
BIOGRAPHICAL SKETCH

NAME: Andres Merits

POSITION TITLE: Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Moscow State University, USSR	M. Sc	06/1990	Biochemistry
Moscow State University, USSR/Russia	Ph.D.	04/1994	Virology (plant viruses)
Institute of Biotechnology, University of Helsinki, Finland	Postdoctoral Fellow	12/1998	Virology (plant viruses)
Institute of Biotechnology, University of Helsinki, Finland	Research Associate	12/2001	Mol. Virology (molecular biology of alpha- and flaviviruses)

A. Personal Statement

In 2002 I obtained position of senior research scientist in Estonian Biocentre (Tartu) and in 01.01.2003 become group leader and Research professor at University of Tartu. In 2007 I was elected to position of Professor of Applied Virology in Institute of Technology, University of Tartu. Current research topics include studies of replication of different RNA genomic viruses, including alphaviruses (Semliki Forest virus, Chikungunya virus, Ross River virus, O'nyong'nyong virus), flaviviruses (Zika virus, Dengue virus) and hepaciviruses (hepatitis C virus), construction of virus-based gene expression vectors. The research also includes construction of systems for antiviral drug screening (Chikungunya virus, Zika virus) and analysis of antiviral properties of low molecular weight compounds and oligonucleotide based inhibitors. The research has led to 130 peer-reviewed publications. According to Thomson Reuters Web of Science database (02.03.2019) they have been cited >3500 times (h-index = 38). My current research group, working at these topics, consists from 8 researchers: three senior scientists (with Ph.D. of equivalent degree), three Ph.D. students and two M.Sc. students. This group is involved in intensive collaboration with other research groups Estonia as well as in world-wide international collaboration. I have successfully supervised 13 PhD students.

B. Positions and Honors

Academic Positions

2002-2003 Senior Research Scientist, Estonian Biocentre, Tartu, Estonia
2003-2006 Research Professor, Institute of Molecular and Cell Biology, University of Tartu, Estonia
2007-2012 Full Professor, Institute of Technology, University of Tartu, Estonia
2013-2019 Full Professor (permanent), Institute of Technology, University of Tartu, Estonia
2019- Academy research professor, Institute of Technology, University of Tartu, Estonia

Other Experience and Professional Memberships

2001-present Docent, University of Helsinki, Helsinki, Finland
2006-present Member of the scientific council of Institute of Technology, University of Tartu, Estonia
2010-present Member of the scientific evaluation committee of ETAG (Estonian Research Council)
2006-present Member of the *American Society for Microbiology*
2013-present Member of the *Society for General Microbiology*

Affiliations

2003- present University of Tartu (professor)
2001 – present University of Helsinki, Finland (docent)

Honors

2015: Estonian State Award in Molecular Biology and Chemistry
2019: Elected as Academy Professor by Estonian Academy of Sciences

C. Contributions to Science

1. Prior starting working with animal/human viruses I was expert on plant viruses; most of my studies from this period were dedicated to analysis of plant virus (potyvirus) replicase complex proteins and to the topic of transport and vector transmission of plant viruses. Several paper from this period are still (15 years later) highly cited:
 - **Merits A**, Guo D, Järvekülg L, Saarma M. Biochemical and genetic evidence for interactions between potato A potyvirus-encoded proteins P1 and P3 and proteins of the putative replication complex. *Virology*, 1999, 263: 15-22.
 - Dorokhov YuL, Mäkinen K, Frolova OYu, **Merits A**, Saarinen J, Kalkkinen N, Atabekov IG, Saarma M. A novel function for ubiquitous plant enzyme pectin methylesterase: the host-cell receptor for the tobacco mosaic virus movement protein. *FEBS Letters*, 1999, 461: 223-228.
 - Ivanov KI, Puustinen P, **Merits A**, Saarma M, Mäkinen KM. Phosphorylation down-regulates the RNA-binding function of the coat protein of potato virus A. 2001. *Journal of Biological Chemistry*, 276: 13530-13540.

2. After focusing my research on the topic of alphaviruses I worked mostly on biogenesis of alphavirus replication complex and the nsP2 protease, a key enzyme involved in regulation of alphavirus replication. These studies were continued after my return to Estonia and establishment of my own research group. I have performed detailed analysis of nsP2, discovered two new functions of this enzyme and demonstrated its role in biogenesis of alphavirus replicase complexes:
 - Vasiljeva L, **Merits A**, Auvinen P, Kääriäinen L. Identification of a novel function of the alphavirus capping apparatus-RNA 5' triphosphatase activity of Nsp2 2000. *Journal of Biological Chemistry* 275: 17281-17287.
 - Vasiljeva L, Valmu L, Kääriäinen L, **Merits A**. Site-specific protease activity of the carboxy-terminal domain of semliki forest virus replicase protein nsP2. 2001. *Journal of Biological Chemistry*, 276: 30786-30793.
 - Salonen A, Vasiljeva L, **Merits A**, Magden Y, Jokitalo E, Kaariainen L. Properly folded nonstructural polyprotein directs the Semliki Forest virus replication complex to endosomal compartment. 2003. *Journal of Virology*, 77: 1691-1702.
 - Vasiljeva L, **Merits A**, Golubtsov A, Sizemskaja V, Kääriäinen L, Ahola T. Regulation of the sequential processing of Semliki Forest virus replicase polyprotein. 2003. *Journal of Biological Chemistry*, 278: 41636-41645.
 - Lulla A, Lulla V, Tints K, Ahola T, **Merits A**. Molecular determinants of substrate specificity for semliki forest virus nonstructural protease. 2006 *Journal of Virology*, 80: 5413-5422.
 - Lulla A, Lulla V, **Merits A**. Macromolecular assembly-driven processing of the 2/3 cleavage site in the alphavirus replicase polyprotein. 2012. *Journal of Virology*, 86: 553-565
 - Lulla V, Karo-Astover L, Rausalu K, **Merits A**, Lulla A. Presentation overrides specificity: probing the plasticity of alphaviral proteolytic activity through mutational analysis. 2013. *Journal of Virology*, 87: 10207-10220
 - Das PK, **Merits A**, Lulla A. (2014). Functional Crosstalk between Distant Domains of Chikungunya Virus Non-Structural Protein 2 Is Decisive For Its RNA-Modulating Activity. 2014. *Journal of Biological Chemistry*. 289: 5635-5653.
 - Utt A, Quirin T, Saul S, Hellström K, Ahola T and **Merits A**. (2016). Versatile trans-replication systems for Chikungunya virus allow functional analysis and tagging of every replicase protein. *PLoS One*, 11, e0151616. doi: 10.1371/journal.pone.0151616
 - Rausalu, K., Utt, A., Quirin, T., Varghese, F.S., Žusinaite, E., Das, P.K., Ahola, T. and **Merits, A**. (2016). Chikungunya virus infectivity, RNA replication and non-structural polyprotein processing depend on the nsP2 protease's active site cysteine residue. *Scientific Reports*, 6, 37124. doi: 10.1038/srep37124
 - Hellström, K., Kallio, K., Utt, A., Quirin, T., Jokitalo, E., **Merits, A**. and Ahola, T. (2017). Partially uncleaved alphavirus replicase forms spherule structures in the presence and absence of RNA template. *Journal of Virology*, 91, pii: e00787-17. doi: 10.1128/JVI.00787-17. Print 2017 Sep 15

3. My studies of functions of nsP2 and virus replication led to analysis of complicated interactions between virus and host. We have studied effects of mutations in alphavirus replicase proteins on ability of virus to persist in infected host cells and identified numerous host proteins interaction with alphavirus replicases. Many of these studies were performed in collaboration with different research groups all over the world.
- Panas MD, Varjak M, Lulla A, Er Eng K, **Merits A**, Karlsson-Hedestam GB, McInerney GM. Sequestration of G3BP coupled with efficient translation inhibits stress granules in Semliki Forest virus infection. 2012. *Molecular Biology of the Cell*, **23**:4701-4012.
 - Varjak M, Saul S, Arike L, Lulla A, Peil L, **Merits A**. Magnetic fractionation and proteomic dissection of cellular organelles occupied by the late replication complexes of Semliki Forest virus. 2013. *Journal of Virology*, **87**: 10295-10312.
 - Nikonov A, Mölder T, Sikut R, Kiiver K, Männik A, Toots U, Lulla A, Lulla V, Utt A, **Merits A**, Ustav M. RIG-I and MDA-5 Detection of Viral RNA-dependent RNA Polymerase Activity Restricts Positive-Strand RNA Virus Replication. 2013. *PLoS Pathogens*, 9: e1003610.
 - Pinggen M, Bryden SR, Pondeville E, Schnettler E, Kohl A, **Merits A**, Fazakerley JK, Graham GJ, McKimmie CS. (2016). Host inflammatory response to mosquito bites defines severity of arbovirus infection. *Immunity*, **44**, 1455-1469, 10.1016/j.immuni.2016.06.002
 - Bartholomeeusen K, Utt A, Coppens S, Rausalu K, Vereecken K, Ariën KK, **Merits A**. A Chikungunya virus trans-replicase system reveals the importance of delayed non-structural polyprotein processing for efficient replication complex formation in mosquito cells. 2018. *Journal of Virology*, pii: JVI.00152-18. doi: 10.1128/JVI.00152-18.
 - Liu X, Mutso M, Utt A, Lepland A, Herrero L, Taylor A, Bettadapura J, Rudd P, **Merits A**, Mahalingam, S. Decreased virulence of Ross River virus harboring mutation in the first cleavage site of non-structural polyprotein is caused by a novel mechanism leading to increased production of interferon-inducing RNAs". 2018. *mBio*, **9**(4). pii: e00044-18. doi: 10.1128/mBio.00044-18.
 - Abraham R, Hauer D, McPherson RL, Utt A, Kirby I, Cohen MS, **Merits A**, Leung, A.K.L. and Griffin, D.E. (2018) ADP ribosyl-binding and hydrolase activities of the alphavirus nsP3 macrodomain are critical for initiation of virus replication. *Proceedings of the National Academy of Sciences of the U S A*, **115**(44):E10457-E10466. doi: 10.1073/pnas.1812130115.
4. The increasing importance of alphaviruses, most notably Chikungunya virus, promoted novel directions including analysis of host mechanisms counter-acting Chikungunya virus infection and development of antiviral strategies (antiviral compounds and vaccine candidates) against this pathogen. These studies also relied heavily on international collaboration; partly because Chikungunya virus is not epidemic in Estonia and therefore we lack clinical samples from virus-infected patients.
- Pohjala L, Utt A, Varjak M, Lulla A, **Merits A**, Ahola T, Tammela P. Inhibitors of alphavirus entry and replication identified with a stable Chikungunya replicon cell line and virus-based assays. 2011. *PLoS ONE*, **6**: e28923.
 - Teng TS, Foo SS, Simamarta D, Lum FM, Teo TH, Lulla A, Yeo NK, Koh EG, Chow A, Leo YS, **Merits A**, Chin KC, Ng LF. Viperin restricts chikungunya virus replication and pathology. 2012 *Journal of Clinical Investigations*, **122**: 4447-4460.
 - Teo TH, Lum FM, Claser C, Lulla V, Lulla A, **Merits A**, Rénia L, Ng LF. A Pathogenic Role for CD4+ T Cells during Chikungunya Virus Infection in Mice. 2013. *Journal of Immunology*, **190**: 259-269.
 - Hallengård D, Lum FM, Kümmerer BM, Lulla A, Lulla V, García-Arriaza J, Fazakerley JK, Roques P, Le Grand R, **Merits A**, Ng LF, Esteban M, Liljeström P. Prime-Boost Immunization Strategies against Chikungunya Virus. 2014. *Journal of Virology*, **88**:13333-13343.
 - Utt A, Das PK, Varjak M, Lulla V, Lulla A, **Merits A**. Mutations conferring a non-cytotoxic phenotype on Chikungunya virus replicons compromise enzymatic properties of non-structural protein 2. 2015. *Journal of Virology*, **89**: 3145-3162.
 - Ching KC, Kam YW, **Merits A**, Ng LF, Chai CL. Trisubstituted thieno[3,2-b]pyrrole 5-carboxamides as potent inhibitors of alphaviruses. 2015. *Journal of Medicinal Chemistry*, **58**: 9196-9213.
 - Karlas A, Berre S, Couderc T, Varjak M, Braun P, Meyer M, Gangneux N, Karo-Astover L, Weege F, Raftery M, Schönrich G, Klemm U, Wurzlbauer A, Bracher F, **Merits A**, Meyer T and Lecuit M (2016). A host genome-wide loss-of-function screen identifies effective chikungunya antiviral drugs. *Nature Communications*, **7**, 11320, doi:10.1038/ncomms11320

- Das, P.K., Puusepp, L., Varghese, F.S., Utt, A., Ahola, T., Kananovich, D.G., Lopp, M., **Merits, A.** and Karelson, M. (2016). Design and validation of novel chikungunya virus protease inhibitors. *Antimicrobial Agents and Chemotherapy*, **60**, 7382-7395
 - Teo, T.H., Chan, Y.H., Lee, W.W., Lum, F.M., Amrun, S.N., Her, Z., Rajarethinam, R., **Merits, A.**, Röttschke, O., Rénia, L. and Ng, L.F. (2017). Fingolimod treatment abrogates chikungunya virus-induced arthralgia. *Sci Transl Med.*, 9, pii: eal1333. doi: 10.1126/scitranslmed.aal1333
 - Roques, P., Ljungberg, K., Kummerer, B.M., Gosse, L., Dereuddre-Bosquet, N., Tchitchek, N., Hallengard, D., Garcia-Arriaza, J., Meinke, A., Esteban, M., **Merits, A.**, Le Grand, R. and Liljestrom, P. (2017) Attenuated and vectored vaccines 1 protect non-human primates against Chikungunya virus. *JCI Insight*, **2**(6), e83527. doi: 10.1172/jci.insight.83527
5. Recent outbreak of Zika virus (ZIKV) has boosted our interest to this pathogen and flaviviruses in general. In a very short time we have been able to contribute to the field by developing a new ZIKV reverse genetics system (currently most commonly used system in world, at least 45 different laboratories have requested and obtained it from us), applying it for studies of anti-ZIKV compounds; developing of novel assay for diagnostics of ZIKV infection and by analyzing ZIKV/mosquito vector interactions:
- Mutso, M., Saul, S., Rausalu, K., Susova, O., Žusinaite, E., Mahalingam, S. and **Merits, A.** (2017). Reverse genetic system, genetically stable reporter viruses and packaged subgenomic replicon based on Brazilian Zika virus isolate. *Journal of General Virology*, **98**, 2712-2724. doi: 10.1099/jgv.0.000938.
 - Varghese, F.S., Rausalu, K., Hakanen, M., Saul, S., Kümmerer, B., Susi, P., **Merits, A.** and Ahola, T. (2017). Obatoclox inhibits alphavirus membrane fusion by neutralizing the acidic environment of endocytic compartments" *Antimicrobial Agents and Chemotherapy*, pii: AAC.02227-16. 61. pii: e02227-16. doi: 10.1128/AAC.02227-16
 - Lum, F.-M., Lin, C., Susova, O.Y., Teo, T.-H., Fong, S.-W., Mak, T.-M., Lee, L.K., Chong, C.-Y., Lye, D.C.B., Lin, R.T.P., **Merits, A.**, Leo, Y.-S. and Ng, L.F.P. (2017). Sensitive detection of Zika virus antigen in patients' whole blood as an alternative diagnostic approach. *The Journal of Infectious Diseases*, **216**, 182-190. doi: 10.1093/infdis/jix276
 - Varjak, M., Donald, C.L., Mottram, T., Sreenu, V.B., **Merits, A.**, Maringer, K., Schnettler, E. and Kohl, A. (2017). Characterization of the Zika virus induced small RNA response in *Aedes aegypti* cells. *PLOS Neglected Tropical Diseases*, **11**:e0006010. doi: 10.1371/journal.pntd.0006010

Complete List of the Publications:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=merits+a>

D. Research Support

Ongoing Research Support

Estonian Research Council IUT20-27. Andres Merits PI 01/01/2014-12/31/2019
 Title: Interaction between virus and host – expanding knowledge for development of biomedical tools". The proposal is aiming studies of alphaviruses and human papillomaviruses; development of antiviral strategies and virus based biotechnological systems.
 Role: PI

The Wellcome Trust Collaboration Award 200171/Z/15/Z. Luke Alpey PI 09/01/2016-08/31/2021
 Title: Genetic approaches to reducing vector competence of *Aedes aegypti* for chikungunya virus.
 Role: co-PI

Estonian Ministry of Science and Education. Tanel Tenson PI 09/01/2016-08/31/2022
 Title: Centre of Excellence in in Molecular Cell Engineering, Estonia. Project aimed use of methods of synthetic and chemical biology on studies of microbes, viruses and cells. It includes development of anti-viral approaches and compounds
 Role: co-PI

The Defence Advanced Research Projects Agency (DARPA), USA, Luke Alphey PI 10/01/2018-03/31/2022
Title: Predicting and preventing flavivirus spillover”
Role: co-PI

Completed Research Support

Estonian Biotechnology Program. Andres Merits PI 01/01/2012-12/31/2013
Title: “Anti-HCV drug development and screening technologies” The proposal was dedicated to development of humanized model for hepatitis C and biological therapeutics inhibiting HCV replication.
Role: PI

European Commission Framework 7 grant, Andes Merits (Partner) 12/01/2010-11/30/2014
Title “Integrated research on Chikungunya virus” Proposal was dedicated to studies of Chikungunya virus replication and pathogenesis; it also aimed to development of vaccine candidates and antiviral compounds
Role: Partner (co-PI)

Estonian Ministry of Science and Education. Tanel Tenson PI 09/01/2008-08/31/2015
Title: Centre of Excellence in Chemical Biology, Estonia. Project aimed use of methods of chemical biology on studies of microbes, viruses and cells. It included development of anti-viral compounds
Role: co-PI

Estonian Ministry of Science and Education. Andres Merits PI 01/01/2008-12/31/2013
Title: Analysis of the replication, viral-host interactions and virus induced pathogenesis of viruses with RNA genomes and inhibition or practical usage of these processes. Project was dedicated to the analysis of alphavirus and hepacivirus replication and development of vectors based on alphavirus genome

European Commission: Framework 5 grant, Andres Merits (Partner) 10/01/2002-09/30/2005
Title “Semliki Forest virus based therapeutic systems”. Project was dedicated to analysis of molecular biology of Semliki forest virus and use of this virus for bio- and gene technology applications
Role. Partner (co-PI)

The Wellcome Trust. Andres Merits, PI 01/01/2003-12/31/2007
Wellcome Trust reference 067575/Z/02/Z, International Senior Research Fellowship in Biomedical Sciences
Title: Alphavirus genomes as models and tools for studies of RNA replication, virus-cell interactions and virus induced pathogenesis of positive strand RNA viruses. The project aimed studies of replication and virus-host interaction of Semliki Forest virus
Role: PI

Estonian Science Foundation. Andres Merits, PI 01/01/1995-12/31/2014
4 different projects titled:
Title 1: Molecular tools based on plant nanovirus genome
Title 2: Mechanisms involved in the Semliki Forest virus replication and virus-host interactions: basic studies and potential use for gene technology.
Title 3: Alphavirus replication, inhibition and virus-host interactions.
Title 4: Exploration of space of alphavirus-encoded short linear interaction motifs mediating hijacking of host pathways and facilities.
All these were small (up to \$20,000/year) projects intended mainly to support PhD/MSc students of the PI
Role: PI in all 4 projects.

E. Collaborators

On-going collaboration with following researchers:
Prof. Luke Alphey, The Pirbright Institute, UK
Prof. Roland Wolkowicz, USA

Dr. Rennos Fragkoudis, University of Nottingham, UK
Dr. Jamal Sam, University of Malaya, Malaysia
Dr. Tero Ahola, University of Helsinki, Finland
Dr. Gerald McInerney, Karolinska Institute, Sweden
Prof. Alain Kohl, University of Glasgow, UK
Prof. Mark Harris, University of Leeds, UK
Prof. Suresh Mahalingam, Griffith University, Australia
Prof. John Fazakerley, University of Melbourne, Australia
Dr. Lisa Ng, A*Star, Singapore