

Editorial

Announcing *Exosomes and Microvesicles*,
the official journal of the American Society for Exosomes and Microvesicles

Stephen J. Gould¹, Douglas Taylor², Antonio Chiesi³ and Winston P. Kuo⁴

¹ Department of Biological Chemistry, the Johns Hopkins University, Baltimore, MD, USA

² Department of Obstetrics, Gynecology & Women's Health, University of Louisville School of Medicine, Louisville, KY, USA

³ Exosomics Siena SpA, Siena, Italy

⁴ Harvard Catalyst, Laboratory for Innovative Translational Technologies, Harvard Medical School, Boston, MA, USA;

Department of Developmental Biology, Harvard School of Dental Medicine, Cambridge, MA, USA

* Corresponding E-mail: exmv@intechopen.com

© 2013 Gould et al.; licensee InTech. This is an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract This editorial article introduces the new scientific journal *Exosomes and Microvesicles (EXMV)*, the official journal of the American Society for Exosomes and Microvesicles (ASEMV), and describes its editorial line and mission in relation to the role of the Society, the state of the art of the study of exosomes and microvesicles, and the overall approach of the publication.

Keywords Exosomes, Microvesicles, ASEMV, Editorial

1. Introduction

The past decade has witnessed an extraordinary explosion of research in the field of exosomes, microvesicles, and other extracellular vesicles. On the wave of the huge interest in this emerging field coming from the academic, industrial and financial communities, in 2012 the *American Society for Exosomes and Microvesicles (ASEMV)* was established by the initiative of a number of stakeholders in the United States. ASEMV is a non-profit scientific society dedicated to advancing exosome and microvesicle research, promoting interactions among researchers, funding agencies, and educating scientists and policy makers about the biological, biomedical and biotechnological importance of secreted vesicles in both basic and applied/clinical sciences. Its mission, in short, is

to advance the field of extracellular vesicle research and to support the scientists working in this domain, both in the academic and industrial environments. The society is already active in sponsoring scientific meetings, partnering with other scientific societies for interdisciplinary developments and working with funding agencies to promote this exciting field of biology. Today, we expand these activities by launching *Exosomes and Microvesicles (EXMV)*, the official journal of our Society, a peer-reviewed, open access scientific publication with an innovative approach, being open to both sides: for readers and for authors (no fee requested). The mission of *Exosomes and Microvesicles* is to publish papers that provide a significant contribution to our understanding, development and translation of knowledge to concrete applications in this field. The Journal is addressed to experts and emerging scientists such as cell and molecular biologists, medical researchers, clinicians and surgeons specializing in exosome-based approaches for the diagnosis or treatment of human diseases, but also to researchers coming from other relevant scientific fields such as biomedical engineers, biomaterials scientists, chemists and pharmacists developing new technologies and applications in the field. The goal of the Journal is to connect all of them and thus enhance the translation of knowledge in the exosome and microvesicle sciences among disciplines and among

academia and industry. No other existing journal focuses on the application of exosomes and microvesicles in the maintenance of human health, and the development of strategies to better diagnose and fight diseases.

2. The field of research

The study of exosomes (nano-scaled lipid-based membrane vesicles of endocytic origin that are shed from most living cells) and other secreted microvesicles (heterogeneously-sized membrane-delimited vesicles shed from the cell membrane) is a domain of biotechnology and biomedicine that crosses multiple disciplines, including the application of molecular and cell biology, biochemistry, genetics, physiology, immunology and biophysics to analytics, to help elucidate the structure, biogenesis, function and trafficking, providing hints on distinctive features and biomedical potential of different vesicle categories [1-4]. Discovered over 30 years ago, exosomes were long considered an alternative secretion pathway for unwanted molecules meant to be discarded from the parent cells [5]. Over last decade, important roles of exosomes have emerged as mediators of intracellular communication and immune regulation, both in physiological and pathological conditions [2, 5-7]. Today, these vesicles are often recognized for their specific molecular composition dependent on parent cell/tissue type and condition, and their involvement in the transferring of proteins, lipids and genetic material affecting the function of the recipient (target) cell [8,9]. The recent increased interest in exosomes and microvesicles has been related to the discovery of their role in intercellular communication vectors in parent cell microenvironments or at a distance, by trafficking through the lymphatic and circulatory system, and can thus be found in a variety of human biofluids such as blood and urine [10-12]. These features make exosome research an appealing field for the discovery of exosome-associated biomarkers and the development of targeted diagnostic applications [8, 13-15]. Recent papers have shown the diagnostic value of exosomes purified from blood and urine in pathological conditions such as cancer [12,13,16]. Moreover, the use of exosomes as therapeutic tools in cancer immunotherapy [17], regenerative medicine [19] and therapeutic vaccine [18] approaches, as well as in targeted drug delivery [20-22], has been the subject of many on-going pioneering studies.

The field of investigation in the domain of exosomes and secreted microvesicles is therefore an exciting and rapidly expanding field of clinical and translational science, with a pressing demand for further insights into the roles of exosomes and their functions in physiologic and pathologic conditions. Further development is needed

in the area of standardizing methodological approaches for the exchange and validation of independently obtained data from an increasing number of on-going exosome research focused groups worldwide. Overall, this field comprises a multidisciplinary scientific arena with unprecedented potential to open new research paths and yield novel biotechnological and medical applications.

3. Publishing approach

As a response to the rapid growth of this research field and to the wide range of topics and applications that it may have in the future, both in basic research and clinical applications, the mission of *Exosomes and Microvesicles* is to facilitate and foster communication among scientists from different backgrounds and with differing provenances, and between academia and industry, for an effective translation of discoveries and applications. Several categories of papers will be published, including Original Research Articles, Technical Reports on methods and protocols, Review Articles, Hypotheses and Opinions on contradictory or visionary issues, Meeting Reports and Letters to the Editor. Submissions are encouraged from all institutions and on all topics related to extracellular vesicles, including:

- biogenesis of extracellular vesicles, both in eukaryotic and prokaryotic cells
- mechanisms of vesicle : cell interactions
- intercellular signalling
- intercellular traffic of proteins, nucleic acids and other macromolecules
- modulation of the extracellular matrix
- roles of extracellular vesicles in normal physiological processes, including differentiation, development, immunity, tissue repair, stem cell biology, etc.
- roles of extracellular vesicles in disease, including cancer, neurodegeneration, diabetes, chronic inflammatory diseases, cardiovascular diseases, infectious disease, ageing, etc.
- virology and bacteriology
- biomarkers
- technical advances in vesicle purification and characterization
- design and production of cell-derived vesicles
- design and production of synthetic vesicles
- use of extracellular vesicles in diagnostics and companion diagnostics
- use of extracellular vesicles in therapeutics delivery
- use of extracellular vesicles in antigen presentation and vaccine development
- use of extracellular vesicles in cell free regenerative medicine
- use of extracellular vesicles in association with other synthetic nanoparticle for different scopes

Exosomes and Microvesicles aims to be the preeminent journal for scientific advances in the field of extracellular vesicle research. To achieve this goal, we have arranged for papers in *EXMV* to be published in an open access, electronic format, with no charge to its readers. Open access will make all published material available to everybody, without the barrier of affordability or copyright ownership. Therefore, all papers will be distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.

In line with the idea of making knowledge free to the scientific community, the Journal currently also offers free of charge publication to all authors. The Journal will take it upon itself to finance the costs of production, processing and publication of all submitted, peer-reviewed and accepted articles for the benefit and advancement of the exosomes and microvesicles field of research, and the scientific community of interest in this particular area of study.

Further on the ASEM and the Journal aim to work on partnering with other scientific societies and industry leaders to advance the field and to allow free access to knowledge.

An additional feature of *EXMV* is its plan to expand its activity to ancillary projects such as special issues and collections of papers, books and events. The first act will be the publication of reports and abstracts from the Exosomes and Microvesicles Conference 2013 that will be held in late September in Orlando, Florida, organized by ASEM, with the *EXMV* Journal as the official conference journal.

EXMV's promise of excellence is certainly evident in its Associate Editors and members of its Editorial Board. They are international experts with diverse expertise mirroring the Journal's scope. On this occasion we would like to thank our reviewers whose skill and rigour contributed to the launch of the Journal.

4. Inaugural papers

The first papers published by *EXMV* consist of four articles that illustrate the Journal's scope.

The paper by Atay et al. [23] addresses exosomes as mediators of cross talk between tumour cells and tumour microenvironments, essential for creating the favourable context for tumour progression and evasion. In this case, the authors report the induction of proinflammatory cytokines production by activated macrophages, thus providing hints for an explanation of increased levels of inflammatory mediators, such as IL-1 β , observed in cancer patients and, more importantly, identifying

possible therapeutic intervention targeting the exosome-related mechanisms leading to tumour stroma "education".

Hendrix et al. [24] address another phenomenon characteristic of tumour microenvironments: intratumoural acidification caused by the switch from oxidative phosphorylation towards aerobic glycolysis that is a fundamental prerequisite for the invasive growth and chemoresistance of metastatic cancers. The authors identify the role of Rab27B in promoting the metabolic switch and so-called filopodia phenotype through a paracrine activation of distinct signalling pathways potentially mediated by exosomes. Indeed Rab27B is one of the essential regulators of exosome biogenesis and release, and are themselves secreted by exosomes. This paper reinforces already published evidence on the close inter-connection between microenvironmental pH and exosome traffic in cancer.

Romagnoli et al. [25] provide data on the incorporation of mature dendritic cell-derived exosomes by diverse tumour cells that thereby acquire the surface display of co-stimulatory molecules involved in antigen presentation. The authors suggest this mechanism of conversion into potentially immunogenic cells as an avenue to be explored in tumour immunotherapy. The real potential of such an approach is that it fosters further investigation. This paper also addresses the molecular mechanisms and components involved in the selective uptake of exosomes by target cells, correlating the rate of uptake with the cell expression of CD9.

Finally, a review article from Suntres et al. [26] gives a timely comment on appealing use of exosomes in a variety of therapeutic applications, ranging from immunotherapy in cancer, vaccines in infective diseases such as parasitic and viral infections, through to their use in the treatment of autoimmune and inflammatory conditions and targeted drug delivery. The authors highlight some unsolved issues that currently hamper full leveraging of enormous exosome potential as therapeutic effectors, in particular, standardization of methodology for their isolation and characterization.

Therefore, the Journal will act as a means of tying together and maintaining a scholarly community around exosomes and microvesicles by staking out the intellectual territory of this new field to serve as a forum to inform/discuss issues around exosomes and microvesicles, whether it is basic science or clinical and translational.

We hope that you will find our first papers and the ones to follow inspiring and insightful. We invite you to consider *Exosomes and Microvesicles* as a means of learning about and contributing to the further development of this evolving field.

5. References

- [1] Keller S, Sanderson MP, Stoeck A, Altevogt P. Exosomes: from biogenesis and secretion to biological function. *Immunol Lett.* 2006 Nov 15;107(2):102-8.
- [2] Théry C, Ostrowski M, Segura E. Membrane vesicles as conveyors of immune responses. *Nat Rev Immunol.* 2009 Aug;9(8):581-93.
- [3] György B, Szabó TG, Pásztói M, Pál Z, Misják P, Aradi B, László V, Pállinger E, Pap E, Kittel A, Nagy G, Falus A, Buzás EI. Membrane vesicles, current state-of-the-art: emerging role of extracellular vesicles. *Cell Mol Life Sci.* 2011 Aug;68(16):2667-88
- [4] Simons M, Raposo G. Exosomes-vesicular carriers for intercellular communication. *Curr Opin Cell Biol.* 2009;21(4):575-81.
- [5] Corrado C, Raimondo S, Chiesi A, Ciccia F, De Leo G, Alessandro R. Exosomes as intercellular signaling organelles involved in health and disease: basic science and clinical applications. *Int J Mol Sci.* 2013 Mar 6;14(3):5338-66
- [6] Pant S, Hilton H, Burczynski ME. The multifaceted exosome: biogenesis, role in normal and aberrant cellular function, and frontiers for pharmacological and biomarker opportunities. *Biochem Pharmacol.* 2012 Jun 1;83(11):1484-94.
- [7] Lai CPK, Breakefield XO. Role of Exosomes/Microvesicles in the Nervous System and Use in Emerging Therapies. *Front Physiol.* 2012; 3: 228.
- [8] Simpson RJ, Lim JW, Moritz RL, Mathivanan S. Exosomes: proteomic insights and diagnostic potential. *Expert Rev Proteomics.* 2009 Jun;6(3):267-83.
- [9] Valadi H, Ekstrom K, Bossios A, Sjostrand M, Lee JJ, Lotvall JO. Exosome-mediated transfer of mRNAs and microRNAs is a novel mechanism of genetic exchange between cells. *Nat Cell Biol.* 2007;9(6):654-9.
- [10] Caby MP, Lankar D, Vincendeau-Scherrer C, Raposo G, Bonnerot C. Exosomal-like vesicles are present in human blood plasma. *Int Immunol.* 2005 Jul;17(7):879-87.
- [11] Mitchell PJ, Welton J, Staffurth J, Court J, Mason MD, Tabi Z, Clayton A. Can urinary exosomes act as treatment response markers in prostate cancer? *Int J Cancer.* 2012;131(7):1674-8. doi: 10.1186/1479-5876-7-4.
- [12] Logozzi M, De Milito A, Lugini L, Borghi M, Calabrò L, Spada M, Perdicchio M, Marino ML, Federici C, Iessi E, Brambilla D, Venturi G, Lozupone F, Santinami M, Huber V, Maio M, Rivoltini L, Fais S. High levels of exosomes expressing CD63 and caveolin-1 in plasma of melanoma patients. *PLoS One.* 2009;4(4):e5219.
- [13] Skog J, Wurdinger T, van Rijn S, Meijer DH, Gainche L, Sena-Esteves M, et al. Glioblastoma microvesicles transport RNA and proteins that promote tumour growth and provide diagnostic biomarkers. *Nat Cell Biol.* 2008;10(12):1470-6.
- [14] Duijvesz D, Luider T, Bangma CH, Jenster G. Exosomes as biomarker treasure chests for prostate cancer. *Eur Urol.* 2011 May;
- [15] Vlassov AV, Magdaleno S, Setterquist R, Conrad R. Exosomes: current knowledge of their composition, biological functions, and diagnostic and therapeutic potentials. *Biochim Biophys Acta.* 2012 Jul;1820(7):940-8.
- [16] Shao H, Chung J, Balaj E, Charest A, Bigner DD, Carter BS, Hochberg FH, Breakefield XO, Weissleder R, Lee H. Protein typing of circulating microvesicles allows real-time monitoring of glioblastoma therapy. *Nat Med.* 2012 Dec;18(12):1835-40.
- [17] Record M, Subra C, Silvente-Poirot S, Poirot M. Exosomes as intercellular signalosomes and pharmacological effectors. *Biochem Pharmacol.* 2011 May 15;81(10):1171-82
- [18] Tan A, De La Peña H, Seifalian AM. The application of exosomes as a nanoscale cancer vaccine. *Int J Nanomedicine.* 2010 Nov 10;5:889-900.
- [19] Lai RC, Yeo RW, Tan KH, Lim SK. Mesenchymal stem cell exosome ameliorates reperfusion injury through proteomic complementation. *Regen Med.* 2013 Mar;8(2):197-209.
- [20] van Dommelen SM, Vader P, Lakhali S, Kooijmans SA, van Solinge WW, Wood MJ, Schiffelers RM. Microvesicles and exosomes: opportunities for cell-derived membrane vesicles in drug delivery. *J Control Release.* 2012 Jul 20;161(2):635-44.
- [21] Sun D, Zhuang X, Xiang X, Liu Y, Zhang S, Liu C, Barnes S, Grizzle W, Miller D, Zhang HG. A novel nanoparticle drug delivery system: the anti-inflammatory activity of curcumin is enhanced when encapsulated in exosomes. *Mol Ther.* 2010 Sep;18(9):1606-14.
- [22] Alvarez-Erviti L, Seow Y, Yin H, Betts C, Lakhali S, Wood MJ. Delivery of siRNA to the mouse brain by systemic injection of targeted exosomes. *Nat Biotechnol.* 2011 Apr;29(4):341-5.
- [23] Atay S, Roberson CD, Taylor CG, Taylor DD. Ovarian Cancer-derived Exosomal Fibronectin Induces Pro-inflammatory IL-1. *Exosomes and Microvesicles.*
- [24] Hendrix A, Ciccone C, Gespach C, Bracke M, De Wever O, Westbroek W. Rab27B-Mediated Metabolic Reprogramming Induces Secretome Acidification and Chemoresistance in Breast Cancer Cells. *Exosomes and Microvesicles.*
- [25] Romagnoli GG, Toniolo PA1, Migliori IK, Caldini EG, Ferreira MA, Pizzo CR, Bergami-Santos PC, Barbuto JAM Tumour Cells Incorporate Exosomes derived from Dendritic Cells through a Mechanism Involving the Tetraspanin CD9. *Exosomes and Microvesicles.*
- [26] Suntres ZE, Smith MG, Momen-Heravi F, Hu J, Zhang X, Wu Y, Zhu H, Wang J, Zhou J, Kuo WP. Therapeutic Uses of Exosomes. *Exosomes and Microvesicles.*