

# Exosome Biomarkers of Disease

## Big Potential from a Little Vesicle

The tiny exosome (30-120 nm) is effecting a big impact on the landscape of molecular diagnostics, making it possible to diagnose and characterize disease with increasingly non-invasive methods. Whether isolated from a liquid biopsy or cell culture, these diminutive vesicles contain valuable information about the health and disease profile of their cell and organ of origin. Learn how scientists are interpreting the language of exosomes to better understand disease processes and prognoses.

### THE LUNG

**Source(s):**  
Bronchoalveolar lavage fluid,  
Sputum, Peripheral blood,  
Urine, Tumor cell-line media

**Diseases Detected:**  
Asthma<sup>13, 14</sup>  
Non-small-cell lung cancer<sup>15, 16</sup>  
Adenocarcinoma<sup>17</sup>  
Hyperoxia-induced  
neonatal lung disease<sup>18</sup>  
Emphysema<sup>19</sup>  
Cystic fibrosis<sup>20</sup>

### THE CIRCULATORY SYSTEM

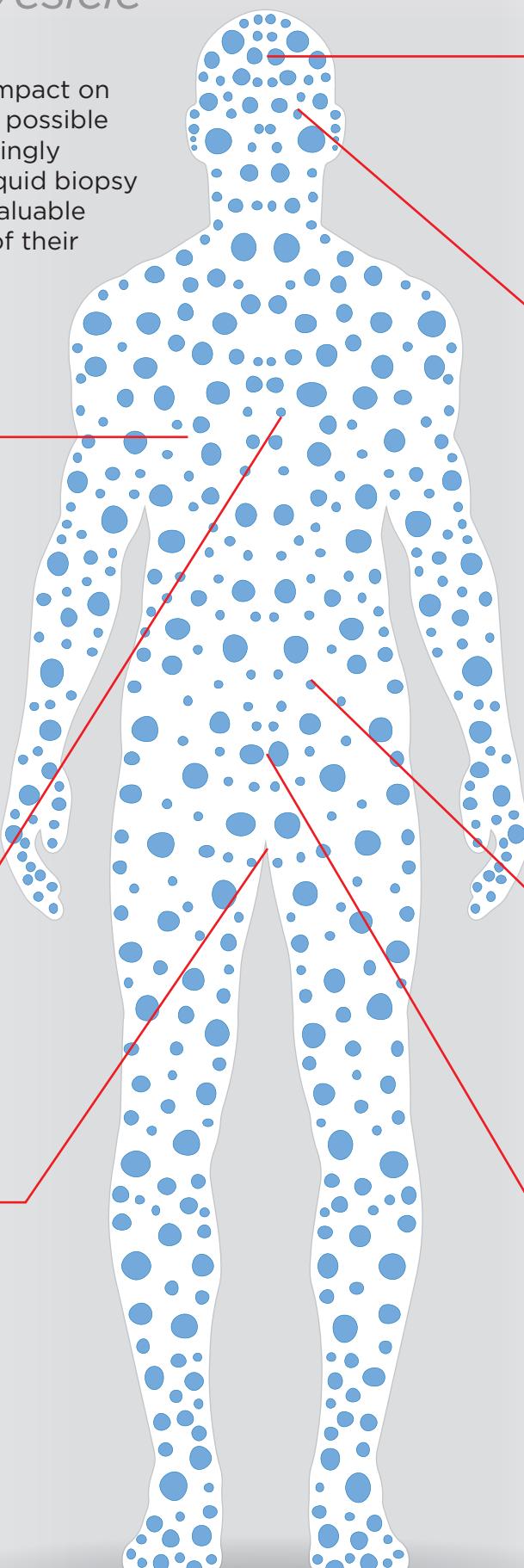
**Source(s):**  
Peripheral blood, Urine,  
Tumor cell-line media

**Diseases Detected:**  
Myocardial infarction<sup>21</sup>  
Atherosclerosis<sup>22</sup>  
Cardiomyopathy<sup>23</sup>

### THE REPRODUCTIVE ORGANS

**Source(s):**  
Breast milk, Vaginal secretions,  
Seminal fluid, Endometrium,  
Peripheral blood, Urine,  
Tumor cell-line media

**Diseases Detected:**  
Cervical cancer<sup>33</sup>  
Ovarian cancer<sup>34</sup>  
Breast cancer<sup>35, 36</sup>  
Prostate cancer<sup>37</sup>  
Endometriosis<sup>38, 39</sup>



### THE BRAIN

**Source(s):**  
Cerebrospinal fluid (CSF),  
Peripheral blood, Urine,  
Tumor cell-line media

**Diseases Detected:**  
Alzheimer's disease<sup>1-3</sup>  
Parkinson's disease<sup>4-5</sup>  
Schizophrenia<sup>6</sup>  
Bipolar disorder<sup>6</sup>  
Glioblastoma<sup>7-9</sup>  
Medulloblastoma<sup>9</sup>  
Autism<sup>9</sup>  
Multiple sclerosis<sup>10</sup>



### THE EYE

**Source(s):**  
Aqueous humor,  
Vitreous humor,  
Lacrimal-gland secretion (tears),  
Urine, Peripheral blood,  
Tumor cell-line media

**Diseases Detected:**  
Uveal melanoma<sup>11</sup>  
Glaucoma<sup>12</sup>



### THE DIGESTIVE SYSTEM

**Source(s):**  
Gastric juices,  
Peripheral blood, Urine,  
Tumor cell-line media

**Diseases Detected:**  
Gastric cancer<sup>24</sup>  
Colon cancer<sup>25</sup>  
Oral cancer<sup>26, 27</sup>  
Periodontitis<sup>28</sup>



### THE URINARY SYSTEM

**Source(s):**  
Urine, Peripheral blood,  
Tumor cell-line media

**Diseases Detected:**  
Bladder cancer<sup>29, 30</sup>  
Renal-cell carcinoma<sup>31, 32</sup>



### REFERENCES:

1. S. Kumar et al., "Are circulating microRNAs peripheral biomarkers for Alzheimer's disease?" *Biochim Biophys Acta*, doi: 10.1016/j.bbadi.2016.06.001, 2016.
2. C.N. Winston et al., "Prediction of conversion from mild cognitive impairment to dementia with neuronally derived blood exosome protein profile," *Alzheimer's Dement (Amst)*, doi: 10.1016/j.jad.2016.04.001, 2016.
3. T. Malm et al., "Exosomes in Alzheimer's disease," *Neurochem Int*, doi: 10.1016/j.neuint.2016.04.011, 2016.
4. M. Shi et al., "CNS tau efflux via exosomes is likely increased in Parkinson's disease but not in Alzheimer's disease," *Alzheimer's Dement*, doi: 10.1016/j.jalz.2016.04.003, 2016.
5. K.B. Fraser et al., "Ser(P)-1292 LRRK2 in urinary exosomes is elevated in idiopathic Parkinson's disease," *Mov Disord*, doi: 10.1002/mds.26686, 2016.
6. M.G. Banigan et al., "Differential expression of exosomal microRNAs in prefrontal cortices of schizophrenia and bipolar disorder patients," *PLoS One*, doi: 10.1371/journal.pone.0048814, 2013.
7. S.M. Evans et al., "Initial evidence that blood-borne microvesicles are biomarkers for recurrence and survival in newly diagnosed glioblastoma patients," *J Neurooncol*, doi: 10.1007/s11060-015-2051-3, 2016.
8. K. Mahmudi et al., "Small extracellular vesicles as tumor biomarkers for glioblastoma," *Mol Aspects Med*, doi: 10.1016/j.mam.2015.06.008, 2015.
9. E. De Smaele et al., "MicroRNAs as biomarkers of CNS cancer and other disorders," *Brain Res*, doi: 10.1016/j.brainres.2010.03.103, 2010.
10. J. Singh et al., "Targeted stage-specific inflammatory microRNA profiling in urine during disease progression in experimental autoimmune encephalomyelitis: Markers of disease progression and drug response," *J Neuroimmune Pharmacol*, doi: 10.1007/s11481-015-9630-0, 2016.
11. M. Ragusa et al., "miRNA profiling in vitreous humor, vitreal exosomes and serum from uveal melanoma patients: Pathological and diagnostic implications," *Cancer Biol Ther*, doi: 10.1080/15384047.2015.1046021, 2015.
12. W.M. Dismuke et al., "Human aqueous humor exosomes," *Exp Eye Res*, doi: 10.1016/j.exer.2015.01.019, 2015.
13. C. Mazzeo et al., "Exosome secretion by eosinophils: A possible role in asthma pathogenesis," *J Allergy Clin Immunol*, doi: 10.1016/j.jaci.2014.11.026, 2015.
14. Y. Fujita et al., "Intercellular communication by extracellular vesicles and their microRNAs in asthma," *Clin Ther*, doi: 10.1016/j.clinthera.2014.05.006, 2014.
15. M. Giallombardo et al., "Exosomal miRNA analysis in non-small cell lung cancer (NSCLC) patients' plasma through qPCR: A feasible liquid biopsy tool," *J Vis Exp*, doi: 10.3791/53900, 2016.
16. S. Taverna et al., "Exosomes isolation and characterization in serum is feasible in non-small cell lung cancer patients: Critical analysis of evidence and potential role in clinical practice," *Oncotarget*, doi: 10.18632/oncotarget.7638, 2016.
17. B. Sandfeld-Paulsen et al., "Exosomal proteins as diagnostic biomarkers in lung cancer," *J Thorac Oncol*, doi: 10.1016/j.jtho.2016.05.034, 2016.
18. A. Veerappan et al., "Mast cells and exosomes in hyperoxia-induced neonatal lung disease," *Am J Physiol Lung Cell Mol Physiol*, doi: 10.1152/ajplung.00299.2015, 2016.
19. H.G. Moon et al., "CCNI secretion and cleavage regulate the lung epithelial cell functions after cigarette smoke," *Am J Physiol Lung Cell Mol Physiol*, doi: 10.1152/ajplung.00102.2014, 2014.
20. C. Porro et al., "Pro-inflammatory effect of cystic fibrosis sputum microparticles in the murine lung," *J Cyst Fibros*, doi: 10.1016/j.jcf.2013.03.002, 2013.
21. D.A. Chistiakov et al., "Cardiac extracellular vesicles in normal and infarcted heart," *Int J Mol Sci*, doi: 10.3390/ijms17010063, 2016.
22. D.A. Chistiakov et al., "Extracellular vesicles and atherosclerotic disease," *Cell Mol Life Sci*, doi: 10.1007/s00108-015-1906-2, 2015.
23. F. Westermeier et al., "New molecular insights of insulin in diabetic cardiomyopathy," *Front Physiol*, doi: 10.3389/fphys.2016.00125, 2016.
24. X. Zhou et al., "Diagnostic value of plasma microRNA signature in gastric cancer: A microRNA expression analysis," *Sci Rep*, doi: 10.1038/srep11251, 2015.
25. H. Ogata-Kawata et al., "Circulating exosomal microRNAs as biomarkers of colon cancer," *PLoS One*, doi: 10.1371/journal.pone.0092921, 2014.
26. A. Zlotogorski-Hurvitz et al., "Morphological and molecular features of oral fluid-derived exosomes: Oral cancer patients versus healthy controls," *J Cancer Res Clin Oncol*, doi: 10.1007/s00432-015-2005-3, 2016.
27. P. Sivadasan et al., "Human salivary proteome – a resource of potential biomarkers for oral cancer," *J Proteomics*, doi: 10.1016/j.jprot.2015.05.039, 2015.
28. T. Tomofuji et al., "MicroRNAs as serum biomarkers for periodontitis," *J Clin Periodontol*, doi: 10.1111/jcpe.12536, 2016.
29. C.R. Silvers et al., "Identification of extracellular vesicle-born periostin as a feature of muscle-invasive bladder cancer," *Oncotarget*, doi: 10.18632/oncotarget.8024, 2016.
30. M. Nagata et al., "Molecular biomarkers in bladder cancer: Novel potential indicators of prognosis and treatment outcomes," *Dis Markers*, doi: 10.1155/2016/8205836, 2016.
31. M. Nawaz et al., "The emerging role of extracellular vesicles as biomarkers for urogenital cancers," *Nat Rev Urol*, doi: 10.1038/nrurol.2014.301, 2016.
32. F. Raimondo et al., "The urinary proteome and peptidome of renal cell carcinoma patients: a comparison of different techniques," *Expert Rev Proteomics*, doi: 10.1586/14789450.2014.926222, 2014.
33. J. Zhang et al., "Exosomal long noncoding RNAs are differentially expressed in the cervicovaginal lavage samples of cervical cancer patients," *J Clin Lab Anal*, doi: 10.1002/jcla.21990, 2016.
34. K.D. Dorayappan et al., "The biological significance and clinical applications of exosomes in ovarian cancer," *Gynecol Oncol*, doi: 10.1016/j.ygyno.2016.03.036, 2016.
35. D.P. Joyce et al., "Exosome-encapsulated microRNAs as circulating biomarkers for breast cancer," *Int J Cancer*, doi: 10.1002/ijc.30179, 2016.
36. Q. Zhao et al., "A direct quantification method for measuring plasma microRNAs identified potential biomarkers for detecting metastatic breast cancer," *Oncotarget*, doi: 10.18632/oncotarget.7990, 2016.
37. E. Endzelins et al., "Diagnostic, prognostic and predictive value of cell-free miRNAs in prostate cancer: A systematic review," *Mol Cancer*, doi: 10.1186/s12943-016-0523-5, 2016.
38. D.C. Muth et al., "Potential role of cervicovaginal extracellular particles in diagnosis of endometriosis," *BMC Vet Res*, doi: 10.1186/s12917-015-0513-7, 2015.
39. L. Texido et al., "Eco-nucleotidases activities in the contents of ovarian endometriomas: Potential biomarkers of endometriosis," *Mediators Inflamm*, doi: 10.1155/2014/120673, 2014.