyceride; ALT: Alanine aminotransferase;
 AST: Aspartate aminotransferase.

Supplementary Table 3 Correlation analysis between the differential metabolites and biochemical indexes in the diabetes mellitus group *versus* diabetes mellitus + human umbilical cord mesenchymal stem cells group comparison

Biochemical index	Differential metabolite ID	Correlation coefficient	P value
FBG	MW0105310	0.876721469	< 0.001
FBG	MEDP2111	0.922384045	< 0.001
FBG	MEDN0161	0.7762638	< 0.01
FBG	MW0053910	0.767131285	< 0.01
FBG	MW0126559	0.75799877	< 0.01
FBG	MW0111511	0.735167482	< 0.01
FBG	MW0006044	0.840191408	< 0.01
FBG	MW0108240	0.812793862	< 0.01
FBG	MW0124440	0.771697543	< 0.01
FBG	MW0107510	0.75799877	< 0.01
FBG	MW0129372	-0.812793861659457	< 0.01
FBG	MW0129025	-0.794528831060368	< 0.01
FBG	ZINC149577	0.68037239	< 0.05
FBG	MEDP1665	0.69863742	< 0.05
FBG	MEDP1440	0.721468709	< 0.05
FBG	MW0109620	0.616444783	< 0.05
FBG	MW0115265	0.662107359	< 0.05
FBG	MW0002133	0.630143556	< 0.05
FBG	MEDL01912	0.730601224	< 0.05
FBG	MW0156774	0.625577298	< 0.05
FBG	MW0063832	0.648408586	< 0.05
FBG	MW0077514	0.694071163	< 0.05
FBG	MW0008605	0.671239875	< 0.05
FBG	MW0009714	0.689504905	< 0.05
FBG	MW0007103	0.730601224	< 0.05
FBG	MW0156686	0.60274601	< 0.05

FBG	MW0063704	-0.602746009769935	< 0.05
TG	MW0126559	0.936363636	< 0.001
TG	MW0009714	0.881818182	< 0.001
TG	ZINC149577	0.818181818	< 0.01
TG	MEDN0161	0.863636364	< 0.01
TG	MEDL01912	0.809090909	< 0.01
TG	MW0111511	0.772727273	< 0.01
TG	MW0006044	0.781818182	< 0.01
TG	MW0108240	0.818181818	< 0.01
TG	MEDP1434	0.772727273	< 0.01
TG	MW0056727	-0.772727272727273	< 0.01
TG	MW0009539	0.654545455	< 0.05
TG	MW0105310	0.718181818	< 0.05
TG	MEDP1381	0.645454545	< 0.05
TG	MEDP2111	0.7	< 0.05
TG	MW0053910	0.681818182	< 0.05
TG	MW0168835	0.7	< 0.05
TG	MW0063832	0.718181818	< 0.05
TG	MW0077514	0.681818182	< 0.05
TG	MW0008605	0.754545455	< 0.05
TG	MW0007103	0.7	< 0.05
TG	MW0107510	0.727272727	< 0.05
TG	MW0156686	0.681818182	< 0.05
TG	MW0063704	-0.690909090909091	< 0.05
TG	MW0137976	-0.690909090909091	< 0.05
ALT	ZINC149577	0.872727273	< 0.001
ALT	MEDL01912	0.918181818	< 0.001
ALT	MW0105310	0.763636364	< 0.01
ALT	MW0115265	0.809090909	< 0.01
ALT	MW0126559	0.8	< 0.01
ALT	MW0002133	0.781818182	< 0.01

ALT	MW0111511	0.836363636	< 0.01
ALT	MW0108240	0.809090909	< 0.01
ALT	MW0063704	-0.845454545454546	< 0.01
ALT	MW0137976	-0.790909090909091	< 0.01
ALT	MW0054746	0.727272727	< 0.05
ALT	MEDP1665	0.627272727	< 0.05
ALT	MEDP1440	0.627272727	< 0.05
ALT	MW0159225	0.618181818	< 0.05
ALT	MEDN0161	0.754545455	< 0.05
ALT	MEDP2111	0.754545455	< 0.05
ALT	MW0053910	0.736363636	< 0.05
ALT	MW0106195	0.718181818	< 0.05
ALT	MW0168835	0.681818182	< 0.05
ALT	MW0077514	0.663636364	< 0.05
ALT	MW0006044	0.736363636	< 0.05
ALT	MW0106596	0.645454545	< 0.05
ALT	MW0008605	0.745454545	< 0.05
ALT	MW0009714	0.727272727	< 0.05
ALT	MW0007103	0.736363636	< 0.05
ALT	MW0107510	0.736363636	< 0.05
ALT	MW0156686	0.718181818	< 0.05
ALT	MW0129025	-0.645454545454545	< 0.05
ALT	MW0160275	-0.681818181818182	< 0.05
ALT	MW0118606	-0.654545454545455	< 0.05
ALT	MW0056727	-0.654545454545455	< 0.05
AST	MW0053910	0.909090909	< 0.001
AST	MW0111511	0.881818182	< 0.001
AST	MW0107510	0.881818182	< 0.001
AST	MW0156686	0.872727273	< 0.001
AST	MW0105310	0.8	< 0.01
AST	MEDN0161	0.772727273	< 0.01

AST	MEDP2111	0.763636364	< 0.01
AST	MW0126559	0.790909091	< 0.01
AST	MW0002133	0.763636364	< 0.01
AST	MEDL01912	0.763636364	< 0.01
AST	MW0063832	0.827272727	< 0.01
AST	MW0006044	0.772727273	< 0.01
AST	MW0108240	0.8	< 0.01
AST	MW0063704	-0.781818181818182	< 0.01
AST	ZINC149577	0.663636364	< 0.05
AST	MW0054746	0.736363636	< 0.05
AST	MW0123852	0.618181818	< 0.05
AST	MEDP1381	0.718181818	< 0.05
AST	MEDP1440	0.645454545	< 0.05
AST	MW0159225	0.709090909	< 0.05
AST	MW0115265	0.690909091	< 0.05
AST	MW0077514	0.690909091	< 0.05
AST	MW0009714	0.654545455	< 0.05
AST	MEDP1434	0.690909091	< 0.05
AST	MW0007103	0.672727273	< 0.05
AST	MW0129372	-0.690909090909091	< 0.05
AST	MW0129025	-0.745454545454545	< 0.05
AST	MW0158316	-0.736363636363636	< 0.05
AST	MW0137976	-0.7	< 0.05
AST	MW0056727	-0.7	< 0.05

FBG: Fasting blood glucose; TG: Triglyceride; ALT: Alanine aminotransferase;
AST: Aspartate aminotransferase.