**Table 1.** **Concentrations of cfNAs in different human body fluids.** In several studies quantities of genetic material were expressed as genome equivalents per milliliter, in such cases, we calculated the amount of DNA with a conversion factor of 6.6 pg of DNA equal to 1 genome equivalent. Interquartile range (IQR).

NA - Not available.

\*Peritoneal dialysis patients without any history of systemic inflammation or peritonitis in the last 3 months.

\*\*Insufficient methodology data.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Phenotype** | **Type of cfNAs** | **Source** | **Samples** | **Concentration** | **Reference** |
| Gastric cancer | cfDNA | Plasma | 130 | 68.7 ± 40.5 ng/ml | [[1]](https://paperpile.com/c/33ouGt/z5al) |
| Gastric cancer | cfDNA | Serum | 130 | 755.9 ± 1203.7 ng/ml | [[1]](https://paperpile.com/c/33ouGt/z5al) |
| Healthy | cfDNA | Saliva | 26 | 1.11 (0.01–67.63) ng/ml | [[2]](https://paperpile.com/c/33ouGt/0Apc) |
| Pulmonary benign disease | cfDNA | Saliva | 15 | 3.26 (0.029–26.30) ng/ml | [[2]](https://paperpile.com/c/33ouGt/0Apc) |
| Non-small-cell lung carcinoma | cfDNA | Saliva | 68 | 0.531 (0.018–285.420) ng/ml | [[2]](https://paperpile.com/c/33ouGt/0Apc) |
| Healthy | cfDNA | Urine | 19 | 6–50 ng/ml | [[3]](https://paperpile.com/c/33ouGt/d3Kh) |
| Prostate cancer | cfDNA | Seminal plasma | 6 | 2243670 ± 1758000 ng/ml | [[4]](https://paperpile.com/c/33ouGt/XxSj) |
| Healthy | cfDNA | Seminal plasma | 3 | 57700 ± 4800 ng/ml | [[4]](https://paperpile.com/c/33ouGt/XxSj) |
| Normozoospermia | cfDNA | Seminal plasma | 11 | 1340 ± 650 (510 to 2730) ng/ml | [[5]](https://paperpile.com/c/33ouGt/mJZH) |
| Azoospermia | cfDNA | Seminal plasma | 9 | 2560 ± 1430 (820 to 5450) ng/ml | [[5]](https://paperpile.com/c/33ouGt/mJZH) |
| Healthy | cfDNA | Tear fluid | 11 | 1400 (200) ng/ml | [[6]](https://paperpile.com/c/33ouGt/m9Sw) |
| Non-autoimmune dry eye disease | cfDNA | Tear fluid | 13 | 2900 (600) ng/ml | [[6]](https://paperpile.com/c/33ouGt/m9Sw) |
| Autoimmune dry eye disease | cfDNA | Tear fluid | 11 | 5200 (1200) ng/ml | [[6]](https://paperpile.com/c/33ouGt/m9Sw) |
| Graft versus host disease | cfDNA | Tear fluid | 12 | 9100 (2300) ng/ml | [[6]](https://paperpile.com/c/33ouGt/m9Sw) |
| Healthy | cfDNA | Sweat | 10 | 11.5 ng/ml | [[7]](https://paperpile.com/c/33ouGt/gP1d) |
| Lung cancer | cfDNA | Sputum | 28 | 312 ± 61 ng/ml | [[8]](https://paperpile.com/c/33ouGt/WKxy) |
| Healthy | cfDNA | Sputum | 68 | 1033 ± 227 ng/ml | [[8]](https://paperpile.com/c/33ouGt/WKxy) |
| Cancer | cfDNA | Ascites | 6 | 3.9–38.4 ng/ml | [[9]](https://paperpile.com/c/33ouGt/QhYO) |
| Cirrhosis | cfDNA | Ascites | 1 | 8.35 ng/ml | [[9]](https://paperpile.com/c/33ouGt/QhYO) |
| Rheumatoid arthritis | cfDNA | Synovial fluid | 80 | 3,182 ng/ml | [[10]](https://paperpile.com/c/33ouGt/xV29) |
| Osteoarthritis | cfDNA | Synovial fluid | 33 | 82 ng/ml | [[10]](https://paperpile.com/c/33ouGt/xV29) |
| Rheumatoid arthritis | cfDNA | Plasma | 80 | 41.3 ng/ml | [[10]](https://paperpile.com/c/33ouGt/xV29) |
| Healthy | cfDNA | Plasma | 50 | 32.1 ng/ml | [[10]](https://paperpile.com/c/33ouGt/xV29) |
| Peritoneal dialysis control\* | cfDNA | Peritoneal effluent | 30 | 0.2 (IQR 0.1–0.3) ng/ml | [[11]](https://paperpile.com/c/33ouGt/S1b9) |
| Peritoneal dialysis | cfDNA | Peritoneal effluent | 23 | 168.5 (IQR 124.3–3033) ng/ml | [[11]](https://paperpile.com/c/33ouGt/S1b9) |
| Continuous ambulatory peritoneal dialysis | cfDNA | Peritoneal effluent | 18 | 1.8–9.5 ng/ml | [[12]](https://paperpile.com/c/33ouGt/jaBY) |
| Lung adenocarcinoma | cfDNA | Bronchoalveolar lavage fluid | 20 | 5490–20130 ng/ml | [[13]](https://paperpile.com/c/33ouGt/CJOa) |
| High risk pancreatic cyst | cfDNA | Cyst fluid | 10 | 44463±39228 ng/ml | [[14]](https://paperpile.com/c/33ouGt/8VII) |
| Low risk pancreatic cyst | cfDNA | Cyst fluid | 20 | 33021±20004 ng/ml | [[14]](https://paperpile.com/c/33ouGt/8VII) |
| Healthy | cfDNA | Serum | 19 | 20±3 ng/ml | [[14]](https://paperpile.com/c/33ouGt/8VII) |
| Pancreatic cancer | cfDNA | Serum | 19 | 36±14 ng/ml | [[14]](https://paperpile.com/c/33ouGt/8VII) |
| Retinoblastoma | cfDNA | Aqueous humour | 12 | 140–394000 (median 1670) ng/ml | [[15]](https://paperpile.com/c/33ouGt/Ls9U) |
| Retinoblastoma | cfDNA | Aqueous humour | 6 | 84–56000 (median 174) ng/ml | [[16]](https://paperpile.com/c/33ouGt/vukL) |
| Central nervous system cancer | cfDNA | Cerebrospinal fluid | 27 | 8440 (100–110000) ng/ml | [[17]](https://paperpile.com/c/33ouGt/dVV2) |
| Pregnant woman with male fetus | cffDNA | Cerebrospinal fluid | 17 | 17.61 (1.51–83.58) ng/ml | [[18]](https://paperpile.com/c/33ouGt/TYGx) |
| Retinoblastoma | cf-miRNA | Aqueous humour | 6 | 79–150000 (median 273) ng/ml | [[16]](https://paperpile.com/c/33ouGt/vukL) |
| Healthy | cfRNA | Saliva | 5 | 1945 (IQR 2495) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Plasma | 4 | 44 (41–51) ng/ml | [[20]](https://paperpile.com/c/33ouGt/sHSQ) |
| Small-cell and non-small-cell lung carcinoma | cfRNA | Plasma | 10+10 | 400 (109–1228) ng/ml | [[20]](https://paperpile.com/c/33ouGt/sHSQ) |
| Healthy | cfRNA | Plasma | 5 | 308 (IQR 104) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Urine | 19 | 24–140 ng/ml | [[3]](https://paperpile.com/c/33ouGt/d3Kh) |
| Healthy | cfRNA | Seminal plasma | 10 | 1750 (870–3640) ng/ml | [[21]](https://paperpile.com/c/33ouGt/i9Mv) |
| Healthy | cfRNA | Seminal plasma | NA\*\* | 17770 (QRI 7673) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Tear fluid | 5 | 564 (IQR 631) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Pleural fluid | 5 | 470 (IQR 190) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Bronchial lavage fluid | 5 | 1128 (IQR 886) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Breast milk | NA\*\* | 47240 (IQR 73180) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Colostrum | 1 | 585 ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Urine | 5 | 94 (IQR 129) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Peritoneal effluent | 5 | 775 (IQR 345) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Central nervous system cancer | cfRNA | Cerebrospinal fluid | 24 | 4210 (300–40600) ng/ml | [[17]](https://paperpile.com/c/33ouGt/dVV2) |
| Healthy | cfRNA | Cerebrospinal fluid | 5 | 111 (IQR 66) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Healthy | cfRNA | Amniotic fluid | NA\*\* | 570 (IQR 354) ng/ml | [[19]](https://paperpile.com/c/33ouGt/nPnE) |
| Retinoblastoma | cfRNA | Aqueous humour | 6 | 400–12800 (median 653) ng/ml | [[16]](https://paperpile.com/c/33ouGt/vukL) |
| HIV‐positive | HIV‐RNA | Cervico‐vaginal secretion | 40 | 250 copies/ml | [[22]](https://paperpile.com/c/33ouGt/Ak7S) |
| HIV-seropositive pregnant | HIV‐RNA | Cervico‐vaginal secretion | 26 | ~550 copies/ml | [[23]](https://paperpile.com/c/33ouGt/RJ4f) |

**Table 2.** **The size range of cfNAs in different human body fluids.** Based on the studies, we summarise the length of the most abundant fraction of cfNAs fragments, however both shorter and longer fragments could also be present in body fluids (not included).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Phenotype** | **Type of cfNAs** | **Source** | **Samples** | **Size** | **Reference** |
| Cancer | cfDNA | Plasma | 51 | 155 bp | [[24]](https://paperpile.com/c/33ouGt/Jeq7) |
| Cancer | cfDNA | Serum | 46 | 150–2000 bp | [[24]](https://paperpile.com/c/33ouGt/Jeq7) |
| Healthy | cfDNA | Urine | 19 | main part 150–400 bp (up to 19000 bp in female) | [[3]](https://paperpile.com/c/33ouGt/d3Kh) |
| Normozoospermia, Azoospermia | cfDNA | Seminal plasma | 11+9 | 180 bp–15000 bp | [[5]](https://paperpile.com/c/33ouGt/mJZH) |
| Non-small-cell lung carcinoma | cfDNA | Plasma | 50 | ~160 bp | [[25]](https://paperpile.com/c/33ouGt/F1ml) |
| Non-small-cell lung carcinoma | cfDNA | Sputum | 50 | ~160 bp | [[25]](https://paperpile.com/c/33ouGt/F1ml) |
| Non-small-cell lung carcinoma | cfDNA | Urine | 50 | ~100 bp | [[25]](https://paperpile.com/c/33ouGt/F1ml) |
| Healthy | cfDNA | Urine | 5 | 150–250 bp | [[26]](https://paperpile.com/c/33ouGt/yOOl) |
| Biliary tract carcinoma | cfDNA | Bile | 10 | ~6000 bp | [[27]](https://paperpile.com/c/33ouGt/MoiH) |
| Cancer | cfDNA | Ascites | 6 | main peak 150–160 bp; smaller peak 300–400 bp | [[9]](https://paperpile.com/c/33ouGt/QhYO) |
| Lung adenocarcinoma | cfDNA | Bronchial lavage fluid | 20 | ~10000 bp | [[13]](https://paperpile.com/c/33ouGt/CJOa) |
| Enucleated eyes | cfDNA | Aqueous humour | 12 | ~133 bp | [[15]](https://paperpile.com/c/33ouGt/Ls9U) |
| Enucleated eyes | cfDNA | Aqueous humour | 6 | 145–165 (median 150 bp) | [[16]](https://paperpile.com/c/33ouGt/vukL) |
| Healthy | cfDNA | Breast milk | NA | ~180 bp | [[28]](https://paperpile.com/c/33ouGt/K4Oa) |
| Pregnant woman | cffDNA | Urine | 5 | 29–45 bp | [[29]](https://paperpile.com/c/33ouGt/Q0IH) |
| Pregnant woman | cfDNA | Urine | 7 | <100 bp | [[29]](https://paperpile.com/c/33ouGt/Q0IH) |

**Table 3.** **The list of collection tubes or stabilization solutions developed for the preservation of cfNAs from different body fluids.** In the table there are summarized different preservation solutions (collection tubes, collection devices or stabilization buffers) for the most known body fluids. Each of the solutions contain information regarding its suitability for the type of the genetic material together with the manufacturer's recommendations for the storage time and temperature and also information about compatibility with downstream analysis. There is also a mention about the preservation reagents, however, in many cases it is proprietary information.

RT - room temperature.

NA - not available.

\* Web page does not work anymore.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Specimen** | **Manufacturer** | **Preservation solution** | **Type of cfNAs** | **Storage time** | **Temperature** | **Reagents** | **Sufficient for downstream analysis and applications** | **References** |
| Blood | Streck (La Vista, NE 68128 USA) | Cell-Free DNA BCT® | cfDNA | 14 days | 6-37 °C | anticoagulant K3EDTA and a cell preservative in a liquid medium | a wide range of downstream applications | [[30]](https://paperpile.com/c/33ouGt/23Vt) |
| CTCs | 7 days | 15-30 °C |
| RNA Complete BCT™ | cfRNA | 7 days | RT | anticoagulant K3EDTA and a cell preservative in a liquid medium | qualitative and quantitative real-time PCR, droplet digital PCR, NGS, and Nanoparticle Tracking Analysis. |
| extracellular vesicles (exosomes) | 7 days | RT |
| CellSearch (Menarini Silicon Biosystems Inc 3401 Masons Mill Road, Suite 100 Huntington Valley, PA) | CellSave Preservative Tubes | CTCs | 4 days | RT | proprietary preservative agent | NA | [[31]](https://paperpile.com/c/33ouGt/aRRr) |
| Qiagen  (PreAnalytiX GmbH  Feldbachstrasse  8634 Hombrechtikon  Switzerland) | PAXgene Blood ccfDNA Tubes | cfDNA | 10 days | RT | proprietary stabilization reagent | PCR, including digital, multiplex and quantitative real-time PCR, methylation-based assays, pharmacogenomic studies, SNP genotyping, NGS | [[32]](https://paperpile.com/c/33ouGt/Xtg6) |
| 7 days | 30 °C | [[33]](https://paperpile.com/c/33ouGt/L2i8) |
| 3 days | 37 °C |
| Roche (F. Hoffmann-La Roche Ltd. CH-4070 Basel, Switzerland) | Cell-Free DNA Collection Tube® | cfDNA | 7 days | 4 °C, RT, 37 °C | anticoagulant K3EDTA and a cell preservative | NA | [[34]](https://paperpile.com/c/33ouGt/TxyL) |
| Norgen (3430 Schmon Parkway, Thorold, ON, Canada, L2V 4Y6) | cf-DNA/cf-RNA Preservative Tubes | cfDNA | 30 days | RT | proprietary anticoagulant and non formaldehyde proprietary preservation agent | PCR, qPCR, rt-qPCR, methylation-sensitive PCR, Southern blot analysis, gene expression analysis, microarrays and NGS. | [[35]](https://paperpile.com/c/33ouGt/O3os) |
| 8 days | 37 °C |
| ctDNA | 30 days | RT |
| 8 days | 37 °C |
| cfRNA | 30 days | RT |
| CTCs | 14 days | RT |
| Biomatrica (5627 Oberlin Drive, Suite 120 San Diego, CA 92121) | LBgard® Blood Tubes | cfDNA | 7 days | 4-25 °C | proprietary reagent | digital PCR, NGS, methylation assays, imaging, immunotyping, prenatal testing, pharmacogenomics, genotyping, cancer diagnostics, allograft acceptance | [[36]](https://paperpile.com/c/33ouGt/7uo5) |
| CTCs | 4 days | 18-30 °C |
| ProTeck (CFGenome LLC, Denver, CO, USA) | Blood Exo DNA ProTeck® | cfDNA | NA | NA | stabilizing reagent very similar to BCTs by Streck; CFGenome is not providing this product anymore | NA | [[37]](https://paperpile.com/c/33ouGt/51WQ) |
| cffDNA |
| MagBio Genomics Inc. (944 Clopper Road  Gaithersburg, MD 20878 USA) | Blood STASIS™ 21-cfDNA Blood Collection Tubes | cfDNA | 21 days | 15-30 °C | proprietary stabilizing reagent | NA | [[38]](https://paperpile.com/c/33ouGt/NEIz) |
| CTCs | 7 days | 4-37 °C | proprietary non-fixative additive |
| Biocept (5810 Nancy Ridge Dr., Suite 150 San Diego, CA 92121) | CEE-Sure™ BCT | cfDNA | 8 days | 6-37 °C | anticoagulant ACD-A (Acid Citrate Dextrose) and a Formaldehyde Releasing Reagent | NA | [[39]](https://paperpile.com/c/33ouGt/BD7f) |
| CTCs | 4 days | 18-25 °C |
| Inresearch Medical Limited (TCL Tower, No.8 Tai Chung Rd, Tsuen Wan, Hongkong) | ImproGene™ Cell Free DNA Tube | cfDNA | 7-14 days | 4-30 °C | anticoagulant with proprietary preservative | NA | [[40]](https://paperpile.com/c/33ouGt/wsML)\* |
| EONE-DIAGNOMICS Genome Center  (#291 Harmony-ro, Yeonsu-gu, Incheon, 22014, South Korea) | NICE® Check cfDNA Tube | cfDNA | NA | NA | NA | NA | [[41]](https://paperpile.com/c/33ouGt/ZWlb) |
| Saliva | Norgen (3430 Schmon Parkway, Thorold, ON, Canada, L2V 4Y6) | Saliva Exosome Collection and Preservation Kit | exosomes, cfRNA | 2 years | RT | proprietary preservative | NA | [[42]](https://paperpile.com/c/33ouGt/aIUn) |
| Oasis Diagnostics® Corporation (15720 NE 31st Avenue,  Vancouver, WA 98686 USA) | Pure•SAL™  Ideal for Liquid Biopsy and Exosomes | cfDNA, cfRNA, exosomes, proteins | NA | NA | proprietary patented  device | PCR, genotyping, sequencing, proteomics and other applications, depending upon the desired results | [[43]](https://paperpile.com/c/33ouGt/gDXV) |
| RNAPro•SAL™  Split Sample Kit for Liquid Biopsy | RNA, cfDNA, cfRNA, exosomes | NA | NA | proprietary patented  device | not specified |
| Urine | Streck (La Vista, NE 68128 USA) | Cell-Free DNA Urine Preserve | cfDNA | 7 days | 6-37 °C | urine enzyme inhibitors and a cell  preservative and PCR compatible blue dye | qPCR, ddPCR, and other methods used to profile circulating DNA. | [[44]](https://paperpile.com/c/33ouGt/gsxi) |
| Hunan UPSBio Inc., (Hunan University National Science Park, Changsha, Hunan, China) | Urine Collection Tube | cfDNA | 7 days | RT | proprietary chemicals from Hunan UPSBio, Inc. | NA | NA |
| Zymo Research (IRVINE 17062 Murphy Ave. Irvine, CA 92614, U.S.A.) | Urine Conditioning Buffer (UCB) | DNA, RNA, cfDNA | 1 month | RT | NA | NA | [[45]](https://paperpile.com/c/33ouGt/AoRo) |
| Norgen (3430 Schmon Parkway, Thorold, ON, Canada, L2V 4Y6) | Urine Preservation | DNA, RNA, miRNA, proteins, cf-miRNA | 2 years | RT | NA | NA | [[46]](https://paperpile.com/c/33ouGt/wAv7) |
| DNA Genotek Inc. (3000 - 500 Palladium Drive Ottawa, Ontario, Canada  K2V 1C2) | Colli-Pee® | not specified | 7 days | RT | the non-toxic Novosanis proprietary Urine Conservation Medium (UCM) | NA | [[47]](https://paperpile.com/c/33ouGt/dMKw) |
| Stool | Zymo Research  (IRVINE 17062 Murphy Ave.  Irvine, CA 92614, U.S.A.) | DNA/RNA Shield Fecal Collection tubes | DNA | 2 years | 4-25 °C | proprietary preservative | NA | [[48]](https://paperpile.com/c/33ouGt/E4JG) |
| RNA | 1 month | 4-25 °C |
| Norgen (3430 Schmon Parkway, Thorold, ON, Canada, L2V 4Y6) | Stool Nucleic Acid Collection and Preservation Tubes | DNA | 2 years | RT | Norgen’s Stool Preservative in a liquid format | NA | [[49]](https://paperpile.com/c/33ouGt/b8iO) |
| RNA | 7 days | RT |
| DNA Genotek (Kanata, ON, Canada) | OMNIgene•GUT | DNA | 1 month | RT | ~2 ml of a proprietary buffer and a large stainless steel bead | 16S rRNA microbiome profiling, shotgun metagenomic sequencing, qPCR and arrays | [[50]](https://paperpile.com/c/33ouGt/5Vga) |

**Table 4. The list of methods developed for the isolation of exosomes from different body fluids.** In the table there are summarized different procedures developed for the extraction of exosomes from various body fluids. They are sorted based on the type of the body fluid from which they were extracted.

|  |  |  |  |
| --- | --- | --- | --- |
| **Source** | **Kit name (Manufacturer)** | **Type** | **References** |
| **Serum** | exo-Spin (Cell Guidance Systems) | Size exclusion-based | [[51]](https://paperpile.com/c/33ouGt/h0Dx) |
| exoEasy Maxi Kit (Qiagen) | Spin column | [[52]](https://paperpile.com/c/33ouGt/Mb2P) |
| Capturem Extracellular Vesicle Isolation Kit (Takara Bio) | Spin column | [[53]](https://paperpile.com/c/33ouGt/4n2K) |
| ExoQuick® ULTRA EV Isolation Kit for Serum and Plasma (System Biosciences) | Bipartate resin columns | [[54]](https://paperpile.com/c/33ouGt/FBb1) |
| The EasySep™ Human Pan-Extracellular Vesicle Positive Selection Kit (STEMCELL Technologies Inc.) | Immunoassay | [[55]](https://paperpile.com/c/33ouGt/1xGx) |
| miRCURY Exosome Kits (Qiagen) | Precipitation | [[56]](https://paperpile.com/c/33ouGt/BjS5) |
| **Plasma** | Total Exosome Isolation Kit (from plasma) (Thermo Fisher Scientific ) | Precipitation-based | [[57]](https://paperpile.com/c/33ouGt/R1Sc) |
| exoEasy Maxi Kit (Qiagen) | Spin column | [[58]](https://paperpile.com/c/33ouGt/KdZC) |
| ExoQuantTM overall exosome capture and quantification assay kit (BioVision Inc.) | Immunoassay | [[59]](https://paperpile.com/c/33ouGt/GtSi) |
| Capturem Extracellular Vesicle Isolation Kit (Takara Bio) | Spin column | [[60]](https://paperpile.com/c/33ouGt/qDMl) |
| ExoQuick® ULTRA EV Isolation Kit for Serum and Plasma (System Biosciences) | Bipartate resin columns | [[61]](https://paperpile.com/c/33ouGt/OVsZ) |
| The Exosome Isolation Kit Pan (Miltenyi Biotec) | Immunoassay | [[62]](https://paperpile.com/c/33ouGt/OdZo) |
| The EasySep™ Human Pan-Extracellular Vesicle Positive Selection Kit (STEMCELL Technologies Inc.) | Immunoassay | [[63]](https://paperpile.com/c/33ouGt/NKcr) |
| ExoFACS™ (BioVision) | Immunoassay | [[64]](https://paperpile.com/c/33ouGt/mD7h) |
| miRCURY Exosome Kits (Qiagen) | Precipitation | [[65]](https://paperpile.com/c/33ouGt/trKp) |
| **Urine** | ExoQuantTM overall exosome capture and quantification assay kit (BioVision Inc.) | Immunoassay | [[59]](https://paperpile.com/c/33ouGt/GtSi) |
| Capturem Extracellular Vesicle Isolation Kit (Takara Bio) | Spin column | [[66]](https://paperpile.com/c/33ouGt/Pb3x) |
| Exo-Urine EV Isolation Kit (System Biosciences) | Size Exclusion Chromatography | [[67]](https://paperpile.com/c/33ouGt/XCEs) |
| The Exosome Isolation Kit Pan (Miltenyi Biotec) | Immunoassay | [[62]](https://paperpile.com/c/33ouGt/OdZo) |
| miRCURY Exosome Kits (Qiagen) | Precipitation | [[68]](https://paperpile.com/c/33ouGt/Lggr) |
| Ultracentrifugation | - | [[69]](https://paperpile.com/c/33ouGt/MZhj) |
| Filtration | - | [[69]](https://paperpile.com/c/33ouGt/MZhj) |
| Precipitation | - | [[69]](https://paperpile.com/c/33ouGt/MZhj) |
| Affinity Purification | - | [[69]](https://paperpile.com/c/33ouGt/MZhj) |
| Microfluidics | - | [[69]](https://paperpile.com/c/33ouGt/MZhj) |
| **Saliva** | ExoFACS™ (BioVision) | Immunoassay | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| Minute™ (Invent Biotechnologies) | SDS-PAGE | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| Exo-spinTM (Cell Guidance Systems) | Size Exclusion Chromatography | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| Saliva Exosome Purification Kit (Norgen) | Resin based separation | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| ExoQuantTM overall exosome capture and quantification assay kit(BioVision Inc.) | Immunoassay | [[59]](https://paperpile.com/c/33ouGt/GtSi) |
| Capturem Extracellular Vesicle Isolation Kit | Spin column | [[71]](https://paperpile.com/c/33ouGt/AxOS) |
| Immuno-affinity | Immunoassay | [[72]](https://paperpile.com/c/33ouGt/yRUH) |
| Ciliated micropillars | Porous silicon nanowire-coated micropillars | [[73]](https://paperpile.com/c/33ouGt/dUms) |
| PMMA-based membrane filters | Porous polymer monoliths filtration | [[74]](https://paperpile.com/c/33ouGt/Z8Dp) |
| Functionalized surfaces (Exochip) | Immunoassay | [[75]](https://paperpile.com/c/33ouGt/wM4Y) |
| **Pleural effusions** | ExoLution Plus Isolation Kit (Exosome Diagnostics) | Precipitation-based | [[76]](https://paperpile.com/c/33ouGt/n5I6) |
| **Breast milk** | Capturem Extracellular Vesicle Isolation Kit (Takara Bio) | Spin column | [[77]](https://paperpile.com/c/33ouGt/HsQG) |
| **Cerebrospinal fluid** | Capturem Extracellular Vesicle Isolation Kit (Takara Bio) | Spin column | [[78]](https://paperpile.com/c/33ouGt/RuBP) |
| miRCURY Exosome Kits (Qiagen) | Precipitation | [[79]](https://paperpile.com/c/33ouGt/sApE) |

**Table 5. The list of methods developed for the isolation of cfNAs from different body fluids.** In the table there are summarized different procedures developed for the extraction of cfNAs from various body fluids.They are sorted based on the recommended source for which were developed and also on the source from which the cfNAs were isolated using a specific kit.

NA - not available.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Source** | **Type of cfNAs** | **Kit name (Manufacturer)** | **Type** | **References** |
| **Serum** | cfDNA | High Pure Viral Nucleic Acid Large Volume Kit (Roche Applied Science) | Spin column | [[80]](https://paperpile.com/c/33ouGt/bKdL) |
| Epi proColon 2.0 (Epigenomics AG) | NA | [[80]](https://paperpile.com/c/33ouGt/bKdL) |
| QIAamp Circulating Nucleic Acid Kit D2 (Qiagen) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| QIAamp DNA Blood Mini Kit (Qiagen) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| QIAsymphony DSP Circulating DNA Kit (Qiagen) | Magnetic beads | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| QIAamp MinElute ccfDNA Kit (Qiagen) | Magnetic beads | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| QIAamp DSP virus Kit (Qiagen) | Silica membrane column | [[82]](https://paperpile.com/c/33ouGt/v6bq) |
| QIAamp UltraSens Virus Kit (Qiagen) | Silica membrane column | [[83]](https://paperpile.com/c/33ouGt/3k6G) |
| MagMax Cell-Free DNA Isolation Kit (Applied Biosystems) | Magnetic beads | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| Maxwell RSC ccDNA Plasma Kit (Promega) | Magnetic beads | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| Chemagic Next Prep cfDNA (Perkin Elmer) | Magnetic beads | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| NextPrep-Mag cfDNA Isolation Kit (Perkin Elmer) | Magnetic beads | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| Nucleospin Plasma XS Kit (Macherey-Nagel) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| FitAmp Plasma/Serum DNA Isolation Kit (EpiGentek) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| GenElute Blood Genomic DNA kit (Sigma) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| Plasma/Serum Cell-Free Circulating DNA Purification Kit (Norgen) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| Quick-cfDNA/cfRNA Serum and Plasma Kit (Zymo Research) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| InviMag® Free Circulating DNA Kit/ IG | Magnetic beads | [[84]](https://paperpile.com/c/33ouGt/sLla) |
| PME free-circulating DNA Extraction Kit (Analytik Jena) | Spin column | [[85–88]](https://paperpile.com/c/33ouGt/szsd+zTkS+arxl+dGz2) |
| Quick-cfDNA Serum & Plasma Kit (Zymo Research) | Combination of chemical and enzymatic methods | [[89]](https://paperpile.com/c/33ouGt/De6b) |
| Sherlock AX (AA Biotechnology) | Spin column | [[90]](https://paperpile.com/c/33ouGt/OHqq) |
| ZR serum DNA Kit (Zymo Research) | Spin column | [[91]](https://paperpile.com/c/33ouGt/sdvq) |
| Phenol-chloroform-based method | Laboratory developed | [[91,92]](https://paperpile.com/c/33ouGt/sdvq+vm8P) |
| Triton/Heat/Phenol-based method | Laboratory developed | [[93]](https://paperpile.com/c/33ouGt/tGeN) |
| cfPure™ cell-free DNA extraction kit (Amsbio) | Magnetic beads | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| cfRNA | MagMAX Cell-Free DNA Isolation Kit (Thermo Fisher Scientific) | Magnetic beads | [[94]](https://paperpile.com/c/33ouGt/6JVn) |
| MagMAX Cell-Free Total Nucleic Acid Isolation Kit (Thermo Fisher Scientific) | Magnetic beads | [[95]](https://paperpile.com/c/33ouGt/NgE6) |
| Plasma/Serum Circulating and Exosomal RNA Purification Kit (Norgen) | Silica membrane column | [[96]](https://paperpile.com/c/33ouGt/0hdT) |
| miRNeasy Serum/Plasma Kit (Qiagen) | Silica membrane column | [[97]](https://paperpile.com/c/33ouGt/cx9S) |
| **Plasma** | cfDNA | High Pure Viral Nucleic Acid Large Volume Kit (Roche Applied Science) | Spin column | [[80]](https://paperpile.com/c/33ouGt/bKdL) |
| InviMag® Free Circulating DNA Kit/ IG | Magnetic beads | [[80]](https://paperpile.com/c/33ouGt/bKdL) |
| Quick-cfDNA™ Serum & Plasma Kit (Zymo Research) | Silica membrane column | [[80]](https://paperpile.com/c/33ouGt/bKdL) |
| InviGenius PLUS (STRATEC Biomedical AG) | Magnetic beads | [[80]](https://paperpile.com/c/33ouGt/bKdL) |
| Plasma/Serum Cell-Free Circulating DNA Purification Midi Kit (Norgen Biotek Corp. ) | Spin column | [[85]](https://paperpile.com/c/33ouGt/szsd) |
| Maxwell RSC ccfDNA Plasma Kit (Promega) | Magnetic beads | [[85,89]](https://paperpile.com/c/33ouGt/szsd+De6b) |
| Circulating Cell Free DNA Kit (NeoGeneStar) | Magnetic beads | [[85]](https://paperpile.com/c/33ouGt/szsd) |
| QIAamp circulating Nucleic Acids Kit (Qiagen) | Silica membrane column | [[83,85–90,92,98–101]](https://paperpile.com/c/33ouGt/szsd+Duns+zTkS+arxl+AheV+n9zb+joHL+vm8P+OHqq+dGz2+3k6G+De6b) |
| QIAamp DNA Blood Mini Kit (Qiagen) | Silica membrane column | [[83,90,91,99,101–103]](https://paperpile.com/c/33ouGt/AheV+mHj2+joHL+sdvq+OHqq+3k6G+GsUB) |
| NucleoSpin Plasma XS Kit (Macherey-Nagel) | Silica membrane column | [[92,99,101]](https://paperpile.com/c/33ouGt/AheV+joHL+vm8P) |
| FitAmp Plasma/Serum DNA Isolation Kit (EpiGentek) | Silica membrane column | [[99,101]](https://paperpile.com/c/33ouGt/AheV+joHL) |
| Plasma/Serum Cell-Free Circulating DNA Purification Midi Kit (Norgen Biotek Corp) | Spin column | [[85,92]](https://paperpile.com/c/33ouGt/szsd+vm8P) |
| Genomic Mini AX Body Fluids (AA Biotechnology) | Spin column | [[90]](https://paperpile.com/c/33ouGt/OHqq) |
| NucleoSpin PlasmaF Kit (Macherey-Nagel) | Spin column | [[102]](https://paperpile.com/c/33ouGt/mHj2) |
| QIAamp DNA Mini Kit (Qiagen) | Silica membrane column | [[104]](https://paperpile.com/c/33ouGt/IHz0) |
| QIAamp DSP virus Kit (Qiagen) | Silica membrane column | [[82]](https://paperpile.com/c/33ouGt/v6bq) |
| QIAamp UltraSens Virus Kit (Qiagen) | Silica membrane column | [[83]](https://paperpile.com/c/33ouGt/3k6G) |
| QIAamp Virus Spin Kit (Qiagen) | Silica membrane column | [[103]](https://paperpile.com/c/33ouGt/GsUB) |
| Quick-cfDNA Serum & Plasma Kit (Zymo Research) | Combination of chemical and enzymatic methods | [[88,89]](https://paperpile.com/c/33ouGt/dGz2+De6b) |
| Plasma/Serum Cell-Free Circulating DNA Purification Mini Kit (Norgen) | Silica membrane column | [[92]](https://paperpile.com/c/33ouGt/vm8P) |
| Sherlock AX (AA Biotechnology) | Spin column | [[90]](https://paperpile.com/c/33ouGt/OHqq) |
| ZR serum DNA Kit (Zymo Research) | Spin column | [[91]](https://paperpile.com/c/33ouGt/sdvq) |
| Maxwell RSC ccfDNA Plasma Kit (Promega) | Magnetic beads | [[85,86,98,100,104]](https://paperpile.com/c/33ouGt/szsd+IHz0+Duns+zTkS+n9zb) |
| ChargeSwitch gDNA Serum Kit, 0.2-1 mL (Invitrogen) | Magnetic beads | [[91,103]](https://paperpile.com/c/33ouGt/sdvq+GsUB) |
| Agencourt Genfind Blood and Serum Genomic DNA Isolation Kit (Agencourt Bioscience Corporation) | Magnetic beads | [[103]](https://paperpile.com/c/33ouGt/GsUB) |
| Chemagic NA Extraction Kit (Perkin-Elmer) | Magnetic beads | [[92]](https://paperpile.com/c/33ouGt/vm8P) |
| COBAS AmpliPrep Total Nucleic Acid Isolation Kit (Roche) | Magnetic beads | [[82]](https://paperpile.com/c/33ouGt/v6bq) |
| QIAsymphony Circulating NA Kit (Qiagen) | Magnetic beads | [[88]](https://paperpile.com/c/33ouGt/dGz2) |
| QIAsymphony DSP Virus/ Pathogen Midi Kit (Qiagen) | Magnetic beads | [[83,87]](https://paperpile.com/c/33ouGt/arxl+3k6G) |
| EpiQuick Circulating Cell- Free DNA Isolation Kit (EpiGentek) | Magnetic beads | [[86]](https://paperpile.com/c/33ouGt/zTkS) |
| Mag-Bind Circulating DNA (Omega Bio-Tek) | Magnetic beads | [[85]](https://paperpile.com/c/33ouGt/szsd) |
| MagMAX Cell-free DNA Isolation Kit (Life Technologies) | Magnetic beads | [[85]](https://paperpile.com/c/33ouGt/szsd) |
| MagNA Pure LC DNA Isolation Kit - Large Volume (Roche) | Magnetic beads | [[102]](https://paperpile.com/c/33ouGt/mHj2) |
| MagNA Pure Compact Nucleic Acid Isolation Kit I (Roche) | Magnetic beads | [[88,98]](https://paperpile.com/c/33ouGt/Duns+dGz2) |
| NEXTprep-Mag cfDNA Isolation Kit (Bioo Scientific) | Magnetic beads | [[86]](https://paperpile.com/c/33ouGt/zTkS) |
| Circulating Cell Free DNA Kit (NeoGeneStar) | Magnetic beads | [[85]](https://paperpile.com/c/33ouGt/szsd) |
| Phenol-chloroform | Laboratory developed | [[91,92]](https://paperpile.com/c/33ouGt/sdvq+vm8P) |
| Sodium iodide method | Laboratory developed | [[91]](https://paperpile.com/c/33ouGt/sdvq) |
| Guanidine-resin method | Laboratory developed | [[91]](https://paperpile.com/c/33ouGt/sdvq) |
| Puregene DNA purification System Cell and Tissue Kit (Gentra) | Precipitation | [[91]](https://paperpile.com/c/33ouGt/sdvq) |
| PME free-circulating DNA Extraction Kit (Analytik Jena) | Spin column | [[85–88]](https://paperpile.com/c/33ouGt/szsd+zTkS+arxl+dGz2) |
| QIAamp MinElute ccfDNA Kit (Qiagen) | Magnetic beads | [[105]](https://paperpile.com/c/33ouGt/MDCQ) |
| EZ1 ccfDNA Kits (Qiagen) | Magnetic beads | [[105]](https://paperpile.com/c/33ouGt/MDCQ) |
| QIAsymphony PAXgene Blood ccfDNA Kit (Qiagen) | Magnetic beads | [[105]](https://paperpile.com/c/33ouGt/MDCQ) |
| cfRNA | miRNeasy Serum/Plasma Kit (Qiagen) | Silica membrane column | [[106]](https://paperpile.com/c/33ouGt/rUMK) |
| miRNeasy 96 Advanced QIAcube HT Kit (Qiagen) | Silica membrane column | [[107]](https://paperpile.com/c/33ouGt/pUYH) |
| QIAamp Circulating Nucleic Acid Kit D2 (Qiagen) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| Plasma/Serum Circulating and Exosomal RNA Purification Kit (Norgen) | Silica membrane column | [[108]](https://paperpile.com/c/33ouGt/xkxT) |
| **Urine** | cfDNA | poly-Lys-coated silica particles | Silica membrane column | [[109]](https://paperpile.com/c/33ouGt/V4L2) |
| Triamine-modified silica particles | Silica membrane column | [[110]](https://paperpile.com/c/33ouGt/RqRD) |
| Hybridization capture | Laboratory developed | [[111]](https://paperpile.com/c/33ouGt/gXbO) |
| Wizard Resin/Guanidinium Thiocyanate | Spin column | [[111]](https://paperpile.com/c/33ouGt/gXbO) |
| Q Sepharose Anion Exchange Resin | Chromatography-based | [[111]](https://paperpile.com/c/33ouGt/gXbO) |
| Urine Cell-Free Circulating DNA Purification Mini Kit (Norgen) | Spin column | [[111,112]](https://paperpile.com/c/33ouGt/gXbO+p8Hx) |
| QIAamp Circulating Nucleic Acid Kit(Qiagen) | Silica membrane column | [[111]](https://paperpile.com/c/33ouGt/gXbO) |
| MagMAX Cell-Free DNA Isolation Kit (Thermo Fisher Scientific ) | Magnetic beads | [[111,112]](https://paperpile.com/c/33ouGt/gXbO+p8Hx) |
| NEXTprep-Mag Urine cfDNA Isolation Kit (PerkinElmer) | Magnetic beads | [[113]](https://paperpile.com/c/33ouGt/rAZo) |
| Urine Cell-Free Circulating DNA Purification Midi Kit(Norgen Biotek) | Silica membrane column | [[113]](https://paperpile.com/c/33ouGt/rAZo) |
| Quick-DNA Urine Kit (ZymoResearch) | Spin column | [[114,115]](https://paperpile.com/c/33ouGt/LIO3+a758) |
| QIAsymphony DSP Circulating DNA Kit (Qiagen) | Magnetic beads | [[116]](https://paperpile.com/c/33ouGt/qVwe) |
| PME free-circulating DNA Extraction Kit (Analytik Jena) | Polymer mediated enrichment followed by centrifugation | [[85–88]](https://paperpile.com/c/33ouGt/szsd+zTkS+arxl+dGz2) |
| cfRNA | Urine Cell-Free Circulating RNA Purification Mini Kit | Spin column | [[115]](https://paperpile.com/c/33ouGt/a758) |
| MicroMini Kit (Qiagen) | NA | [[117]](https://paperpile.com/c/33ouGt/LkRP) |
| QIAamp Circulating Nucleic Acid Kit D2 (QIAgen) | Silica membrane column | [[81]](https://paperpile.com/c/33ouGt/rNgt) |
| **Saliva** | cfDNA | GeneFixTM Saliva DNA isolation kit (Cell projects) | Spin column | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| Oragene®-DNA (DNA Genotek) | Ethanol precipitation | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| Saliva DNA Isolation Kit (Norgen ) | Spin column | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| Saliva DNA Isolation Kit (BioChain Institute) | Spin column | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| Mini·SAL™ Saliva DNA Isolation Kit (Oasis Diagnostics® Corporation) | Spin column | [[70]](https://paperpile.com/c/33ouGt/6gY2) |
| Sherlock AX (AA Biotechnology) | Spin column | [[90]](https://paperpile.com/c/33ouGt/OHqq) |
| Quick-cfDNA Serum & Plasma Kit (Zymo Research) | Combination of chemical and enzymatic methods | [[118]](https://paperpile.com/c/33ouGt/ZeW7) |
| Chitosan coated PMMA high surface area | Functionalized surface | [[119]](https://paperpile.com/c/33ouGt/wf7D) |
| Digital PCR using droplet based microfluidics | Droplet based microfluidics | [[120]](https://paperpile.com/c/33ouGt/58mR) |
| Tagmentation chemistry and solid phase reversible immobilization (SPRI) based integrated microfluidics | Tagmentation chemistry: Extraction DNA  SPRI: Purification DNA | [[121]](https://paperpile.com/c/33ouGt/diea) |
| DNA purification and PCR amplification based integrated microfluidics | Micro-sample processing device (μSPD)  DNA purification process | [[122]](https://paperpile.com/c/33ouGt/UKYL) |
| DNA extraction, amplification, detection based integrated microfluidics | Monolithic aluminum oxide membrane for DNA extraction: seven parallel reaction wells | [[123]](https://paperpile.com/c/33ouGt/UTRg) |
| cfRNA | mirVana Isolation Kit (Thermo Fisher Scientific) | Organic extraction followed by purification on a GFF under specialized binding and wash conditions. | [[124]](https://paperpile.com/c/33ouGt/LOqt) |
| **Stool** | cfDNA | QIAamp Circulating Nucleic Acid Kit (Qiagen) | Silica membrane column | [[125]](https://paperpile.com/c/33ouGt/TZep) |
|  |  | NucleoSpin® Gel and PCR Clean-up kit (Macherey-Nagel) | Spin column | [[125]](https://paperpile.com/c/33ouGt/TZep) |
|  |  | NucleoSpin® Plasma XS kit (Macherey-Nagel) | Spin column | [[125]](https://paperpile.com/c/33ouGt/TZep) |
|  |  | cfPure® Cell-Free DNA Extraction Kit (BioChain) | Magnetic beads | [[125]](https://paperpile.com/c/33ouGt/TZep) |
|  |  | MagMAX™ Cell-Free DNA Isolation Kit (Thermo Fisher Scientific) | Magnetic beads | [[125]](https://paperpile.com/c/33ouGt/TZep) |
|  |  | MagNA Pure 24 System (Roche) | Magnetic beads | [[125]](https://paperpile.com/c/33ouGt/TZep) |
| **Seminal plasma** | cfDNA | QIAamp Circulating Nucleic Acid Kit (Qiagen) | Silica membrane column | [[4]](https://paperpile.com/c/33ouGt/XxSj) |
|  |  | QIAamp DNA Mini Kit (Qiagen) | Silica membrane column | [[126]](https://paperpile.com/c/33ouGt/iGgR) |
| **Pleural effusions** | cfDNA | High Pure PCR Template Preparation Kit (Roche) | Spin column | [[127]](https://paperpile.com/c/33ouGt/WaGH) |
|  |  | QIAsymphony DSP DNA Midi Kit (Qiagen) | Silica membrane column | [[128]](https://paperpile.com/c/33ouGt/VA5t) |
|  |  | QIAamp Circulating Nucleic Acid Kit (Qiagen) | Silica membrane column | [[76]](https://paperpile.com/c/33ouGt/n5I6) |
| **Breast milk** | cfDNA | cfDNA purification kit (SummerBio) | NA | [[28]](https://paperpile.com/c/33ouGt/K4Oa) |
| cfRNA | cfRNA purification kit (SummerBio) | NA | [[28]](https://paperpile.com/c/33ouGt/K4Oa) |
| **Cerebrospinal fluid** | cfDNA | Quick-cfDNA Serum & Plasma Kit (Zymo Research) | Combination of chemical and enzymatic methods | [[89]](https://paperpile.com/c/33ouGt/De6b) |
| **Amniotic fluid** | cfDNA | Quick-cfDNA Serum & Plasma Kit (Zymo Research) | Combination of chemical and enzymatic methods | [[89]](https://paperpile.com/c/33ouGt/De6b) |
| cfRNA | QIAamp Circulating Nucleic Acid kit (Qiagen) | Silica membrane column | [[129]](https://paperpile.com/c/33ouGt/AdeJ) |

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