

Exosomal Shuttle RNA

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- I. Ekstrom, K., Valadi, H., Bossios, A., Sjostrand, M., Lee, J. J., and Lotvall, J. O. (2007). Exosome-mediated transfer of mRNAs and microRNAs is a novel mechanism of genetic exchange between cells. *Nat Cell Biol* 9, 654-659.
Valadi and Ekström have contributed equally to this work.
- II. Ekstrom, K., Valadi, H., Sjostrand, M., Bossios, A., Malmhall, C., and Lotvall, J. O. Human mast cell exosomes shuttle RNA between mast cells and to CD34 cells
In manuscript

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Exosomes are small membrane nanovesicles of endocytic origin that can be released by many different cells to the extracellular environment. Exosomes have been found in a number of body fluids such as blood plasma, breast milk, bronchoalveolar lavage fluid and urine, indicating relevance *in vivo*. Exosomes have been suggested to have a number of different functions and are believed to take part in the communication between cells. Previously, exosomes were believed to consist of a lipid bilayer and proteins, but no nucleic acids. The aim of this thesis was to assess the composition and functions of mast cell exosomes, with focus on the content of nucleic acids and cell to cell communication. We utilized exosomes released from two mast cell lines as well as mouse primary bone marrow derived mast cells. Exosomes were isolated and detected as small 40-80 nm membrane vesicles, which were positive for the tetraspanins CD9, CD63 and CD81 as assessed by electron microscopy and flow cytometry. We showed for the first time that mast cell exosomes contain RNA but no DNA. The exosomal RNA differs from the donor cell RNA. Exosomes contain very little or no ribosomal RNA but a substantial amount of small RNA. We further characterized the RNA using Affymetrix DNA microarray and microRNA array analysis, which revealed that exosomes contain a selection of both microRNA and mRNA. Interestingly, a number of mRNAs were detected in the exosomes but not in their donor cells. Transfer experiments revealed that the exosomal RNA is shuttled to other mast cells and to CD34 positive progenitor cells. Exosomal RNA is functional, as shown by *in vitro* translation and the translation of mouse exosomal RNA to mouse protein after transfer to a human mast cell. In summary, mast cell exosomes contain mRNAs and microRNAs, which can be delivered to another cell. Exosomal RNA shuttle may be a powerful mode of communication between cells, either in the microenvironment or over a distance. We propose that this RNA be called “exosomal shuttle RNA” (esRNA).

Keywords: exosomes, exosomal, shuttle, RNA, esRNA, RNA, vesicles, mast cell, gene transfer, microRNA

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