**SUPPL TABLE 1**. Percentages of single, double, double membrane, multilayer and vesicles with electron dense cargo visualized in vesicle samples of pooled plasma and total blood from HFs and BCP.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Source of exosomes | | % of vesicles | | | | |
| single | double | double membrane | multilayer | with electron dense cargo |
| HFs | Plasma | 91 | 3 | 0 | 2 | 4 |
| Total blood | 37 | 20 | 22 | 8 | 13 |
| BCPs | Plasma | 81 | 8 | 3 | 3 | 5 |
| Total blood | 70 | 10 | 9 | 5 | 6 |

**SUPPL TABLE 2** Exosomal proteins identified in the plasma of HF blood

|  |  |
| --- | --- |
| Gene | Protein |
| A2M | Alpha-2-macroglobulin |
| AARD | Alanine and arginine-rich domain-containing protein |
| ADAM10 | Disintegrin and metalloproteinase domain-containing protein 10 |
| AHSG | Alpha-2-HS-glycoprotein |
| AIFM1 | Apoptosis-inducing factor 1, mitochondrial |
| AIM2 | Interferon-inducible protein AIM2 |
| ALB | Serum albumin |
| AMBP | Alpha-1-microglycoprotein |
| AMPD1 | AMP deaminase 1 |
| APOA1 | Apolipoprotein A-I |
| APOA4 | Apolipoprotein A-IV |
| APOB | Apolipoprotein B-100 |
| APOE | Apolipoprotein E |
| BANF1 | Barrier-to-autointegration factor |
| BARD1 | BRCA1-associated RING domain protein 1 |
| C3 | Complement C3 |
| CAMKK1 | Calcium/calmodulin-dependent protein kinase kinase 1 |
| CCDC85A | Coiled-coil domain-containing protein 85A |
| CD24 | Signal transducer CD24 |
| CD63 | CD63 antigen |
| CD81 | CD81 antigen |
| CD9 | CD9 antigen |
| CFAP97D2 | Uncharacterized protein CFAP97D2 |
| CFH | Complement factor H |
| CHD5 | Chromodomain-helicase-DNA-binding protein 5 |
| CLBA1 | Uncharacterized protein CLBA1 |
| CLU | Clusterin |
| COPS2 | COP9 signalosome complex subunit 2 |
| CORO6 | Coronin-6 |
| COX6A1 | Cytochrome c oxidase subunit 6A1, mitochondrial |
| ENF34 | E3 ubiquitin-protein ligase RNF34 |
| FBF1 | Fas-binding factor 1 |
| FGA | Fibrinogen alpha chain |
| FGB | Fibrinogen beta chain |
| FGF10 | Fibroblast growth factor 10 |
| FGG | Fibrinogen gamma chain |
| FN1 | Fibronectin |
| FXYD5 | FXYD domain-containing ion transport regulator 5 |
| GAS7 | Growth arrest-specific protein 7 |
| GSN | Gelsolin |
| HAND1 | Heart- and neural crest derivatives-expressed protein 1 |
| HBB | Hemoglobin subunit beta |
| HP | Haptoglobin |
| HPR | Haptoglobin-related protein |
| HPX | Hemopexin |
| IGHG2 | Ig gamma-2 chain C region |
| IGHM | Ig mu chain C region |
| IGKC | Ig kappa chain C region |
| IGLC7 | Ig lambda-7 chain C region |
|  | Immunoglobulin mu heavy chain |
| LRG | Leucine-rich alpha-2-glycoprotein |
| MFAP5 | Microfibrillar-associated protein 5 |
| MIA | Melanoma-derived growth regulatory protein |
| NAGS | N-acetylglutamate synthase, mitochondrial |
| NANOS3 | Nanos homolog 3 |
| NAP1L1 | Nucleosome assembly protein 1-like 1 |
| NDUFA2 | NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 2 |
| NIF3L1 | NIF3-like protein 1 |
| NPVF | Pro-FMRFamide-related neuropeptide VF |
| P2RX3 | P2X purinoceptor 3 |
| PIK3CD | Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit delta isoform |
| PIP4K2B | Phosphatidylinositol 4-kinase type 2-beta |
| PLEKHA7 | Pleckstrin homology domain-containing family A member 7 |
| PSKH1 | Serine/threonine-protein kinase H1 |
| RAB22A | Ras-related protein Rab-22A |
| RAB40A | Ras-related protein Rab-40A |
| RAP1B | Ras-related GTP-binding protein B |
| RASGRP4 | RAS guanyl-releasing protein 4 |
| RASSF2 | Ras association domain-containing protein 2 |
| RBMXL2 | RNA-binding motif protein, X-linked-like-2 |
| RFC3 | Replication factor C subunit 3 |
| SNTA1 | Alpha-1-syntrophin |
| TF | Serotransferrin |
| TMEM74B | Transmembrane protein 74B |
| TNFSF14 | Tumor necrosis factor ligand superfamily member 14 |
| TPD52L2 | Tumor protein D54 |
| TTR | Transthyretin |
| ZAP70 | Tyrosine-protein kinase ZAP-70 |
| ZKSCAN8 | Zinc finger protein with KRAB and SCAN domains 8 |
| ZNF835 | Zinc finger protein 835 |
| ZSCAN12 | Zinc finger and SCAN domain-containing protein 12 |

**SUPPL TABLE 3** Exosomal proteins identified in the HF total blood

|  |  |
| --- | --- |
| Gene Name | Protein |
| A2M | Alpha-2-macroglobulin |
| AARD | Alanine and arginine-rich domain-containing protein |
| ACADVL | Very long-chain specific acyl-CoA dehydrogenase, mitochondrial |
| ADAM10 | Disintegrin and metalloproteinase domain-containing protein 10 |
| AHSG | Alpha-2-HS-glycoprotein |
| AIFM1 | Apoptosis-inducing factor 1, mitochondrial |
| AIM2 | Interferon-inducible protein AIM2 |
| AKT1 | RAC-alpha serine/threonine-protein kinase |
| ALB | Serum albumin |
| AMBP | Alpha-1-microglycoprotein |
| AMPD1 | AMP deaminase 1 |
| ANKRD33B | Ankyrin repeat domain-containing protein 33B |
| APOA4 | Apolipoprotein A-IV |
| B3GAT1 | Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 1 |
| BANF1 | Barrier-to-autointegration factor |
| C17orf100 | Uncharacterized protein C17orf100 |
| C3orf14 | Uncharacterized protein C3orf14 |
| CD24 | Signal transducer CD24 |
| CD63 | CD63 antigen |
| CD81 | CD81 antigen |
| CD9 | CD9 antigen |
| CDC73 | Parafibromin |
| CLU | Clusterin |
| CPS1 | Carbamoyl-phosphate synthase [ammonia], mitochondrial |
| CRYBB1 | Beta-crystallin B1 |
| DKC1 | H/ACA ribonucleoprotein complex subunit 4 |
| DNM1P46 | Putative GED domain-containing protein DNM1P46 |
| EHHADH | Peroxisomal bifunctional enzyme |
| FGF10 | Fibroblast growth factor 10 |
| GCLC | Glutamate--cysteine ligase catalytic subunit |
| GDF2 | Growth/differentiation factor 2 |
| GSN | Gelsolin |
| HPR | Haptoglobin-related protein |
| HPX | Hemopexin |
| IGHM | Ig mu chain C region |
| IGHM | Immunoglobulin heavy constant mu |
| IGLC7 | Immunoglobulin lambda constant 7 |
|  | Immunoglobulin mu heavy chain |
| IVD | Isovaleryl-CoA dehydrogenase, mitochondrial |
| KDM6B | Lysine-specific demethylase 6B |
| LMNA | Prelamin-A/C |
| LRG | Leucine-rich alpha-2-glycoprotein |
| MAP9 | Microtubule-associated protein 9 |
| MDGA2 | MAM domain-containing glycosylphosphatidylinositol anchor protein 2 |
| MFAP5 | Microfibrillar-associated protein 5 |
| MIDN | Midnolin |
| MYL1 | Myosin light chain 1/3, skeletal muscle isoform |
| MYPOP | Myb-related transcription factor, partner of profilin |
| PGF | Placenta growth factor |
| PIP4K2B | Phosphatidylinositol 4-kinase type 2-beta |
| POLR1A | DNA-directed RNA polymerase I subunit RPA1 |
| PSKH1 | Serine/threonine-protein kinase H1 |
| RANBP3 | Ran-binding protein 3 |
| RAP1B | Ras-related GTP-binding protein B |
| SPECC1L | Cytospin-A |
| ST3GAL1 | CMP-N-acetylneuraminate-beta-galactosamide-alpha-2,3-sialyltransferase 1 |
| TF | Serotransferrin |
| TPD52L2 | Tumor protein D54 |
| ZNF229 | Zinc finger protein 229 |
| ZNF781 | Zinc finger protein 781 |
| ZNF876P | Putative zinc finger protein 876 |

**SUPPL TABLE 4** Exosomal proteins identified in the BCP plasma

|  |  |
| --- | --- |
| Gene | Protein |
| ABCB7 | ATP-binding cassette sub-family B member 7, mitochondrial |
| ACADM | Medium-chain specific acyl-CoA dehydrogenase, mitochondrial |
| ACSM3 | Acyl-coenzyme A synthetase ACSM3, mitochondrial |
| ADAM10 | Disintegrin and metalloproteinase domain-containing protein 10 |
| AHSG | Alpha-2-HS-glycoprotein |
| ALB | Serum albumin |
| AMBP | Alpha-1-microglycoprotein |
| ANKRD20A8P | Ankyrin repeat domain-containing protein 20B |
| ANO3 | Anoctamin-3 |
| APOA1 | Apolipoprotein A-I |
| APOA4 | Apolipoprotein A-IV |
| APOB | Apolipoprotein B-100 |
| ARMCX1 | Armadillo repeat-containing X-linked protein 1 |
| BANF1 | Barrier-to-autointegration factor |
| BMP7 | Bone morphogenetic protein 7 |
| C3 | Complement C3 |
| CACNA1A | Voltage-dependent P/Q-type calcium channel subunit alpha-1A |
| CAPN2 | Calpain-2 catalytic subunit |
| CCDC158 | Coiled-coil domain-containing protein 158 |
| CD24 | Signal transducer CD24 |
| CD63 | CD63 antigen |
| CD81 | CD81 antigen |
| CD9 | CD9 antigen |
| CEP350 | Centrosome-associated protein 350 |
| CKMT2 | Creatine kinase S-type, mitochondrial |
| CLU | Clusterin |
| CRYAA | Alpha-crystallin A chain |
| CRYAA2 | Alpha-crystallin A2 chain |
| CRYAB | Alpha-crystallin B chain |
| DNM1L | Dynamin-1-like protein |
| DTNA | Dystrobrevin alpha |
| EXD3 | Exonuclease mut-7 homolog |
| EXOC8 | Exocyst complex component 8 |
| FBF1 | Fas-binding factor 1 |
| FGG | Fibrinogen gamma chain |
| GTSE1 | G2 and S phase-expressed protein 1 |
| HBB | Hemoglobin subunit beta |
| HIF1AN | Hypoxia-inducible factor 1-alpha inhibitor |
| HPA | Haptoglobin alpha chain |
| HP | Haptoglobin |
| HPR | Haptoglobin-related protein |
| HPX | Hemopexin |
| IGF2R | Cation-independent mannose-6-phosphate receptor |
| IGHA1 | Immunoglobulin heavy constant alpha 1 |
| IGHG1 | Immunoglobulin heavy constant gamma 1 |
| IGKC | Immunoglobulin kappa constant |
| IGKV3-20 | Immunoglobulin kappa light chain |
| KCNIP3 | Calsenilin |
| KIF20B | Kinesin-like protein KIF20B |
| KIF3B | Kinesin-like protein KIF3B |
| KIFC3 | Kinesin-like protein KIFC3 |
| LRG | Leucine-rich alpha-2-glycoprotein |
| MMAB | Corrinoid adenosyltransferase |
| MRPL52 | 39S ribosomal protein L52, mitochondrial |
| MTHFD1 | C-1-tetrahydrofolate synthase, cytoplasmic |
| NOXO1 | NADPH oxidase organizer 1 |
| OCM | Oncomodulin-1 |
| PDS5A | Sister chromatid cohesion protein PDS5 homolog A |
| PIBF1 | Progesterone-induced-blocking factor 1 |
| POLR2D | DNA-directed RNA polymerase II subunit RPB4 |
| PPHLN1 | Periphilin-1 |
| RAB24 | Ras-related protein Rab-24 |
| RPL28 | 60S ribosomal protein L28 |
| SERPINA1 | Alpha-1-antitrypsin |
| SHE | SH2 domain-containing adapter protein E |
| TCHP | Trichoplein keratin filament-binding protein |
| TF | Serotransferrin |
| TMEM9B | Transmembrane protein 9B |
| TPD52L2 | Tumor protein D54 |
| TRANK1 | TPR and ankyrin repeat-containing protein 1 |
| TTR | Transthyretin |
| VAV3 | Guanine nucleotide exchange factor VAV3 |
| VPS13A | Vacuolar protein sorting-associated protein 13A |
| ZNF622 | Zinc finger protein 622 |
| ZNF638 | Zinc finger protein 638 |

**SUPPL TABLE 5** Exosomal proteins identified in the BCP total blood

|  |  |
| --- | --- |
| Gene | Protein |
| A1BG | Alpha-1B-glycoprotein |
| ADAM10 | Disintegrin and metalloproteinase domain-containing protein 10 |
| AHSG | Alpha-2-HS-glycoprotein |
| ALB | Serum albumin |
| AMBP | Alpha-1-microglycoprotein |
| APOA1 | Apolipoprotein A-I |
| APOA4 | Apolipoprotein A-IV |
| APPBP2 | Amyloid protein-binding protein 2 |
| ATR | Serine/threonine-protein kinase ATR |
| BANF1 | Barrier-to-autointegration factor |
| BMP1 | Bone morphogenetic protein 1 |
| C11orf97 | Uncharacterized protein C11orf97 |
| C1orf131 | Uncharacterized protein C1orf131 |
| C3 | Complement C3 |
| CABP1 | Calcium-binding protein 1 |
| CACNG8 | Voltage-dependent calcium channel gamma-8 subunit |
| CCDC146 | Coiled-coil domain-containing protein 146 |
| CCDC152 | Coiled-coil domain-containing protein 152 |
| CCDC158 | Coiled-coil domain-containing protein 158 |
| CCDC85A | Coiled-coil domain-containing protein 85A |
| CD24 | Signal transducer CD24 |
| CD63 | CD63 antigen |
| CD81 | CD81 antigen |
| CD9 | CD9 antigen |
| CKAP2L | Cytoskeleton-associated protein 2-like |
| CLK3 | Dual specificity protein kinase CLK3 |
| CLU | Clusterin |
| COG4 | Conserved oligomeric Golgi complex subunit 4 |
| COX7A2P2 | Putative cytochrome c oxidase subunit 7A3, mitochondrial |
| DUPD1 | Dual specificity phosphatase DUPD1 |
| EHHADH | Peroxisomal bifunctional enzyme |
| ELL2 | RNA polymerase II elongation factor ELL |
| EPHX4 | Epoxide hydrolase 4 |
| ERC2 | ERC protein 2 |
| EXD3 | Exonuclease mut-7 homolog |
| EXOSC7 | Exosome complex component RRP42 |
| FAM50A | Protein FAM50A |
| FARSB | Phenylalanine-tRNA ligase beta subunit |
| FGA | Fibrinogen alpha chain |
| FGB | Fibrinogen beta chain |
| FGG | Fibrinogen gamma chain |
| GATM | Glycine amidinotransferase, mitochondrial |
| GLRB | Glycine receptor subunit beta |
| HAGH | Hydroxyacylglutathione hydrolase, mitochondrial |
| HMOX1 | Heme oxygenase 1 |
| HPA | Haptoglobin alpha chain |
| HP | Haptoglobin |
| HPR | Haptoglobin-related protein |
| HPX | Hemopexin |
| IGHG2 | Immunoglobulin heavy constant gamma 2 |
| IGHV3-74 | Immunoglobulin heavy variable 3-74 |
| IGKC | Immunoglobulin kappa constant |
| IL16 | Pro-interleukin-16 |
| ITIH4 | Inter-alpha-trypsin inhibitor heavy chain H4 |
| ITPR2 | Inositol 1,4,5-trisphosphate receptor type 2 |
| KRT1 | Keratin, type II cytoskeletal 1 |
| KRT6A | Keratin, type II cytoskeletal 6A |
| KRT6B | Keratin, type II cytoskeletal 6B |
| KRT9 | Keratin, type I cytoskeletal 9 |
| LPCAT2 | Lysophosphatidylcholine acyltransferase 2 |
| LRG | Leucine-rich alpha-2-glycoprotein |
| MAEA | E3 ubiquitin-protein transferase MAEA |
| MBD4 | Methyl-CpG-binding domain protein 4 |
| MIEF1 | Mitochondrial dynamics protein MID51 |
| MYO3B | Myosin-IIIb |
| PCNT | Pericentrin |
| PDZD2 | PDZ domain-containing protein 2 |
| PHB2 | Prohibitin-2 |
| PLB1 | Phospholipase B1, membrane-associated |
| PNLIP | Pancreatic triacylglycerol lipase |
| PPM1A | Protein phosphatase 1A |
| PRAMEF9 | PRAME family member 9/15 |
| PRDM12 | PR domain zinc finger protein 12 |
| RABGAP1L | Rab GTPase-activating protein 1-like |
| RANBP3 | Ran-binding protein 3 |
| RUBCN | Run domain Beclin-1-interacting and cysteine-rich domain-containing protein |
| SACS | Sacsin |
| SERPINA1 | Alpha-1-antitrypsin |
| SERPINB7 | Serpin B7 |
| SKIV2L | Helicase SKI2W |
| SNTA1 | Alpha-1-syntrophin |
| SOCS3 | Suppressor of cytokine signaling 3 |
| SPTBN2 | Spectrin beta chain, non-erythrocytic 2 |
| SRARP | Steroid receptor-associated and regulated protein |
| SSX9P | Putative protein SSX9 |
| TF | Serotransferrin |
| TOR3A | Torsin-3A |
| TPD52L1 | Tumor protein D53 |
| TPD52L2 | Tumor protein D54 |
| TRANK1 | TPR and ankyrin repeat-containing protein 1 |
| TRBV4-3 | T cell receptor beta variable |
| UBA52 | Ubiquitin-60S ribosomal protein L40 |
| VAV3 | Guanine nucleotide exchange factor VAV3 |
| ZKSCAN8 | Zinc finger protein with KRAB and SCAN domains 8 |
| ZNF451 | E3 SUMO-protein ligase ZNF451 |
| ZNF585B | Zinc finger protein 585B |
| ZNF630 | Zinc finger protein 630 |

**SUPPL FIGURE 1** Heat map and dendrogram of the results of GO functional enrichment analysis of exosomal proteins from BCPs and HFs by Biological Processes obtained via STRING (<https://string-db.org/>) and visualized using R (<https://www.r-project.org/>).



**SUPPL TABLE 6** Unique exosomal proteins identified in total blood of BCPs

|  |  |
| --- | --- |
| Gene | Protein |
| A1BG | Alpha-1B-glycoprotein |
| APPBP2 | Amyloid protein-binding protein 2 |
| ATR | Serine/threonine-protein kinase ATR |
| BMP1 | Bone morphogenetic protein 1 |
| C11orf97 | Uncharacterized protein C11orf97 |
| C1orf131 | Uncharacterized protein C1orf131 |
| CABP1 | Calcium-binding protein 1 |
| CACNG8 | Voltage-dependent calcium channel gamma-8 subunit |
| CCDC146 | Coiled-coil domain-containing protein 146 |
| CCDC152 | Coiled-coil domain-containing protein 152 |
| CKAP2L | Cytoskeleton-associated protein 2-like |
| CLK3 | Dual specificity protein kinase CLK3 |
| COG4 | Conserved oligomeric Golgi complex subunit 4 |
| COX7A2P2 | Putative cytochrome c oxidase subunit 7A3, mitochondrial |
| DUPD1 | Dual specificity phosphatase DUPD1 |
| ELL2 | RNA polymerase II elongation factor ELL |
| EPHX4 | Epoxide hydrolase 4 |
| ERC2 | ERC protein 2 |
| EXOSC7 | Exosome complex component RRP42 |
| FAM50A | Protein FAM50A |
| FARSB | Phenylalanine-tRNA ligase beta subunit |
| GATM | Glycine amidinotransferase, mitochondrial |
| GLRB | Glycine receptor subunit beta |
| HAGH | Hydroxyacylglutathione hydrolase, mitochondrial |
| HMOX1 | Heme oxygenase 1 |
| IGHV3-74 | Immunoglobulin heavy variable 3-74 |
| IL16 | Pro-interleukin-16 |
| ITIH4 | Inter-alpha-trypsin inhibitor heavy chain H4 |
| ITPR2 | Inositol 1,4,5-trisphosphate receptor type 2 |
| KRT1 | Keratin, type II cytoskeletal 1 |
| KRT6A | Keratin, type II cytoskeletal 6A |
| KRT6B | Keratin, type II cytoskeletal 6B |
| KRT9 | Keratin, type I cytoskeletal 9 |
| LPCAT2 | Lysophosphatidylcholine acyltransferase 2 |
| MAEA | E3 ubiquitin-protein transferase MAEA |
| MBD4 | Methyl-CpG-binding domain protein 4 |
| MIEF1 | Mitochondrial dynamics protein MID51 |
| MYO3B | Myosin-IIIb |
| PCNT | Pericentrin |
| PDZD2 | PDZ domain-containing protein 2 |
| PHB2 | Prohibitin-2 |
| PLB1 | Phospholipase B1, membrane-associated |
| PNLIP | Pancreatic triacylglycerol lipase |
| PPM1A | Protein phosphatase 1A |
| PRAMEF9 | PRAME family member 9/15 |
| PRDM12 | PR domain zinc finger protein 12 |
| RABGAP1L | Rab GTPase-activating protein 1-like |
| RUBCN | Run domain Beclin-1-interacting and cysteine-rich domainaining protein |
| SACS | Sacsin |
| SERPINB7 | Serpin B7 |
| SKIV2L | Helicase SKI2W |
| SOCS3 | Suppressor of cytokine signaling 3 |
| SPTBN2 | Spectrin beta chain, non-erythrocytic 2 |
| SRARP | Steroid receptor-associated and regulated protein |
| SSX9P | Putative protein SSX9 |
| TOR3A | Torsin-3A |
| TPD52L1 | Tumor protein D53 |
| TRBV4-3 | T cell receptor beta variable |
| UBA52 | Ubiquitin-60S ribosomal protein L40 |
| ZNF451 | E3 SUMO-protein ligase ZNF451 |
| ZNF585B | Zinc finger protein 585B |
| ZNF630 | Zinc finger protein 630 |