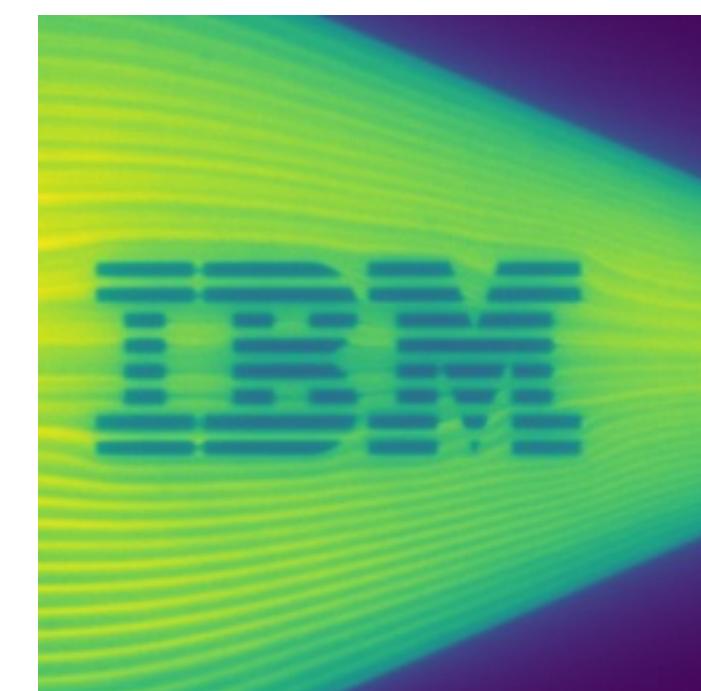


# exRNA Sequence Projects

Sung-cheol Kim  
2019/05/19



# exRNA Atlas

[www.exrna-atlas.org](http://www.exrna-atlas.org)

**Bringing exRNA Data and Analysis Tools Together**

Type in mature miRNAs of interest  ?

The exRNA Atlas is the data repository of the Extracellular RNA Communication Consortium (ERCC). The repository includes small RNA sequencing and qPCR-derived exRNA profiles from human and mouse biofluids. All RNA-seq datasets are processed using [version 4](#) of the [exceRpt small RNA-seq pipeline](#) (Rozowsky et al., 2019) and ERCC-developed quality metrics are uniformly applied to these datasets. If you're interested in submitting your RNA-seq or qPCR data to the Atlas, view our [Submission Guide](#).

Above, in the upper right corner of this panel, you can use the **ncRNA search bar** to search the exRNA Atlas data for specific ncRNAs of interest. If your browser window is smaller, you will need to click the "hamburger" options icon to reveal the ncRNA search bar.

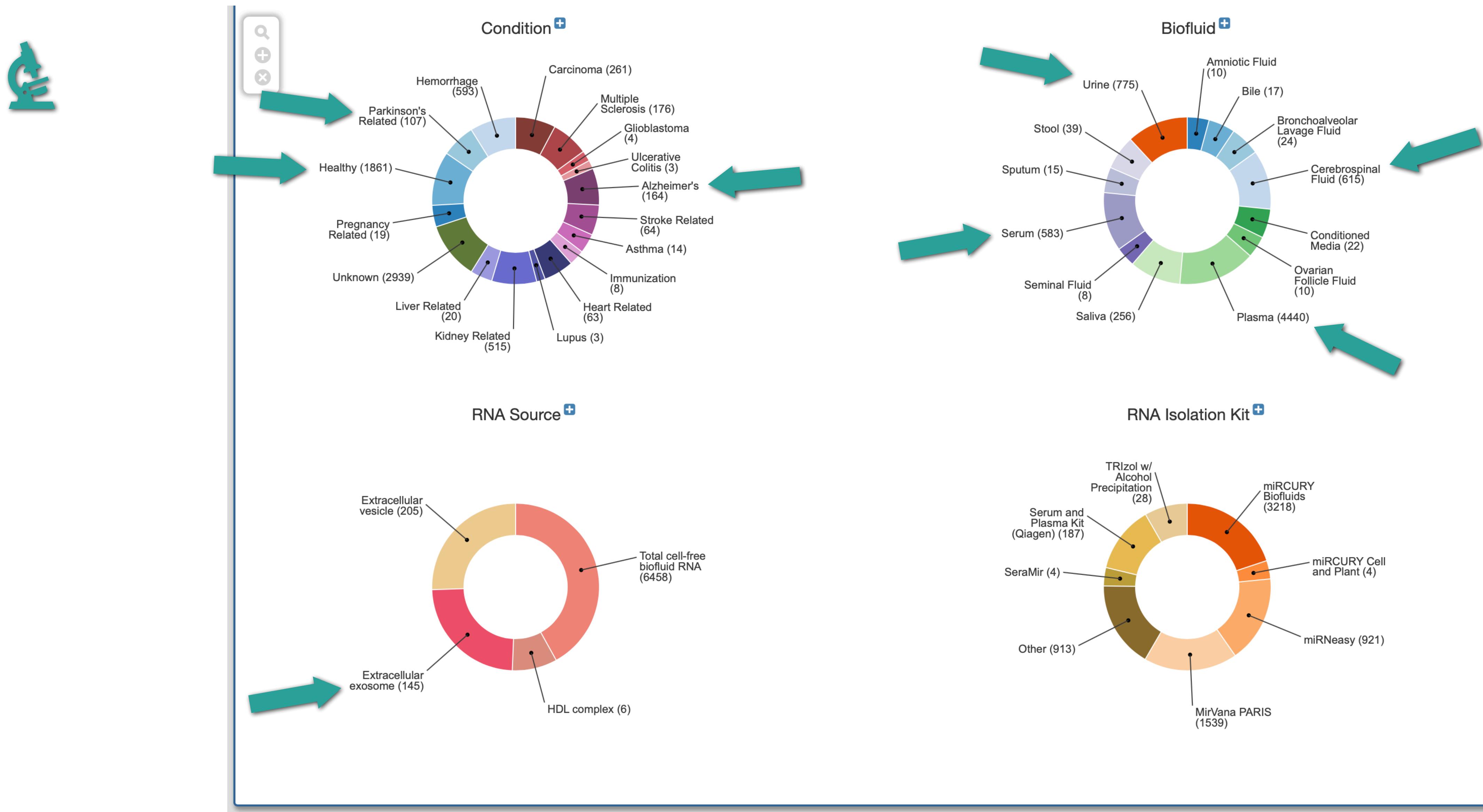
We also have a dedicated JSON-LD API that can be used for programmatic access to Atlas data and metadata. More information can be found on our [API Documentation](#) page.

**Attention:** If you're interested in viewing the version of the Atlas used in the *Cell* paper "ExRNA Atlas Analysis Reveals Distinct Extracellular RNA Cargo Types and Their Carriers Present Across Human Biofluids" (Murillo et al., 2019), please see the associated [Atlas Snapshot](#).

**Getting Started**

exRNA Atlas Analysis Reveals Distinct Extracellular RNA Cargo Types and Their Carriers Present across Human Biofluids

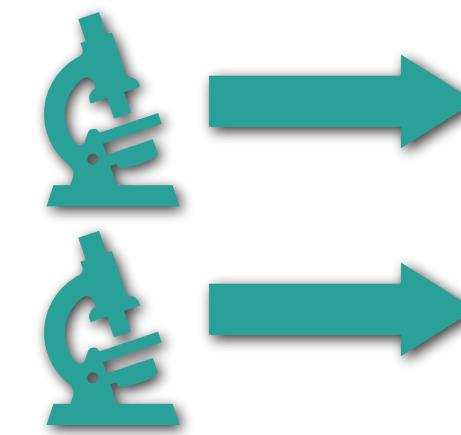
# Condition, Biofluid, RNA Source, RNA Isolation Kit



# Studies on exRNA-Atlas (7 out 29)

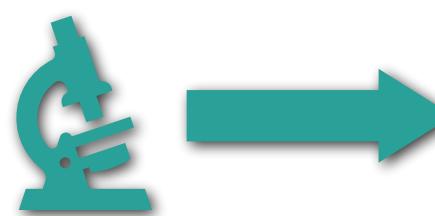
Overview of Studies (25 of 29 Shown)					
PI Name ↑	Organization ↑	Study Title ↑	Samples ↓	Published? ↓	Other Databases
Ansel, Mark	University of California San Francisco	Testing the composition and sources of miRNAs in bronchoalveolar lavage fluid and serum after the induction of allergic lung inflammation. <a href="#">(EXR-MANSE1oCqMmF-AN)</a>	28		
Bitzer, Markus	University of Michigan	Identifying urinary RNA as non-invasive biomarkers for progression of chronic kidney disease <a href="#">(EXR-MBITZ1SHVlr-AN)</a>	80		GEO
Bitzer, Markus	University of Michigan	Identifying urinary RNA from biopsy associated urine as non-invasive biomarkers for kidney transplant patients <a href="#">(EXR-MBITZ1WCKgCw-AN)</a>	207		GEO
Bitzer, Markus	University of Michigan	Identifying urinary RNA from prospective urine as non-invasive biomarkers for kidney transplant patients <a href="#">(EXR-MBITZ1KPWlgP-AN)</a>	228		GEO
Das, Saumya	Massachusetts General Hospital	Small RNA-seq during acute maximal exercise reveal RNAs involved in vascular inflammation and cardiometabolic health <a href="#">(EXR-SADAS1EXER1-AN)</a>	62	✓	GEO
Das, Saumya	Massachusetts General Hospital	Identifying novel small RNA biomarkers for electrical and mechanical remodeling post-MI (myocardial infarction) <a href="#">(EXR-SADAS1UJ0CzW-AN)</a>	43	✓	GEO
Erle, David	University of California-San Francisco	Large differences in small RNA composition between 12 human biofluids - protected access <a href="#">(EXR-DERLE1PHASE1PROT-AN)</a>	117	✓	dbGaP dbGaP dbGaP dbGaP

# Studies on exRNA-Atlas (10 out of 29)



<b>Erle, David</b>	University of California-San Francisco	Large differences in small RNA composition between 12 human biofluids - open access (EXR-DERLE1PHASE1OPEN-AN)	12	✓	GEO
<b>Franklin, Jeff</b>	Vanderbilt University School of Medicine	RNAseq analysis of colorectal cancer cells: KRAS regulation of secreted RNAs. (EXR-JFRAN16VDql8-AN)	18	✓	GEO SRA
<b>Freedman, Jane</b>	University of Massachusetts Medical School	Diverse human extracellular RNAs are widely detected in human plasma. (EXR-JFREE1UH2qPCR-AN, EXR-JFREE1eZDUKB-AN)	2979	✓	dbGaP
<b>Galas, David</b>	Pacific Northwest Diabetes Research Institute	The Complex Exogenous RNA Spectra in Human Plasma: An Interface with Human Gut Biota? (EXR-DGALA1V5h5va-AN)	9	✓	SRA EBI
<b>Gandhi, Roopali</b>	Brigham and Women's Hospital	Search for Novel miRNA Serum Biomarkers in Multiple Sclerosis (EXR-RGAND1UH2001-AN)	193		
<b>Jensen, Kendall</b>	Translational Genomics Research Institute	Plasma small RNASeq comparison with Illumina TruSeq and Biooscientific NextFlex (EXR-KJENS17CZMbP-AN)	12		GEO
<b>Jensen, Kendall</b>	Translational Genomics Research Institute	Blood-Based Extracellular RNAs Are Biomarkers Predictive of Stroke Subtype (EXR-KJENS10IPCIY-AN)	187		
<b>Jensen, Kendall</b>	Translational Genomics Research Institute	Profiles of Extracellular miRNA in Cerebrospinal Fluid and Serum from Patients with Alzheimer's and Parkinson's Diseases Correlate with Disease Status and Features of Pathology (EXR-KJENS1sPlvS2-AN)	345	✓	dbGaP
<b>Jensen, Kendall</b>	Translational Genomics Research Institute	Profiles of Extracellular RNA in Cerebrospinal Fluid and Plasma from Subarachnoid Hemorrhage Patients (EXR-KJENS1WBaSro-AN)	523		GEO dbGaP
<b>Jensen, Kendall</b>	Translational Genomics Research Institute	Total Extracellular Small RNA Profiles from Plasma, Saliva, and Urine of Healthy Subjects. (EXR-KJENS1RID1-AN)	428	✓	dbGaP

# Studies on exRNA-Atlas (10 out of 29)



Jensen, Kendall	Translational Genomics Research Institute	small RNA Sequencing of CSF Samples from Patients with IVH (EXR-KJENS12WGutU-AN)	70	GEO
Krichevsky, Anna	Brigham and Women's Hospital	Extracellular RNA levels for glioblastoma multiforme patients via extracellular exosomes in conditioned media (EXR-AKRIC157ITEI-AN)	4	
Laurent, Louise	University of California-San Diego	Identifying novel small RNA biomarkers unique to patients with placental dysfunction (EXR-LLAUR1s0A1mX-AN)	48	
Naccarati, Alessio	University of Turin	Small non-coding RNA profiling in human biofluids and surrogate tissues from healthy individuals (EXR-ANACC1S6IJ1C-AN)	209	✓ GEO
Patel, Tushar	Mayo Clinic	Identifying and analyzing extracellular RNA found in mouse samples (EXR-TPATE10baswA-AN)	3	
Patel, Tushar	Mayo Clinic	Plasma extracellular RNA profiles in healthy and cancer patients (EXR-TPATE1OqELFf-AN)	192	✓ SRA GEO
Patel, Tushar	Mayo Clinic	Identifying and analyzing circulating extracellular RNA found in human serum. (EXR-TPATE1NUsA7E-AN)	5	
Saugstad, Julie	Oregon Health and Sciences University	TLDA miRNA Screen for Candidate AD Biomarkers in CSF from Living Donors (EXR-JSAUG1UH2001-AN)	99	✓
Tewari, Muneesh	University of Michigan	ULMC Plasma and serum exRNA from healthy donors at University of Michigan (EXR-MTEWA1cHYLo6-AN)	197	GEO
Tuschl, Thomas	Rockefeller University	exRNA reference profiling at 12 intervals over 2 months, addressing the effect of biofluid (serum vs. EDTA plasma), gender, fasting and female hormonal cycle (EXR-TTUSC1gCrGDH-AN)	312	✓ GEO



# Studies on exRNA-Atlas (2 out of 29)

Vickers, Kasey	Vanderbilt University School of Medicine	High-Density Lipoproteins - small RNA Signatures in Systemic Erythematosus Lupus. (EXR-KVICK1olp40e-AN)	6	GEO
Wong, David	University of California-Los Angeles	Identifying novel small RNA biomarkers unique to patients with gastric cancer (EXR-DWONG1qf3tcS-AN)	198	✓ GEO dbGaP

Total 14 published studies

Cell. 2019 Apr 4;177(2):463-477.e15. doi: 10.1016/j.cell.2019.02.018.

## exRNA Atlas Analysis Reveals Distinct Extracellular RNA Cargo Types and Their Carriers Present across Human Biofluids.

Murillo OD<sup>1</sup>, Thistlethwaite W<sup>1</sup>, Rozowsky J<sup>2</sup>, Subramanian SL<sup>1</sup>, Lucero R<sup>1</sup>, Shah N<sup>1</sup>, Jackson AR<sup>1</sup>, Srinivasan S<sup>3</sup>, Chung A<sup>4</sup>, Laurent CD<sup>3</sup>, Kitchen RR<sup>5</sup>, Galeev T<sup>2</sup>, Warrell J<sup>2</sup>, Diao JA<sup>6</sup>, Welsh JA<sup>7</sup>, Hanspers K<sup>8</sup>, Riutta A<sup>8</sup>, Burgstaller-Muehlbacher S<sup>9</sup>, Shah RV<sup>10</sup>, Yeri A<sup>10</sup>, Jenkins LM<sup>11</sup>, Ahsen ME<sup>12</sup>, Cordon-Cardo C<sup>13</sup>, Dogra N<sup>14</sup>, Gifford SM<sup>15</sup>, Smith JT<sup>15</sup>, Stolovitzky G<sup>14</sup>, Tewari AK<sup>16</sup>, Wunsch BH<sup>15</sup>, Yadav KK<sup>17</sup>, Danielson KM<sup>10</sup>, Filant J<sup>18</sup>, Moeller C<sup>3</sup>, Nejad P<sup>19</sup>, Paul A<sup>19</sup>, Simonson B<sup>10</sup>, Wong DK<sup>4</sup>, Zhang X<sup>5</sup>, Balaj L<sup>20</sup>, Gandhi R<sup>19</sup>, Sood AK<sup>21</sup>, Alexander RP<sup>22</sup>, Wang L<sup>23</sup>, Wu C<sup>9</sup>, Wong DTW<sup>24</sup>, Galas DJ<sup>22</sup>, Van Keuren-Jensen K<sup>25</sup>, Patel T<sup>26</sup>, Jones JC<sup>7</sup>, Das S<sup>10</sup>, Cheung KH<sup>27</sup>, Pico AR<sup>8</sup>, Su AI<sup>9</sup>, Raffai RL<sup>4</sup>, Laurent LC<sup>3</sup>, Roth ME<sup>1</sup>, Gerstein MB<sup>28</sup>, Milosavljevic A<sup>29</sup>.

### Author information

### Abstract

To develop a map of cell-cell communication mediated by extracellular RNA (exRNA), the NIH Extracellular RNA Communication Consortium created the exRNA Atlas resource (<https://exrna-atlas.org>). The Atlas version 4P1 hosts 5,309 exRNA-seq and exRNA qPCR profiles from 19 studies and a suite of analysis and visualization tools. To analyze variation between profiles, we apply computational deconvolution. The analysis leads to a model with six exRNA cargo types (CT1, CT2, CT3A, CT3B, CT3C, CT4), each detectable in multiple biofluids (serum, plasma, CSF, saliva, urine). Five of the cargo types associate with known vesicular and non-vesicular (lipoprotein and ribonucleoprotein) exRNA carriers. To validate utility of this model, we re-analyze an exercise response study by deconvolution to identify physiologically relevant response pathways that were not detected previously. To enable wide application of this model, as part of the exRNA Atlas resource, we provide tools for deconvolution and analysis of user-provided case-control studies.

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**KEYWORDS:** ERCC; deconvolution; exRNA; exosomes; extracellular RNA; extracellular vesicles; lipoproteins; ribonucleoproteins

PMID: 30951672 DOI: [10.1016/j.cell.2019.02.018](https://doi.org/10.1016/j.cell.2019.02.018)

Nat Commun. 2016 Apr 26;7:11106. doi: 10.1038/ncomms11106.

## Diverse human extracellular RNAs are widely detected in human plasma.

Freedman JE<sup>1</sup>, Gerstein M<sup>2</sup>, Mick E<sup>3</sup>, Rozowsky J<sup>2</sup>, Levy D<sup>4,5</sup>, Kitchen R<sup>2</sup>, Das S<sup>6</sup>, Shah R<sup>6</sup>, Danielson K<sup>6</sup>, Beaulieu L<sup>1</sup>, Navarro FC<sup>2</sup>, Wang Y<sup>7</sup>, Galeev TR<sup>2</sup>, Holman A<sup>7</sup>, Kwong RY<sup>8</sup>, Murthy V<sup>9</sup>, Tanriverdi SE<sup>1</sup>, Koupenova-Zamor M<sup>1</sup>, Mikhalev E<sup>1</sup>, Tanriverdi K<sup>1</sup>.

### Author information

### Erratum in

Corrigendum: Diverse human extracellular RNAs are widely detected in human plasma. [Nat Commun. 2016]

### Abstract

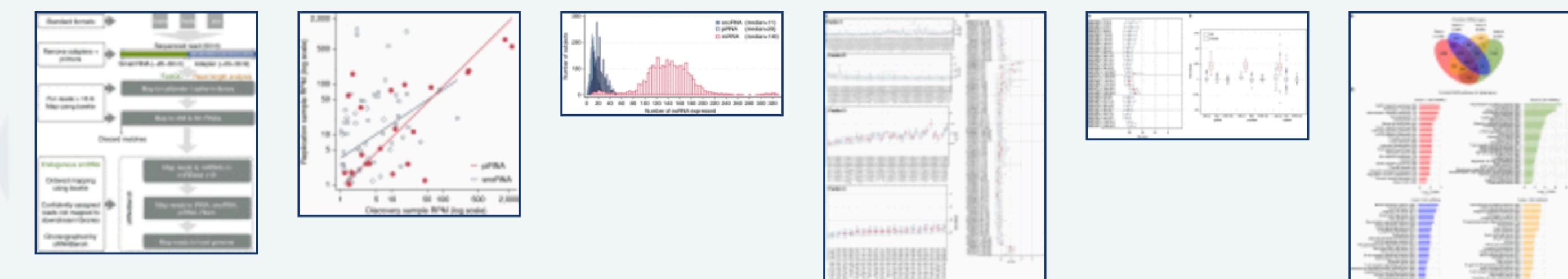
There is growing appreciation for the importance of non-protein-coding genes in development and disease. Although much is known about microRNAs, limitations in bioinformatic analyses of RNA sequencing have precluded broad assessment of other forms of small-RNAs in humans. By analysing sequencing data from plasma-derived RNA from 40 individuals, here we identified over a thousand human extracellular RNAs including microRNAs, piwi-interacting RNA (piRNA), and small nucleolar RNAs. Using a targeted quantitative PCR with reverse transcription approach in an additional 2,763 individuals, we characterized almost 500 of the most abundant extracellular transcripts including microRNAs, piRNAs and small nucleolar RNAs. The presence in plasma of many non-microRNA small-RNAs was confirmed in an independent cohort. We present comprehensive data to demonstrate the broad and consistent detection of diverse classes of circulating non-cellular small-RNAs from a large population.

PMID: 27112789    PMCID: [PMC4853467](#)    DOI: [10.1038/ncomms11106](#)

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PLoS One. 2012;7(12):e51009. doi: 10.1371/journal.pone.0051009. Epub 2012 Dec 10.

## The complex exogenous RNA spectra in human plasma: an interface with human gut biota?

Wang K<sup>1</sup>, Li H, Yuan Y, Etheridge A, Zhou Y, Huang D, Wilmes P, Galas D.

### Author information

#### Abstract

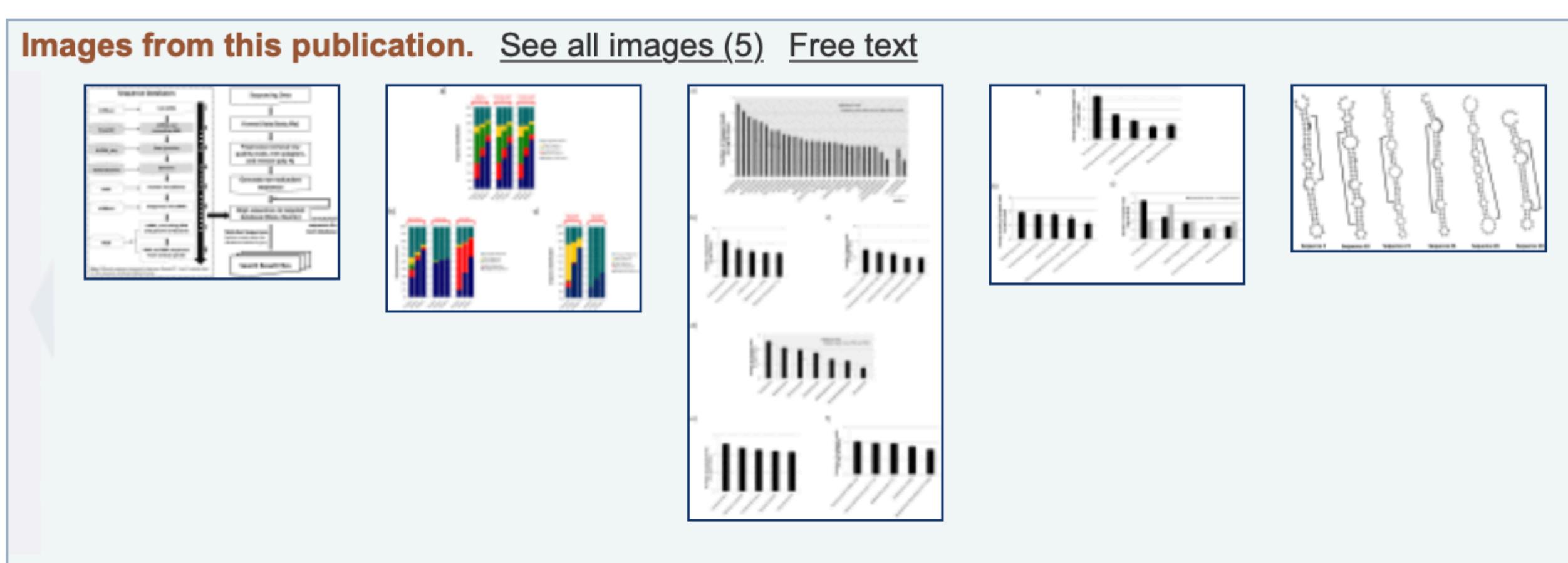
Human plasma has long been a rich source for biomarker discovery. It has recently become clear that plasma RNA molecules, such as microRNA, in addition to proteins are common and can serve as biomarkers. Surveying human plasma for microRNA biomarkers using next generation sequencing technology, we observed that a significant fraction of the circulating RNA appear to originate from exogenous species. With careful analysis of sequence error statistics and other controls, we demonstrated that there is a wide range of RNA from many different organisms, including bacteria and fungi as well as from other species. These RNAs may be associated with protein, lipid or other molecules protecting them from RNase activity in plasma. Some of these RNAs are detected in intracellular complexes and may be able to influence cellular activities under in vitro conditions. These findings raise the possibility that plasma RNAs of exogenous origin may serve as signaling molecules mediating for example the human-microbiome interaction and may affect and/or indicate the state of human health.

PMID: 23251414    PMCID: [PMC3519536](#)    DOI: [10.1371/journal.pone.0051009](#)

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PLoS One. 2014 May 5;9(5):e94839. doi: 10.1371/journal.pone.0094839. eCollection 2014.

## Profiles of extracellular miRNA in cerebrospinal fluid and serum from patients with Alzheimer's and Parkinson's diseases correlate with disease status and features of pathology.

Burgos K<sup>1</sup>, Malenica I<sup>1</sup>, Metpally R<sup>1</sup>, Courtright A<sup>1</sup>, Rakela B<sup>1</sup>, Beach T<sup>2</sup>, Shill H<sup>2</sup>, Adler C<sup>3</sup>, Sabbagh M<sup>2</sup>, Villa S<sup>1</sup>, Tembe W<sup>1</sup>, Craig D<sup>1</sup>, Van Keuren-Jensen K<sup>1</sup>.

### Author information

#### Abstract

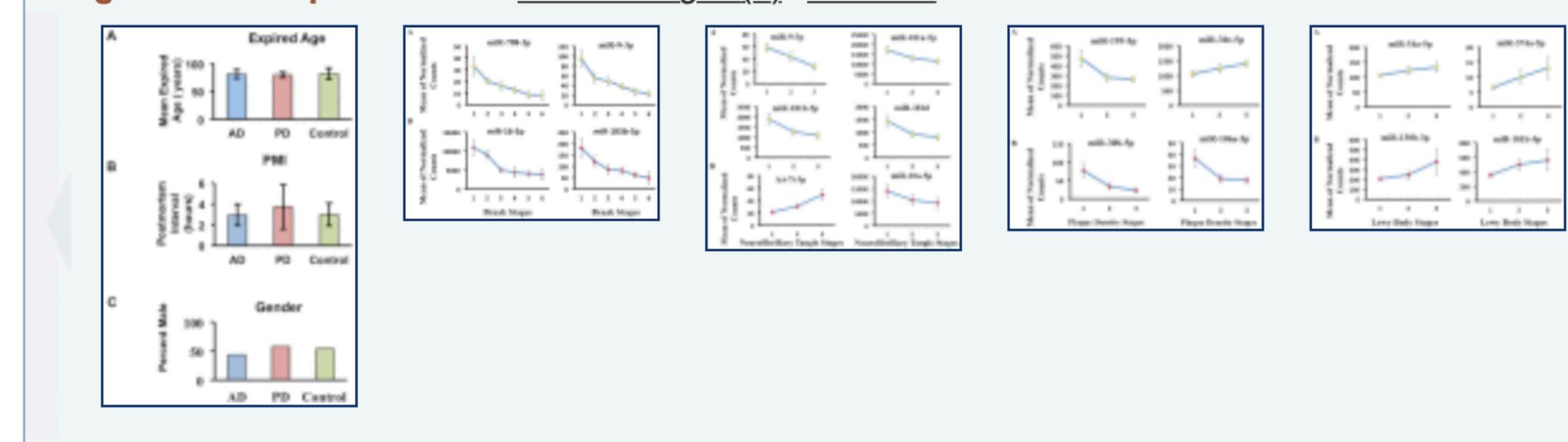
The discovery and reliable detection of markers for neurodegenerative diseases have been complicated by the inaccessibility of the diseased tissue--such as the inability to biopsy or test tissue from the central nervous system directly. RNAs originating from hard to access tissues, such as neurons within the brain and spinal cord, have the potential to get to the periphery where they can be detected non-invasively. The formation and extracellular release of microvesicles and RNA binding proteins have been found to carry RNA from cells of the central nervous system to the periphery and protect the RNA from degradation. Extracellular miRNAs detectable in peripheral circulation can provide information about cellular changes associated with human health and disease. In order to associate miRNA signals present in cell-free peripheral biofluids with neurodegenerative disease status of patients with Alzheimer's and Parkinson's diseases, we assessed the miRNA content in cerebrospinal fluid and serum from postmortem subjects with full neuropathology evaluations. We profiled the miRNA content from 69 patients with Alzheimer's disease, 67 with Parkinson's disease and 78 neurologically normal controls using next generation small RNA sequencing (NGS). We report the average abundance of each detected miRNA in cerebrospinal fluid and in serum and describe 13 novel miRNAs that were identified. We correlated changes in miRNA expression with aspects of disease severity such as Braak stage, dementia status, plaque and tangle densities, and the presence and severity of Lewy body pathology. Many of the differentially expressed miRNAs detected in peripheral cell-free cerebrospinal fluid and serum were previously reported in the literature to be deregulated in brain tissue from patients with neurodegenerative disease. These data indicate that extracellular miRNAs detectable in the cerebrospinal fluid and serum are reflective of cell-based changes in pathology and can be used to assess disease progression and therapeutic efficacy.

PMID: 24797360    PMCID: PMC4010405    DOI: [10.1371/journal.pone.0094839](https://doi.org/10.1371/journal.pone.0094839)

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#### Images from this publication. [See all images \(5\)](#) [Free text](#)



Sci Rep. 2017 Mar 17;7:44061. doi: 10.1038/srep44061.

## Total Extracellular Small RNA Profiles from Plasma, Saliva, and Urine of Healthy Subjects.

Yeri A<sup>1</sup>, Courtright A<sup>1</sup>, Reiman R<sup>1</sup>, Carlson E<sup>1</sup>, Beecroft T<sup>1</sup>, Janss A<sup>1</sup>, Siniard A<sup>1</sup>, Richholt R<sup>1</sup>, Balak C<sup>1</sup>, Rozowsky J<sup>2</sup>, Kitchen R<sup>2</sup>, Hutchins E<sup>1</sup>, Winarta J<sup>1</sup>, McCoy R<sup>3</sup>, Anastasi M<sup>3</sup>, Kim S<sup>4</sup>, Huentelman M<sup>1</sup>, Van Keuren-Jensen K<sup>1</sup>.

### Author information

#### Abstract

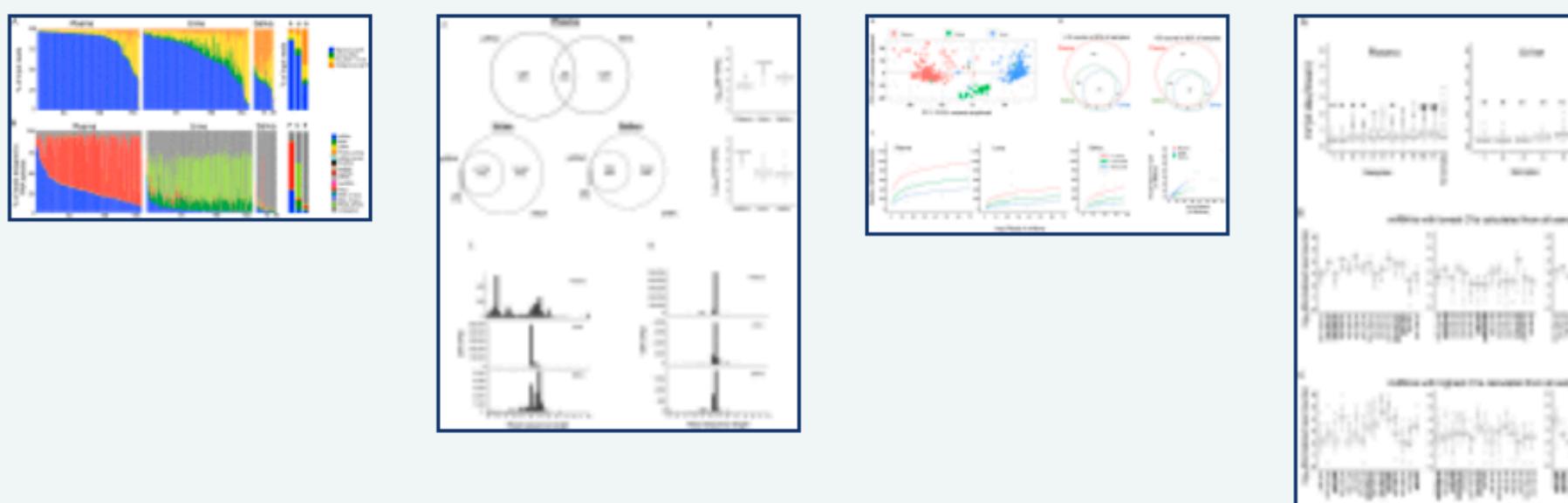
Interest in circulating RNAs for monitoring and diagnosing human health has grown significantly. There are few datasets describing baseline expression levels for total cell-free circulating RNA from healthy control subjects. In this study, total extracellular RNA (exRNA) was isolated and sequenced from 183 plasma samples, 204 urine samples and 46 saliva samples from 55 male college athletes ages 18-25 years. Many participants provided more than one sample, allowing us to investigate variability in an individual's exRNA expression levels over time. Here we provide a systematic analysis of small exRNAs present in each biofluid, as well as an analysis of exogenous RNAs. The small RNA profile of each biofluid is distinct. We find that a large number of RNA fragments in plasma (63%) and urine (54%) have sequences that are assigned to YRNA and tRNA fragments respectively. Surprisingly, while many miRNAs can be detected, there are few miRNAs that are consistently detected in all samples from a single biofluid, and profiles of miRNA are different for each biofluid. Not unexpectedly, saliva samples have high levels of exogenous sequence that can be traced to bacteria. These data significantly contribute to the current number of sequenced exRNA samples from normal healthy individuals.

PMID: 28303895 PMCID: [PMC5356006](#) DOI: [10.1038/srep44061](https://doi.org/10.1038/srep44061)

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Oncotarget. 2017 Dec 14;9(3):3097-3111. doi: 10.18632/oncotarget.23203. eCollection 2018 Jan 9.

## Small non-coding RNA profiling in human biofluids and surrogate tissues from healthy individuals: description of the diverse and most represented species.

Ferrero G<sup>1,2</sup>, Cordero F<sup>1,3</sup>, Tarallo S<sup>3</sup>, Arigoni M<sup>4</sup>, Riccardo F<sup>4</sup>, Gallo G<sup>5,6</sup>, Ronco G<sup>7</sup>, Alasia M<sup>8</sup>, Kulkarni N<sup>4</sup>, Matullo G<sup>3,9</sup>, Vineis P<sup>3,10</sup>, Calogero RA<sup>4</sup>, Pardini B<sup>3,9</sup>, Naccarati A<sup>3,11</sup>.

### Author information

#### Abstract

The role of non-coding RNAs in different biological processes and diseases is continuously expanding. Next-generation sequencing together with the parallel improvement of bioinformatics analyses allows the accurate detection and quantification of an increasing number of RNA species. With the aim of exploring new potential biomarkers for disease classification, a clear overview of the expression levels of common/unique small RNA species among different biospecimens is necessary. However, except for miRNAs in plasma, there are no substantial indications about the pattern of expression of various small RNAs in multiple specimens among healthy humans. By analysing small RNA-sequencing data from 243 samples, we have identified and compared the most abundantly and uniformly expressed miRNAs and non-miRNA species of comparable size with the library preparation in four different specimens (plasma exosomes, stool, urine, and cervical scrapes). Eleven miRNAs were commonly detected among all different specimens while 231 miRNAs were globally unique across them. Classification analysis using these miRNAs provided an accuracy of 99.6% to recognize the sample types. piRNAs and tRNAs were the most represented non-miRNA small RNAs detected in all specimen types that were analysed, particularly in urine samples. With the present data, the most uniformly expressed small RNAs in each sample type were also identified. A signature of small RNAs for each specimen could represent a reference gene set in validation studies by RT-qPCR. Overall, the data reported hereby provide an insight of the constitution of the human miRNome and of other small non-coding RNAs in various specimens of healthy individuals.

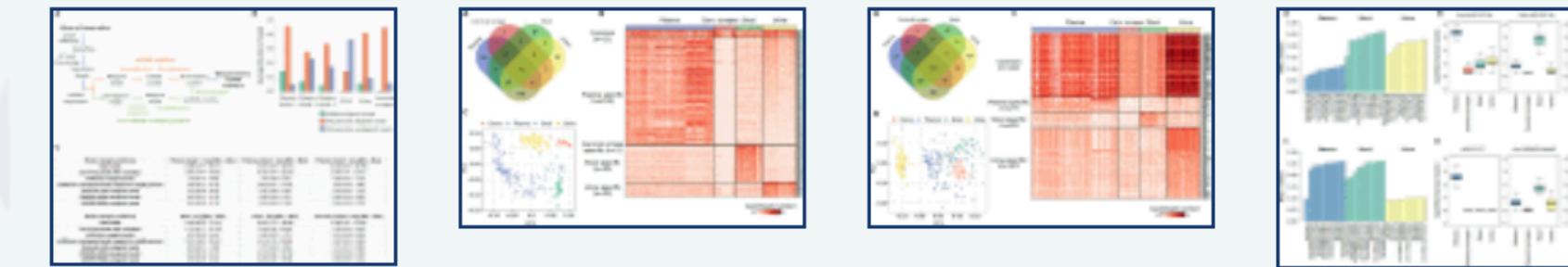
**KEYWORDS:** microRNAs; next-generation sequencing; non-invasive biomarkers; small non-coding RNA profiling; surrogate tissues

PMID: 29423032   PMCID: [PMC5790449](#)   DOI: [10.18632/oncotarget.23203](https://doi.org/10.18632/oncotarget.23203)

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Proc Natl Acad Sci U S A. 2018 Jun 5;115(23):E5334-E5343. doi: 10.1073/pnas.1714397115. Epub 2018 May 18.

## Human plasma and serum extracellular small RNA reference profiles and their clinical utility.

Max KEA<sup>1,2</sup>, Bertram K<sup>1,2</sup>, Akat KM<sup>1,2</sup>, Bogardus KA<sup>1,2</sup>, Li J<sup>1,2</sup>, Morozov P<sup>1,2</sup>, Ben-Dov IZ<sup>3</sup>, Li X<sup>4</sup>, Weiss ZR<sup>4</sup>, Azizian A<sup>5</sup>, Sopeyin A<sup>1,2</sup>, Diacovo TG<sup>6,7</sup>, Adamidi C<sup>1,2</sup>, Williams Z<sup>8</sup>, Tuschl T<sup>9,2</sup>.

### Author information

#### Abstract

Circulating extracellular RNAs (exRNAs) have the potential to serve as biomarkers for a wide range of medical conditions. However, limitations in existing exRNA isolation methods and a lack of knowledge on parameters affecting exRNA variability in human samples may hinder their successful discovery and clinical implementation. Using combinations of denaturants, reducing agents, proteolysis, and revised organic extraction, we developed an automated, high-throughput approach for recovery of exRNAs and exDNA from the same biofluid sample. We applied this method to characterize exRNAs from 312 plasma and serum samples collected from 13 healthy volunteers at 12 time points over a 2-month period. Small RNA cDNA library sequencing identified nearly twofold increased epithelial-, muscle-, and neuroendocrine-cell-specific miRNAs in females, while fasting and hormonal cycle showed little effect. External standardization helped to detect quantitative differences in erythrocyte and platelet-specific miRNA contributions and in miRNA concentrations between biofluids. It also helped to identify a study participant with a unique exRNA phenotype featuring a miRNA signature of up to 20-fold elevated endocrine-cell-specific miRNAs and twofold elevated total miRNA concentrations stable for over 1 year. Collectively, these results demonstrate an efficient and quantitative method to discern exRNA phenotypes and suggest that plasma and serum RNA profiles are stable over months and can be routinely monitored in long-term clinical studies.

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**KEYWORDS:** biofluid DNA isolation; biofluid RNA isolation; exRNA biomarker; exRNA reference profiling; extracellular nucleic acids

PMID: 29777089 DOI: [10.1073/pnas.1714397115](https://doi.org/10.1073/pnas.1714397115)

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# Computational deconvolution method

[Cell Rep.](#) 2016 Nov 15;17(8):2075-2086. doi: 10.1016/j.celrep.2016.10.057.

## Epigenomic Deconvolution of Breast Tumors Reveals Metabolic Coupling between Constituent Cell Types.

Onuchic V<sup>1</sup>, Hartmaier RJ<sup>2</sup>, Boone DN<sup>2</sup>, Samuels ML<sup>3</sup>, Patel RY<sup>4</sup>, White WM<sup>5</sup>, Garovic VD<sup>6</sup>, Oesterreich S<sup>2</sup>, Roth ME<sup>4</sup>, Lee AV<sup>2</sup>, Milosavljevic A<sup>7</sup>.

### Author information

#### Abstract

Cancer progression depends on both cell-intrinsic processes and interactions between different cell types. However, large-scale assessment of cell type composition and molecular profiles of individual cell types within tumors remains challenging. To address this, we developed epigenomic deconvolution (EDec), an *in silico* method that infers cell type composition of complex tissues as well as DNA methylation and gene transcription profiles of constituent cell types. By applying EDec to The Cancer Genome Atlas (TCGA) breast tumors, we detect changes in immune cell infiltration related to patient prognosis, and a striking change in stromal fibroblast-to-adipocyte ratio across breast cancer subtypes. Furthermore, we show that a less adipose stroma tends to display lower levels of mitochondrial activity and to be associated with cancerous cells with higher levels of oxidative metabolism. These findings highlight the role of stromal composition in the metabolic coupling between distinct cell types within tumors.

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**KEYWORDS:** DNA methylation; Warburg effect; breast cancer; cancer; cell type composition; deconvolution; gene expression; heterotypic interaction; metabolic coupling; metabolism

PMID: 27851969 PMCID: [PMC5115176](#) DOI: [10.1016/j.celrep.2016.10.057](#)

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