NACIONALNI INŠTITUT ZA BIOLOGIJO

Večna pot 111, SI-1000 Ljubljana

Nacionalni inštitut za biologijo Vas vabi, da se udeležite predavanja:

»Heparin blocks horizontal transfer of glioma-derived extracellular vesicles «,

ki ga bo predstavila Nadia A. Atai,
Department of Neurology and Program in Neuroscience, Massachusetts General Hospital and Harvard Medical School, Boston (USA); Department of Cell Biology and Histology, Academic Medical Center (AMC), University of Amsterdam, Amsterdam (The Netherlands)

Predavanje bo potekalo v ponedeljek, 18.11.2013 ob 9.00 uri,
v vhodnem objektu NIB-a, Večna pot 111, v Ljubljani, v predavalnici B7.

Povzetek predavanja:

Heparin blocks horizontal transfer of glioma-derived extracellular vesicles

Nadia A. Atai[1,2], Leonora Balaj[1], Henk van Veen[2], Xandra O. Breakefield[1], Peter A. Jarzyna[3], Cornelis J. F. Van Noorden[2], Johan Skog[4], Casey A. Maguire[1*]

[1]Department of Neurology and Program in Neuroscience, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114, USA; [2]Department of Cell Biology and Histology, Academic Medical Center (AMC), University of Amsterdam, 1105 AZ Amsterdam, The Netherlands; [3]Molecular Imaging Laboratory, MGH/MIT/HMS Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, Harvard Medical School, Boston, MA 02129, USA; [4]Exosome Diagnostic, Inc., New York, NY 10032, USA

Abstract

Extracellular vesicles (EVs) have been implicated in tumorigenesis. Biomolecules which can block EV binding and uptake into recipient cells may be of therapeutic value. Here, we show that heparin interacts with uptake of tumor-derived EVs into recipient cells. Incubation of glioma cell-derived EVs with heparin resulted in micron-sized structures observed by transmission electron microscopy (TEM), with EVs clearly visible within these structures. Inclusion of heparin greatly diminished transfer of labeled EVs from donor to recipient tumor cells. We also show a direct interaction between heparin and EVs using binding assays and microscopy. We found that the block in EVs uptake was at the level of cell binding and not internalization. Finally, incubation of glioma-derived EVs containing EGFRvIII mRNA with heparin reduced transfer of this message to recipient cells. The effect of heparin on EVs uptake may provide a unique tool to study EV function. It may also foster research of heparin as a therapeutic for disease in which EVs play a role.

Acknowledgments
This work was supported by NIH/NINDS 1 R21 NS081374-01 (C.A.M.) NIH/NCI grants CA069246 (X.O.B), CA141226 (X.O.B.); CA156009 (X.O.B.) CA141150 (X.O.B.), an American Brain Tumor Association Fellowship (C.A.M.), and a 2010 AMC Scholarship, University of Amsterdam (N.A.A.). We gratefully acknowledge the Neuroscience Center PCR Core facility, which is funded by PHS grant P30NS045776. We acknowledge the MGH Neuroscience Center Microscopy and Image Analysis Core, which is funded by NIH grant P30NS045776. We thank the van Leeuwenhoek Center for Advanced Microscopy (LCAM) at the Academic Medical Center (University of Amsterdam, the Netherlands) for performing the transmission electron microscopy sample processing and imaging. We thank Lori LoGuidice and Ard Jonker (University of Amsterdam) for technical help. C.A.M. has a financial interest in Exosome Diagnostics, Inc. C.A.M.'s interests were reviewed and are managed by the Massachusetts General Hospital and Partners HealthCare in accordance with their conflict of interest policies. J.S. is an inventor on the exosome/EVs technology used in this study which has been licensed to Exosome Diagnostics, Inc. He holds equity in, and is now an employee of that company. X.O.B. is on the Scientific Advisory Board of Exosome Diagnostics, Inc.

Predavanje bo potekalo v angleškem jeziku.

Vljudno vabljeni!