

AUTOIMMUNE DISEASE RESEARCH IN RĪGA STRADIŅŠ UNIVERSITY



The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 952376

Table of Contents

VirA Project.....	4
Objectives.....	6
Activities.....	7
Project Partners.....	8
Consortium.....	9
Rīga Stradiņš University (RSU).....	11
University of Ferrara (Unife).....	12
Ulm University (UULM).....	14
Zabludowicz Center for Autoimmune Diseases at Sheba Medical Center (SMC).....	15
VirA’s operational scheme.....	17
Autoimmunity research projects in RSU (2020–2022).....	18
Relevant publications in RSU (2020–2022).....	19
Potential directions of collaboration.....	25
Areas of expertise.....	26

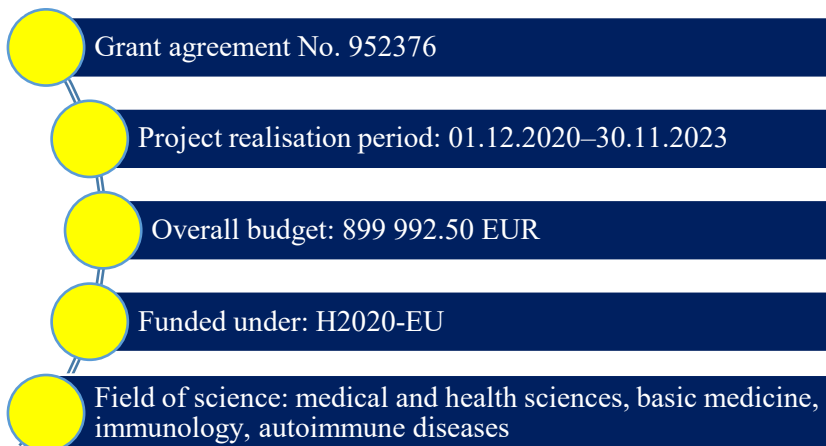
VirA Project

The specific challenge of VirA Twinning project “**Reducing networking gaps between Rīga Stradiņš University (RSU) and internationally-leading counterparts in viral infection-induced autoimmunity research**” is to enhance networking activities between the RSU located in Latvia as a Widening country and internationally-leading counterparts at the European Union (EU) level in the field of autoimmunity research. Over several decades, both on a local and regional level RSU has proven itself as an important island of research excellence in viral infection-induced autoimmunity research. Raising the research excellence further requires widening the network and establishing closer cooperation with global leaders in science, sharpening the institutional profile of RSU.

The project **aims** at strengthening close scientific cooperation with counterparts: in Italy – University of Ferrara, in Germany – Ulm University, and in Israel – Zabludowicz Center for Autoimmune Diseases at Sheba Medical Center (SMC). Partner universities are excellence centres (world leaders) that are forerunners in immunology, virology, morphology and clinical data management and modelling, and are capable of inspiring positive change in the research field and significantly influence future developments at RSU via joint activities.

Systemic autoimmune diseases (SAD) are a significant cause of morbidity and mortality worldwide, creating a **challenge** for researchers and clinicians to find evidence-based solutions for SAD diagnostics, treatment and prevention. Due to complexity of autoimmune disease research, which requires multidisciplinary

approaches, a problem is insufficient research capacity at low-performing EU Member State research institutions. Research capacity, able to deliver precise and early diagnostic is of high importance to move towards the development of methods for personalised medicine and better understanding of triggers and mechanisms in autoimmunity, leading to better understanding of chronic diseases and comorbidities and searching for therapy options. VirA project will optimally address the challenges and strengthen the European Research Area in autoimmunity.



Objectives

#1

Increase research excellence of the coordinating institution in the field of research as a result of the twinning exercise

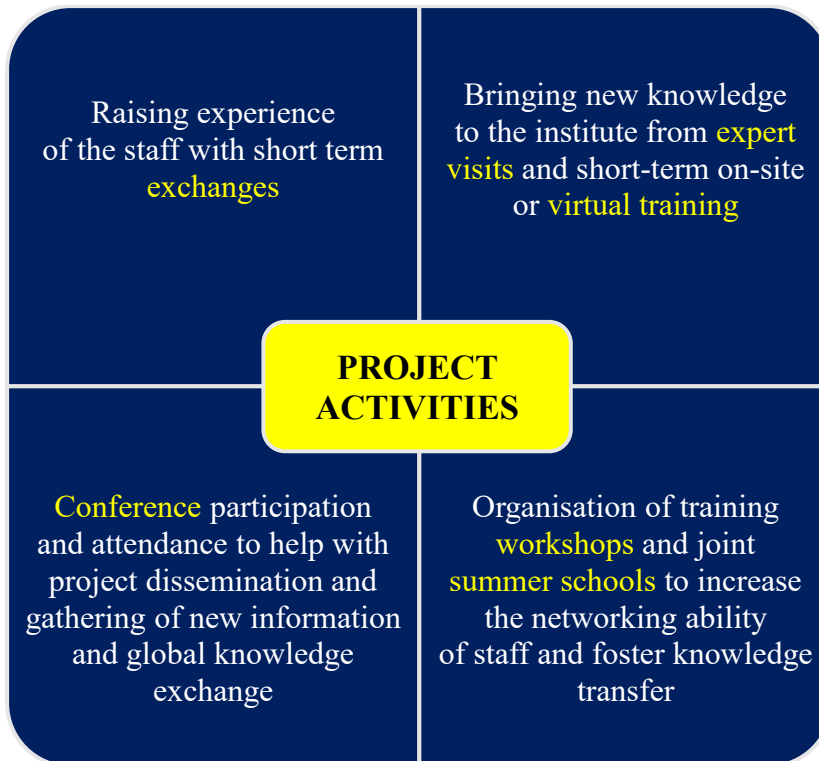
#2

Enhance reputation, attractiveness and networking channels of the coordinating institution

#3

Enhance scientific and technological capacity of the linked institutions with a principal focus on the university or research organisation from the Widening Country

Activities



Project Partners

Coordinated by:



Rīga Stradiņš University
Latvia

Project partners:



**Università
degli Studi
di Ferrara**

University of Ferrara
Italy



universität
uulm

Ulm University
Germany



SHEBA
Tel HaShomer
City of Health

**Zabludowicz Center
for Autoimmune Diseases
at Sheba Medical Center**
Israel

Consortium

The VirA overall consortium structure includes four partners from four different countries. The present consortium has the required multidisciplinary know-how and expertise to carry out diverse project activities and create an impact on European level.

The consortium will enhance RSU research capacity in the field of autoimmune diseases and strengthen links, not only between institutions of the low-performing Member States and internationally leading institutions from the EU, but it will also strengthen collaboration between the EU and Israel. It will increase excellence in autoimmune disease research by establishing a multidisciplinary research unit including four platforms at RSU:

- Immunology,
- Virology,
- Morphology,
- Clinical data management and modelling.

Upgrading research capacity and omitting limitations of research potential in Latvia is a valuable contribution to EU research competitiveness, synergistically joining resources and creating niches of excellence with a global future in convergence regions.

Infections and autoimmune diseases, due to their impact on global health and uneven sharing of burden between countries, make research a driving force for achieving more equal access to care, delivering prompt answers to new challenges and opening of new research fields.

Figure 1

Geographic locations of partners (Latvia, Germany, Italy, Israel)



Rīga Stradiņš University (RSU)



RĪGAS STRADIŅA
UNIVERSITĀTE

RSU is a public University in Latvia covering 66 study programmes, among which seven are English-taught programmes. The University has 9,290 students and is one of the largest entities in the Baltic States in the area of medicine, health sciences and pharmacy, and the only universal medical university in Latvia. RSU holds a unique place in Latvia's scientific field, providing a full research cycle from laboratory to hospital bed. RSU has a high level of internationalisation with 2,523 international students from 65 countries. RSU processes are ISO 9001:2008 certified (*Bureau Veritas*) and, therefore, RSU possesses a managerial capacity required by complex projects.

RSU has been recognised as the university with the best reputation in Latvia, gaining the highest rating among the 10 largest Latvian universities according to a study conducted by market research company Kantar TNS in 2017–2021. RSU has been included, for the first time, in the Times Higher Education Emerging Economies Ranking 2022. The 115th place of the RSU is not only the best rating among Latvian higher educational institutions but also the highest historical place which any university in Latvia has achieved so far in any of the ratings created by the Times Higher Education. Success is largely based on the quality of scientific activity and successful international operations. An ever-increasing attention is paid to the transfer of knowledge and technologies by integrating knowledge in the basic functions of the University, and transforming knowledge in to products and services that are useful to society.

www.rsu.lv

University of Ferrara (Unife)



**Università
degli Studi
di Ferrara**

The Unife, founded in 1391, is one of the oldest in Italy. It consists of 12 Departments: Architecture, Humanities, Life Science and Biotechnology; Chemical, Pharmaceutical and Agricultural Sciences, Neurosciences and Rehabilitation, Translational Medicine, Medical Sciences, Engineering, Physics and Earth Science, Law, Management and Economics, Mathematics and Informatics.

The School of Medicine of the Unife is responsible for teaching activities to approximately 4,000 students (MD, dentistry, nursing, physiotherapy degrees and sanitary/technical degrees, such as radiology, biomedical lab, audiology, etc). The School of Medicine also coordinates all clinical activities of the three Medical Departments, which are mainly carried out in the S. Anna University Hospital (*Azienda Ospedaliero-Universitaria*), located in Ferrara.

Some facts and figures about the University: approximately 25,000 students enrolled (6 % are international students); 230 Socrates/Erasmus partners; 41 international research projects funded by FP7, of which four Coordinated by Unife and three funded in *Horizon 2020*, several projects funded by other European research programmes; approximately 500 international cooperation agreements. There are 11 PhD programmes operating in the different subject areas, including Molecular Medicine and Pharmacology; Biomedical and Biotechnological Sciences.

Relevance of the participation of the University of Ferrara to this project is the availability of both Clinical Units (Endocrinology, Rheumatology, Neurology, Gynaecology) and Basic Science research groups of international relevance.

www.unife.it

Ulm University (UULM)



universität
uulm

UULM founded in 1967, enjoys an excellent reputation for innovative research and interdisciplinary training. It is part of a strong network of international partnerships, which creates opportunities for students and researchers alike and strengthens the reputation of Ulm as excellent and future-oriented University.

UULM is the youngest university in Germany, which has five faculties (i.e. Computer Science, Engineering, Mathematics and Economics, Medicine, Natural Sciences) and currently more than 10,000 students. Biomedicine and Biotechnology are at the major focus of the university's research program. With help by university network InnoSüd at UULM, there is unique support for technology transfer to small and medium-sized enterprises (<https://www.uni-ulm.de/en/technology-transfer/business-start-ups/>). Most recently, ERC-Proof of Concept projects by Prof. Jelezko (NDI) und Prof. Kirchhoff (Epi-X4Health) have been founded. These concepts provide a new focus on the use of peptides and technologies to understand immune deviations such as autoimmune dysfunction, and eventually lead to new treatment and disease prevention. Experiences at UULM will be highly useful to transfer to young investigators from the Baltic area. Knowledge transfer will be part of summer school initiatives as well.

www.uni-ulm.de

Zabludowicz Center for Autoimmune Diseases at Sheba Medical Center (SMC)



Zabludowicz Center for Autoimmune Diseases (3,000 sqm) at the Sheba Medical Center is affiliated to Tel-Aviv University, Sackler Faculty of Medicine. This unique centre entails departments, outpatient clinic as well as a large day care centre for treatment with biological and other therapies and a clinical study centre for evaluation of new treatments. The centre encompasses research and diagnostic laboratories that enable hospital service, Israeli and international collaboration between physicians and researchers from different fields (i.e., Internal Medicine, Clinical Immunology, Autoimmunity, Rheumatology, Neurology, Gastroenterology, Obstetrics and Gynaecology), as well as a large auditorium, meeting rooms and student teaching rooms.

In the Zabludowicz Center patients with different autoimmune diseases can be diagnosed and treated by a multidisciplinary team including old and new therapies, complementary medicine, psychological treatments etc. The research plans of the Zabludowicz Center are in collaboration with others physician and scientists in Israel and around the world. The centre was founded by Prof. Yehuda Shoenfeld, a leading clinical immunologist and an expert in immunology and allergy, and a prolific researcher and author.

Sheba Medical Center at Tel HaShomer, Israel is the largest medical centre in the Middle East. Sheba Medical Center includes a general hospital, maternity hospital, paediatric hospital, and a rehabilitation hospital. Sheba's staff consists of over 1,600 physicians committed to the highest standards of diagnostic, therapeutic and rehabilitative medicine and a total staff of approximately 10,000 employees.

Sheba Medical Center is the national leader in clinical research in Israel. It conducts nearly one fourth of all clinical studies in Israel: Sheba accommodates over 90 research teams and approximately 4,000 research studies take place annually. Sheba is Israel's leading medical institution in terms of publication quality and quantity – the medical centre staff publishes approximately 1,800 scientific articles a year.

A goal of the research teams at Sheba is to collaborate with leading teaching and research academic institutes, both domestically and internationally. Sheba's academic authority promotes multidisciplinary health and medical studies – thousands teach and study at Sheba every year. An academic campus is under construction and will include research institutes, technological incubators, start-up companies, and an innovation centre. This academic facility will operate jointly with medical supercentres worldwide.

Tel-Aviv University (TAU) has over 2,200 faculty members, among them internationally renowned scientists who have made significant contributions to advancement of knowledge in fields as diverse as particle physics, cell biology, biotechnology, genetics, fibre optics, humanities, arts and social sciences. Israel's largest and most comprehensive university. TAU is comprised of nine faculties, 27 schools, 98 departments and some 130 research institutes and centres.

TAU runs Israel's largest bio-medical research and teaching framework with 1,400 scientist-clinicians at 17 affiliated hospitals. The scientists team up with pharmaceutical companies to develop new drugs and medical technologies.

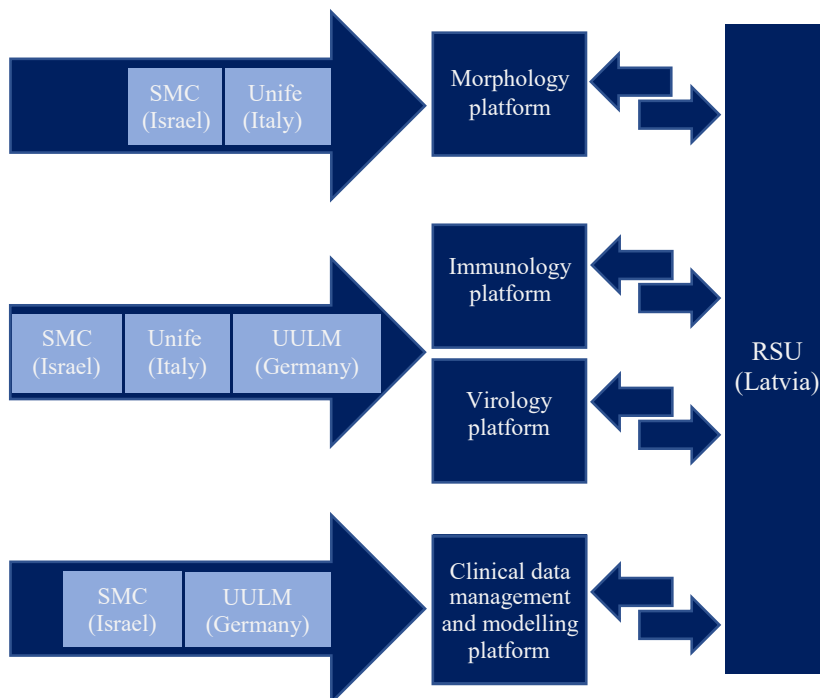
www.eng.sheba.co.il

VirA's operational scheme

Figure 2

Project operational scheme

SMC – Zabludowicz Center for Autoimmune Diseases at Sheba Medical Center; Unife – University of Ferrara; UULM – Ulm University; RSU – Rīga Stradiņš University.



Autoimmunity research projects in RSU (2020–2022)

Human herpesvirus 6 chemokine receptor mediated immunomodulating mechanism involvement in autoimmune thyroiditis development

Sultanova, A., Čistjakovs, M., Sokolovska, L. & Strojeva, S.

Project realisation period: 01.12.2020 → 31.12.2021

Project: The Latvian Council of Science Programme → Fundamental and Applied Research Projects

VirA: Reducing networking gaps between Rīga Stradiņš University (RSU) and internationally-leading counterparts in viral infection-induced autoimmunity research

Murovska, M., Lunga, A., Doniņa, S., Nora-Krūkle, Z., Groma, V., Krūmiņa, A. & Rasa-Dzelzkalēja, S.

Project realisation period: 01.12.2020 → 30.11.2023

Project: EU Programmes → Horizon 2020

Selection of biomarkers in ME/CFS for patient stratification and treatment surveillance / optimisation

Murovska, M., Berķis, U., Krūmiņa, A., Svirskis, Š., Grāvelsiņa, S., Arāja, D., Vilmane, A., Vecvagare, K. & Maksimova, I.

Project realisation period: 01.01.2020 → 30.06.2023

Project: The Latvian Council of Science Programme → Fundamental and Applied Research Projects

Dissecting the interplay between intestinal dysbiosis and B cell function in the pathogenesis of immunoglobulin A nephropathy

Čerņevskis, H., Oļeiņika, K., Kroiča, J., Kuzema, V., Pētersons, A., Berga-Švītiņa, E., Rācenis, K., Popova, A., Šlisere, B., Vasiļvolfa, A. & Saulīte, A. J.

Project realisation period: 01.01.2020 → 30.06.2023

Project: The Latvian Council of Science Programme → Fundamental and Applied Research Projects

Relevant publications in RSU (2020–2022)

Shikova, E., Reshkova, V., Kumanova, A. & Murovska, M., European Network on ME/CFS (EUROMENE) (2020). Cytomegalovirus, Epstein-Barr virus, and human herpesvirus-6 infections in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Journal of Medical Virology*, 92(12), 3682–3688. <https://doi.org/10.1002/jmv.25744> (IF 2.3)

Araja, D., Berkis, U., Lunga, A., & Murovska, M. (2021). PMU29 Burden of COVID-19 consequences: an example of post-viral chronic fatigue syndrome: an example of post-viral chronic fatigue syndrome. *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, 24(S1), S149–S150. [PMU29]. <https://doi.org/10.1016/j.jval.2021.04.741> (IF 5.725)

Vasconcelos, M. H., Alcaro, S., Arechavala-Gomez, V., Baumbach, J., Borges, F., Brevini, T. A. L., Rivas, J. D. L., Devaux, Y., Hozak, P., Keinänen-Toivola, M. M., Lattanzi, G., Mohr, T., Murovska, M., Prusty, B. K., Quinlan, R. A., Pérez-Sala, D., Scheibenbogen, C., Schmidt, H. H. H. W., Silveira, I., Riganti, C. (2021). Joining European scientific forces to face pandemics. *Trends in Microbiology*, 29(2), 92–97. <https://doi.org/10.1016/j.tim.2020.10.008> (IF 17.079)

Grāvelsiņa, S., Caselli, E., Nora-Krūkle, Z., Svirskis, S., Vilmane, A., Di Luca, D., & Murovska, M. (2021). Prevalence of KIR2DL2/DS2 and KIR2DL3 and presence of B19V in patients with thyroid disorders. *Proceedings of the Latvian Academy of Sciences, Section B: Natural, Exact, and Applied Sciences*, 75(1), 16–19. <https://doi.org/10.2478/prolas-2021-0003> (IF 0.35)

Friedman, K. J., Murovska, M., Pheby, D. F. H., & Zalewski, P. (2021). Our evolving understanding of ME/CFS. *Medicina (Lithuania)*, 57(3), 1–5. [200]. <https://doi.org/10.3390/medicina57030200>

(IF 2.43)

Skuja, S., Svirskis, S., & Murovska, M. (2021). Human herpesvirus-6 and -7 in the brain microenvironment of persons with neurological pathology and healthy people. *International Journal of Molecular Sciences*, 22(5), 1–19. [2364]. <https://doi.org/10.3390/ijms22052364>

(IF 5.924)

Kadiša, A., Nora-Krūkle, Z., Sokolovska, L., Grāvelsiņa, S., Vecvagare, K., Svirskis, Š., Lejnieks, A., & Murovska, M. (2021). Does the course of disease influence the development of fatigue in rheumatoid arthritis patients? *Proceedings of the Latvian Academy of Sciences, Section B: Natural, Exact, and Applied Sciences*, 75(2), 106–112.

<https://doi.org/10.2478/prolas-2021-0017>

(IF 0.35)

Kujawski, S., Cossington, J., Słomko, J., Zawadka-Kunikowska, M., Tafil-Klawe, M., Klawe, J. J., Buszko, K., Jakovljevic, D. G., Kozakiewicz, M., Morten, K. J., Dawes, H., Strong, J. W. L., Murovska, M., Oosterwijck, J. V., Estevez-Lopez, F., Newton, J. L., Hodges, L., & Zalewski, P. (2021). Relationship between cardiopulmonary, mitochondrial and autonomic nervous system function improvement after an individualised activity programme upon chronic fatigue syndrome patients. *Journal of Clinical Medicine*, 10(7), [1542].

<https://doi.org/10.3390/jcm10071542>

(IF 4.242)

Nacul, L., Authier, F. J., Scheibenbogen, C., Lorusso, L., Helland, I. B., Martin, J. A., Sirbu, C. A., Mengshoel, A. M., Polo, O., Behrends, U., Nielsen, H., Grabowski, P., Sekulic, S., Sepulveda, N., Estévez-López, F., Zalewski, P., Pheby, D. F. H., Castro-Marrero, J., Sakkas, G. K., ... Lacerda, E. M. (2021). European network on myalgic encephalomyelitis/chronic fatigue syndrome (EUROMENE): Expert consensus on the diagnosis, service provision, and care of people with ME/CFS in Europe. *Medicina* (Lithuania), 57(5), [510]. <https://doi.org/10.3390/medicina57050510>
(IF 2.43)

Kujawski, S., Słomko, J., Hodges, L., Pheby, D. F. H., Murovska, M., Newton, J. L., & Zalewski, P. (2021). Post-exertional malaise may be related to central blood pressure, sympathetic activity and mental fatigue in chronic fatigue syndrome patients. *Journal of Clinical Medicine*, 10(11), [2327]. <https://doi.org/10.3390/jcm10112327>
(IF 4.242)

Kujawski, S., Bach, A. M., Słomko, J., Pheby, D. F. H., Murovska, M., Newton, J. L., & Zalewski, P. (2021). Changes in the allostatic response to whole-body cryotherapy and static-stretching exercises in chronic fatigue syndrome patients vs. Healthy individuals. *Journal of Clinical Medicine*, 10(13), [2795]. <https://doi.org/10.3390/jcm10132795>
(IF 4.242)

Araja, D., Berkis, U., Lunga, A., & Murovska, M. (2021). Shadow burden of undiagnosed myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) on society: Retrospective and prospective – in light of Covid-19. *Journal of Clinical Medicine*, 10(14), [3017]. <https://doi.org/10.3390/jcm10143017>
(IF 4.242)

Gravelsina, S., Nora-Krukle, Z., Vilmane, A., Svirskis, S., Vecvagare, K., Krūmiņa, A., & Murovska, M. (2021). Potential of activin B as a clinical biomarker in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Biomolecules*, 11(8), [1189]. <https://doi.org/10.3390/biom11081189> (IF 4.879)

Zaķe, T., Kalere, I., Upmale-Engela, S., Svirskis, S., Gersono, G., Skesters, A., Groma, V., & Konrāde, I. (2021). Plasma levels of Th17-associated cytokines and selenium status in autoimmune thyroid diseases. *Immunity, inflammation and Disease*, 9(3), 792–803. <https://doi.org/10.1002/iid3.433> (IF 0.9)

Jain, N., Smirnovs, M., Strojēva, S., Murovska, M., & Skuja, S. (2021). Chronic alcoholism and HHV-6 infection synergistically promote neuroinflammatory microglial phenotypes in the *substantia nigra* of the adult human brain. *Biomedicines*, 9(9), [1216]. <https://doi.org/10.3390/biomedicines9091216> (IF 6.081)

Krumina, A., Vecvagare, K., Svirskis, S., Gravelsina, S., Nora-Krukle, Z., Gintere, S., & Murovska, M. (2021). Clinical profile and aspects of differential diagnosis in patients with ME/CFS from Latvia. *Medicina (Lithuania)*, 57(9), [958]. <https://doi.org/10.3390/medicina57090958> (IF 2.43)

Pheby, D. F. H., Friedman, K. J., Murovska, M., & Zalewski, P. (2021). Turning a corner in ME/CFS research. *Medicina (Lithuania)*, 57(10), [1012]. <https://doi.org/10.3390/medicina57101012> (IF 2.43)

Arāja, D., Rovīte, V., Murovska, M., Terentjeva, A., Vaidere, D., Vecvagare, K., & Vīksna, L. (2021). Severity of COVID-19: Causes and consequences – from obesity to chronic fatigue syndrome. *Proceedings of the Latvian Academy of Sciences. Section B. Natural, Exact, and Applied Sciences*, 75 (6), 411–416. <https://doi.org/10.2478/prolas-2021-0061>
(IF 0.35)

Xu, M., Leskinen, K., Gritti, T., Groma, V., Arola, J., Lepistö, A., Sipponen, T., Saavalainen, P., & Söderlund-Venermo, M. (2022). Prevalence, Cell Tropism, and Clinical Impact of Human Parvovirus Persistence in Adenomatous, Cancerous, Inflamed, and Healthy Intestinal Mucosa. *Frontiers in Microbiology*, 13, 914181. <https://doi.org/10.3389/fmicb.2022.914181>
(IF 6.064)

Kujawski, S., Słomko, J., Godlewska, B., Cudnoch-Jędrzejewska, A., Murovska, M., Newton, J., Sokołowski, Ł. & Zalewski, P. (2022). Combination of whole body cryotherapy with static stretching exercises reduces fatigue and improves functioning of the autonomic nervous system in Chronic Fatigue Syndrome. *Journal of Translational Medicine*, 20(1), [273]. <https://doi.org/10.1186/s12967-022-03460-1>
(IF 4.965)

Sultanova, A., Čistjakovs, M., Sokolovska, L., Cunskis, E. & Murovska, M. (2022). Investigation of the Involvement of HHV-6 Encoded Viral Chemokine Receptors in Autoimmune Thyroiditis Development. *Microbiology Spectrum*, 10(3), [e02369-21]. <https://doi.org/10.1128/spectrum.02369-21>
(IF 9.43)

Araja, D., Berkis, U. & Murovska, M. (2022). COVID-19 Pandemic-Revealed Consistencies and Inconsistencies in Healthcare: A Medical and Organizational View. *Healthcare* (Basel, Switzerland), 10(6), [1018]. <https://doi.org/10.3390/healthcare10061018>
(IF 3.160)

Potential directions of collaboration

Life sciences

Persistent viral infections

Newly discovered viruses

Bioimmunology

Medical biotechnology

Statistics and mathematical modelling

Areas of expertise

Diseases of central nervous system

- Multiple sclerosis
- Encephalopathy
- Meningitis
- Epilepsy

Autoimmune diseases

- Autoimmune thyroid diseases
- Rheumatoid arthritis
- Fibromyalgia
- Myalgic encephalomyelitis/chronic fatigue syndrome

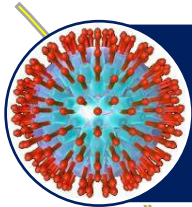
Malignant processes

- Prostate cancer
- Chronic lymphocytic leukemia

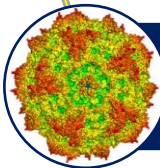
Paediatric diseases

- Lower Respiratory Tract Illnesses
- Acute Gastroenteritis

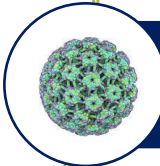
Areas of expertise



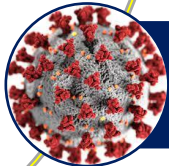
Epstein-Barr virus
Cytomegalovirus
Human Herpesvirus 6A and 6B
Human Herpesvirus 7



Parvovirus B19
Bocavirus 1-4
Human parvovirus 4



Papillomaviruses



Severe acute respiratory syndrome coronavirus 2
(SARS-CoV-2)

CONTACT INFORMATION



Project Coordinator
Assoc. Prof., MD, Ph.D.
Modra Murovska

Address:
Rīga Stradiņš University
Institute of Microbiology and Virology
5 Rātsupītes Street, Riga, LV-1067, Latvia

Phone:
+371 67060834

E-mail:
Modra.Murovska@rsu.lv