

NAME: Metka Lenassi

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PI of Laboratory for Extracellular Vesicle Research

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PERSONAL STATEMENT:

I am an Associate Professor of biochemistry and molecular biology and the head of the Laboratory for extracellular vesicle research, at the Faculty of Medicine, University of Ljubljana.

My research work is focused on advancing the knowledge of extracellular vesicles (EVs) in cell-pathogen communication, using human-HIV interaction as a model system. Specifically, my group explores the role of EVs released from cells expressing HIV protein Nef and their role in HIV-associated neurocognitive disorders in aviremic (infected) individuals. We are also heavily involved in EV-biomarker studies, including the use of Nef-EVs in HIV diagnostics, urine EVs as biomarkers of kidney allograft rejection, and plasma EVs in cancer diagnostics. To that end, we collaborate with several international and local clinical partners.

I am also dedicated to promoting EVs among the wider research and medical community, through involvement in teaching activities at the undergraduate and graduate levels, organization of EV-focused meetings and training programs, and through roles in local (president of the Slovenian Network for Extracellular Vesicles, SiN-EV) and international (serving as Executive Chair of Science and Journals Committee of the International Society for Extracellular Vesicles, ISEV) EV societies. Please consult the below CV for details.

EDUCATION/TRAINING:

DEGREE	COMPLETION DATE	FIELD OF STUDY	INSTITUTION AND LOCATION
Postdoc.	Oct. 2008	Virology	Univ. of California San Francisco, USA
PhD	June 2007	Biochemistry and molecular biology	Univ. of Ljubljana, Faculty of Medicine, SI
B. Sc.	Sept. 2002	Microbiology	Univ. of Ljubljana, Biotechnical faculty, SI

POSITIONS AND EMPLOYMENT:

ACTIVITY/OCCUPATION	TIME	FIELD	INSTITUTION/COMPANY
Associate professor (academic position)	Mar. 2019-present	Biochemistry/Molecular genetics	UL Faculty of Medicine (MF), Institute of biochemistry and molecular genetics
Specialist lecturer	Sep. 2018-Dec. 2018	Molecular biology/Genetics	Oxford Brookes University
Visiting scholar	Aug. 2014-Dec. 2014	Virology	Univ. California San Francisco

ACTIVITY/ OCCUPATION	TIME	FIELD	INSTITUTION/ COMPANY
Assistant professor	Feb. 2014-Mar. 2019	Biochemistry/Molecular Biology	UL, MF, Institute of Biochemistry (IBK)
Teaching assistant	April 2010-Feb. 2014	Biochemistry/Molecular Biology	UL, MF, IBK
Postdoctoral fellow	Jan. 2009-April 2010	Biochemistry/Microbiology	UL, MF, IBK
Research fellow	April 2007-Jan. 2009	Biochemistry/Microbiology	UL, MF, IBK
Postdoctoral fellow	Oct. 2007-Nov. 2008	Virology	Univ. California San Francisco
Marie Curie Early Stage Research Training fellow	Jan. 2007-March 2007	Biochemistry/Microbiology	University of Gothenburg
PhD student	Sep. 2003-April 2007	Biochemistry and molecular biology	UL, MF, IBK

LEADERSHIP EXPERIENCE:

- 2018-present PI of the Laboratory for extracellular vesicle research (University of Ljubljana, Faculty of Medicine); <http://ibk.mf.uni-lj.si/groups/lenassi/home.html>
- 2024-present Executive Chair of Science & Journals on the Board of the International Society of Extracellular Vesicles (ISEV); <https://www.isev.org/board-of-directors>
- 2022-present member of the ISEV Rigor & Standardization subcommittee, ISEV Blood Task force and Urine Task force, <https://www.isev.org/rigor-standardization>
- 2022-2024 Executive Chair of Science & Meetings on the Board of the International Society of Extracellular Vesicles (ISEV)
- 2019-present President of the Slovenian network for extracellular vesicles (SiN-EV); <https://sin-ev.org/>
- 2023- Deputy coordinator of the scientific field Biochemistry and molecular biology at the interdisciplinary Biomedicine doctoral programme
- 2023- Part of the expert council of the Medical Experimental Center (MEC) at the University of Ljubljana, Faculty of Medicine
- 2021-present Co-organizer of 3 ISEV annual meetings, 3 ISEV focused meetings, 6 ISEV workshops and several other international meetings
- 2019-present Chair of the organizing committee of the annual meetings of the Slovenian Network for EVs (SiN-EV)

TEACHING EXPERIENCE, MENTORSHIP:

- 2019 Recipient of award "Lavričeva nagrada" for the best teaching assistant at the UL Faculty of Medicine
- 2018 Specialist lecturer at Oxford Brookes University during 3 months visit
- 2018-present Teaching courses, designed and developed by me, at the MSc (Clinical application of extracellular vesicles) and PhD (Extracellular vesicles-biological relevance and clinical potential) level
- 2010-present Lecturer in Concepts of Biochemistry and Research in Medicine, first year modules at UL Faculty of Medicine
- 2011-present Part of tutorship program for medical students

2011-present Under my mentorship students were four-times awarded with a top undergraduate student award Prešernova nagrada, twice with student research award Krkina nagrada, once nominated for Lindau Nobel meeting, once awarded American Slovenian Education Foundation (ASEF) mobility fellowship; and once awarded the Lapanjetovo priznanje by Slovenian biochemical society for outstanding work by early career researcher

EXPERT COMMITTEES AND AWARDS:

2021 Recipient of award Excellence in Science, given by the ARIS for the most visible scientific achievements

2019 Recipient of award "Lavričeva nagrada" for the best teaching assistant at UL MF

2018 Section Editor leader for journal AMS

2007 Marie Curie Early Stage Research Training Grant

2013-present Grant evaluator for Horizon 2020, Research Foundation Flanders (FWO, Belgium), Dutch Research Council (NWO), Paracelsus Medical University Salzburg (Austria), Czech Science Foundation (GACR), National innovation Office (NKFIH; Hungary), French National Research Agency (ANR, France) and British Heart Foundation (BHF; UK)

-present Reviewer for Nature Communications, Nature Nanotechnology, Journal of extracellular vesicles, Journal of Extracellular Biology, European Journal of Cell Biology, Journal of Leukocyte Biology, Frontiers Physiology, ACS Applied Materials & Interfaces, Molecular Immunology, Communications Biology, BBA - Biomembranes, Cells, PlosOne, New Journal of Chemistry, BMC Microbiology and others

-present Member of ISEV, SiN-EV, Slovenian Biochemistry Society (SBD) and Slovenian Microbiological Society (SMD)

CONTRIBUTIONS TO SCIENCE:

(1) We showed that viral protein Nef is released from HIV-infected human T cells, astrocytes and microglia with EVs, which were also detected in the plasma of virally suppressed HIV-infected individuals. With our collaborators, we were the first to propose that EVs can accumulate in CD81 immunopositive organelles that originate from the plasma membrane and not from the endosomal pathway. Nef-containing EVs contribute to the HIV pathogenesis of uninfected cells. Thereby we identified a novel mechanism of communication between HIV and the human host.

(2) Using an *in vitro* model of latent HIV infection, we are investigating the role of Nef-containing EVs in neural stem cell homeostasis, neuronal differentiation, and neuronal senescence. Our work aims to elucidate the mechanisms underlying Nef-mediated neurotoxicity and neuroinflammation, contributing to a better understanding of the role of Nef-containing EVs in the onset and persistence of HIV-associated neurocognitive disorders.

(3) We co-developed a method to size-separate, characterize and quantify EVs by asymmetrical-flow field-flow fractionation (AF4) technique coupled to a multi-detection system. We were also the first to show that the commonly used method for labelling EVs with fluorescent dye PKH is unsuitable for functional studies of the vesicles and have suggested improvements.

(4) Extracellular vesicles as biomarkers of disease: We have established workflows for (i) collection and storage of blood plasma and urine that is compatible with EV research, (ii) isolation of EVs from blood plasma and urine and (iii) characterization of EV size/concentration, RNA, DNA and protein

content. We are applying them in several ongoing collaborative biomarker studies with clinical partners on diverse diseases like HIV-1 infection, kidney allograft rejection, and different cancers.