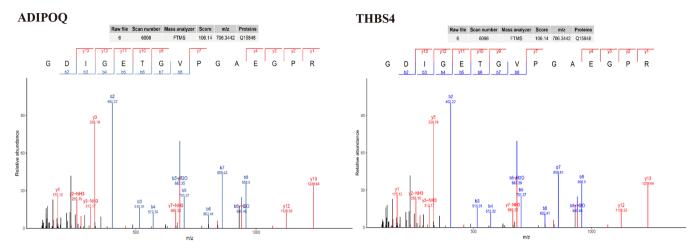
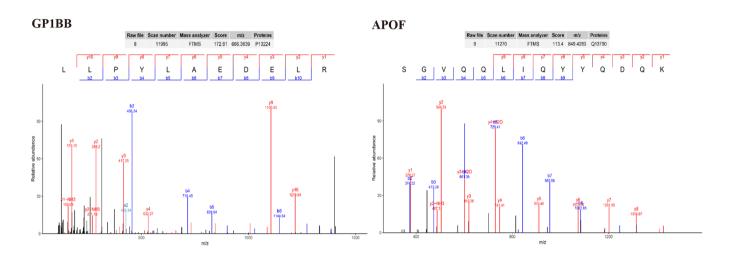
Figure S1. Representative mass spectra images of the identified proteins. ADIPOQ, adiponectin, C1Q and collagen domain containing; THBS4, thrombospondin 4; GP1BB, glycoprotein Ib platelet subunit β ; APOF, apolipoprotein F; PSG9, pregnancy specific β -1-glycoprotein 9; APCS, amyloid P component, serum.





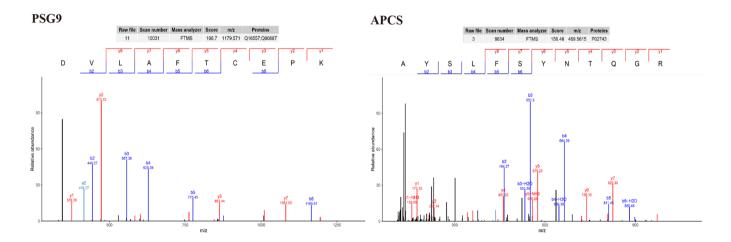


Figure S2. A heatmap was generated from the hierarchical clustering of the Gene Ontology analysis results, showing that umbilical cord serum proteins were enriched in cellular component terms that were related to cell junction, cell adhesion and extracellular matrix components. The differentially expressed proteins were categorized into four groups according to their fold change: Q1 (0-0.5), Q2 (0.5-0.67), Q3 (1.5-2) and Q4 (>2), with P<0.05 in all cases. The functional annotation following enrichment, together with the corresponding enrichment P-value, were first collected. The functional classifications that were enriched in at least one of the clusters (with P<0.05) were then screened. The filtered P-value data matrix was -log10 transformed. The transformed data matrix was classified by Z transformation for each functional category. Lastly, the dataset obtained following Z transformation was analyzed using one-way hierarchical clustering.

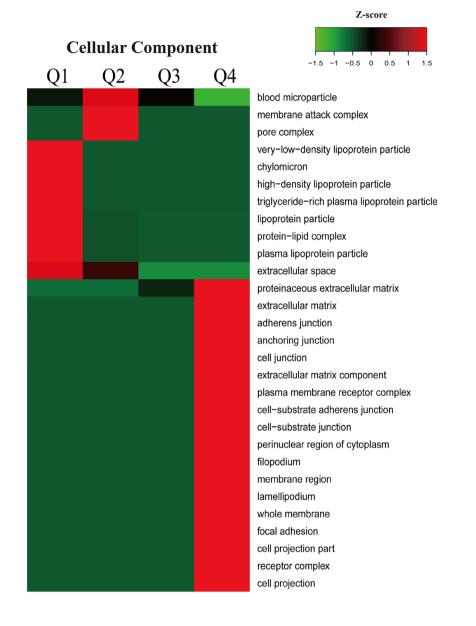


Figure S3. A heatmap was generated from hierarchical clustering of the Gene Ontology analysis results, showing that umbilical cord serum proteins were enriched in biological process terms that were related to gene regulation, as well as cell growth, differentiation, motility and adhesion. The differentially expressed proteins were categorized into four groups according to their fold change: Q1 (0-0.5), Q2 (0.5-0.67), Q3 (1.5-2) and Q4 (>2), with P<0.05 in all cases.

Biological Process	Z-score
Q1 Q2 Q3 Q4	
	positive regulation of immune response -1.5 -1 -0.5 o o.5 1 1.5 protein activation cascade
	adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains activation of immune response
	lymphocyte mediated immunity proteolysis
	B cell mediated immunity regulation of immune response
	immunoglobulin mediated immune response negative regulation of hydrolase activity
	negative regulation of response to external stimulus positive regulation of response to external stimulus
	regulation of inflammatory response negative regulation of response to wounding
	negative regulation of coagulation negative regulation of hemostasis
	regulation of proteolysis regulation of response to stress
	regulation of protein maturation regulation of protein metabolic process
	regulation of response to external stimulus regulation of macromolecule metabolic process
	regulation of primary metabolic process regulation of defense response
	acute inflammatory response acute-phase response
	lipoprotein metabolic process cholesterol metabolic process
	regulation of lipoprotein particle clearance sterol metabolic process accondary alcohol metabolic process
	secondary alcohol metaolic process sterol transport regulation of lipid biosynthetic process
	steroid metabolic process lipid transport
	npu unsport negative regulation of lipid metabolic process positive regulation of respiratory burst
	positive regulation of respiratory burst regulation of respiratory burst protein-light complex remodeling
	protein-spin compiex emotening plasma lipoprotein particle remodeling plasma lipoprotein particle organization
	prestein-lipid complex subunit organization macromolecular complex remodeling
	negative regulation of macromolecule metabolic process regulation of gene expression
	Pagetalanter of gene capacitation homotypic cell adhesion platelet activation
	positive regulation of cellular metabolic process regulation of anatomical structure morphogenesis
	regulation of multicellular organismal development regulation of cell growth
	positive regulation of gene expression negative regulation of developmental process
	cell-matrix adhesion extracellular matrix organization
	single organismal cell-cell adhesion negative regulation of gene expression
	regulation of cell migration regulation of cellular component movement
	regulation of cell motility circulatory system development
	cellular response to organic substance negative regulation of nucleobase-containing compound metabolic process
	regulation of cell size cell morphogenesis
	negative regulation of macromolecule biosynthetic process regulation of cell proliferation
	regulation of cellular localization positive regulation of cell proliferation
	positive regulation of epithelial cell poliferation regulation of cellular protein localization regulation of cell morphogenesis
	regulation of cell in Comparelations negative regulation of cellular biosynthetic process positive regulation of signal transduction
	power regulation of extend of cell growth developmental cell growth
	cellular response to oxygen-containing compound negative regulation of biosynthetic process
	regulation of RNA metabolic process interaction with host
	cellular response to organic cyclic compound cardiovascular system development
	developmental growth involved in morphogenesis regulation of nervous system development
	regulation of cell development system development
	regulation of transport regulation of cell differentiation
	anatomical structure formation involved in morphogenesis regulation of signal transduction
	regulation of protein localization regulation of nitrogen compound metabolic process
	cell differentiation regulation of protein localization to membrane
	cell morphogenesis involved in differentiation cell development
	regulation of developmental growth positive regulation of cell motility
	renal system development entry into cell of other organism involved in symbiotic interaction
	cell junction assembly morphogenesis of an epithelium
	negative regulation of nitrogen compound metabolic process regulation of phosphate metabolic process
	positive regulation of macromolecule metabolic process animal organ morphogenesis entry into other organism involved in symbiotic interaction
	cellular response to nitrogen compound
	animal organ development urogenital system development integrin-mediated signaling pathway
	response to transforming growth factor beta positive regulation of cellular component movement
	posterio comparato subunit organization regulation of phosphorus metabolic process
	rervous system development response to growth factor
	positive regulation of phosphorus metabolic process positive regulation of metabolic process
	tissue morphogenesis cellular response to growth factor stimulus
	cellular component morphogenesis neurogenesis
	cellular response to transforming growth factor beta stimulus positive regulation of locomotion
	entry into host

Figure S4. A heatmap was generated from hierarchical clustering of the Gene Ontology analysis results, showing that umbilical cord serum proteins were enriched in molecular function terms that were related to molecule binding, including integrin binding and enzyme binding. The differentially expressed proteins were categorized into four groups according to their fold change: Q1 (0-0.5), Q2 (0.5-0.67), Q3 (1.5-2) and Q4 (>2), with P<0.05 in all cases.

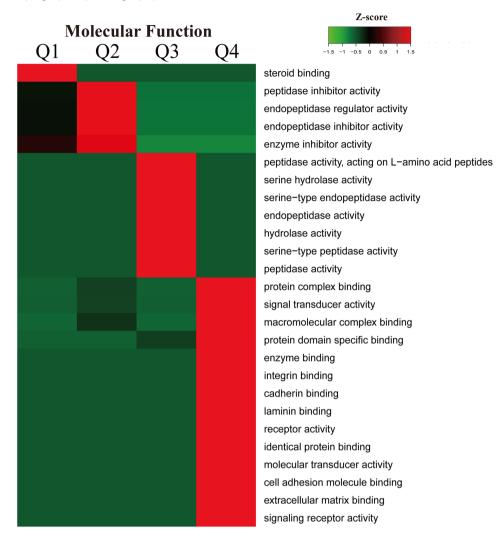


Figure S5. Flow cytometry was used to determine apoptotic cell death of MHCC97H cells treated with exosomes from the negative control, ME and UE groups. The data are presented as the mean \pm SEM. *P<0.05, **P<0.01, ***P<0.001. ME, maternal serum exosome; UE, umbilical serum exosome; PI, propidium iodide. The different quadrants Q1, Q2, Q3 and Q4 represent necrotic cells, late apoptotic cells, early apoptotic cells and viable cells, respectively.

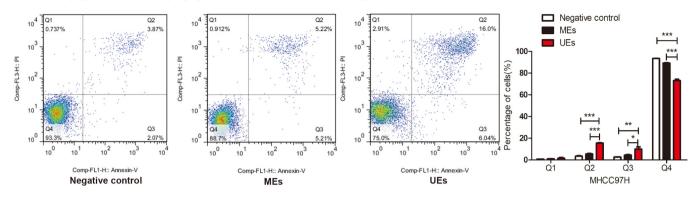


Table SI. Representative mass spectra of some differentially expressed proteins.

Gene name	Protein description	UEs/MEs ratio	MW (kDa)	Score
ADIPOQ	Adiponectin	5.724 Up	26.413	35.253
THBS4	Thrombospondin-4	5.211 Up	105.87	156.01
GP1BB	Platelet glycoprotein Ib beta chain	5.067 Up	21.717	55.474
COL1A1	Collagen alpha-1(I) chain	4.956 Up	138.94	18.486
THBS3	Thrombospondin-3	4.78 Up	104.2	40.532
TNXB	Tenascin-X	4.373 Up	458.22	131.96
PPIA	Peptidyl-prolyl cis-trans isomerase A	4.283 Up	18.012	29.025
PF4V1	Platelet factor 4 variant	4.197 Up	11.553	13.468
MSN	Moesin	3.998 Up	67.819	24.523
GP1BA	Platelet glycoprotein Ib alpha chain	3.848 Up	71.539	25.828
CRP	C-reactive protein	0.062 Down	25.038	47.518
IGHA2	Ig α -2 chain C region	0.086 Down	36.526	54.714
PZP	Pregnancy zone protein	0.104 Down	163.86	228.85
APOL1	Apolipoprotein L1	0.106 Down	43.974	81.534
HP	Haptoglobin	0.108 Down	45.205	190.31
IGHA1	Ig alpha-1 chain C region	0.115 Down	37.654	227.22
PSG4	Pregnancy-specific beta-1-glycoprotein 4	0.116 Down	47.112	79.15
APOF	Apolipoprotein F	0.117 Down	35.399	25.247
PSG9	Pregnancy-specific beta-1-glycoprotein 9	0.147 Down	48.272	26.244
APCS	Serum amyloid P-component	0.155 Down	25.387	88.277

ME, maternal serum exosome; UE, umbilical serum exosome; MW, molecular weight.