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Proteomic profiling of exosomes released by cancer cells reveals a tissue specific signature

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Abstract

Exosomes are 40-100-nm-diameter nanovesicles of endocytic origin that are released from diverse cell types. To better understand the biological role of exosomes and to avoid confounding data arising from proteinaceous contaminants, it is important to work with highly purified material. Here, we describe an immunoaffinity capture method using the colon epithelial cell-specific A33 antibody to purify colorectal cancer cell (LIM1215)-derived exosomes. LC-MS/MS revealed 394 unique exosomal proteins of which 112 proteins (28%) contained signal peptides and a significant enrichment of proteins containing coiled coil, RAS, and MIRO domains. A comparative protein profiling analysis of LIM1215-, murine mast cell-, and human urine-derived exosomes revealed a subset of proteins common to all exosomes such as endosomal sorting complex required for transport (ESCRT) proteins, tetraspanins, signaling, trafficking, and cytoskeletal proteins. A conspicuous finding of this comparative analysis was the presence of host cell-specific (LIM1215 exosome) proteins such as A33, cadherin-17, carcinoembryonic antigen, epithelial cell surface antigen (EpCAM), proliferating cell nuclear antigen, epidermal growth factor receptor, mucin 13, misshapen-like kinase 1, keratin 18, mitogen-activated protein kinase 4, claudins (1, 3, and 7), centrosomal protein 55 kDa, and ephrin-B1 and -B2. Furthermore, we report the presence of the enzyme phospholipid scramblase implicated in transbilayer lipid distribution membrane remodeling. The LIM1215-specific exosomal proteins identified in this study may provide insights into colon cancer biology and potential diagnostic biomarkers.

Biography

Mathivanan obtained his Ph.D. from Johns Hopkins University, USA and Institute of Bioinformatics, India in proteomics and bioinformatics. He undertook his postdoctoral studies at the Ludwig Institute for Cancer Research, Australia. He received a NH&MRC fellowship to study exosomes in cancer. He is currently a group head in La Trobe University, Melbourne, Australia. He has published more than 32 papers in international peer-reviewed journals and serving as an editorial board member of repute. His research articles have been cited at an average of 85 citations per article.