



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



Materials on successful workshop accomplishment

Deliverable D3.1

Project Number - 952376 - VirA

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Executive Summary

Due to the ongoing COVID-19 pandemic the workshop “**Viral Infections as Aetiological or Trigger Factors of Autoimmune Diseases**” was conducted virtually on November 9th and 10th 2021. In total, 170 participants attended the online workshop, representing for example academic researchers from Rīga Stradiņš university (RSU), University of Daugavpils, Latvian Biomedical research and study centre; national hospitals – Riga East Clinical University hospital, Pauls Stradiņš Clinical University hospital, Riga 1st hospital; regulators from national competent authorities and industry representatives.

Participants in the event included leading researchers, young scientists and students, as well as medical practitioners and residents. Most of the participants, as listeners, came from Latvia on both days of the event, but the lectures were mainly given by VirA project partners from Italy (University of Ferrara), Germany (Ulm University) and Israel (Medical Research Infrastructure Development and Health Services Fund by the Sheba Medical Center).

The attachment of this report contains workshop agenda, the list of participants, the evaluation form and pool reports which shows how many participants participated and what answers they chose in the multi-answer online question and answer sessions. A full recording of the seminar is available on the VirA project website, and anyone interested can listen to it at a time convenient to them (<https://vira-twinning.eu/events/workshop-viral-infections-aetiological-or-trigger-factors-autoimmune-diseases>; <https://panopto.rsu.lv/Panopto/Pages/Viewer.aspx?id=2a4e30eb-3948-45e5-aedf-adde008494e6>; <https://panopto.rsu.lv/Panopto/Pages/Viewer.aspx?id=1fe32d44-fac2-45ab-b3c6-adde007a9055>).

The intention of the workshop was to get into a theoretical and practical knowledge on viruses as aetiological or trigger factors of autoimmune diseases. During the event, we listened to both theoretical lectures and lectures with a practical orientation, where experts showed and told about various available and applicable research methods, thus exchanging experience and expertise and providing valuable input to the horizons of young scientists' knowledge. Lectures on the effects of viruses on autoimmune diseases, both autoimmune thyroiditis and autoimmune neurological and dermatological diseases, were certainly relevant information for practitioners and residents, as evidenced by the results of the workshop evaluation questionnaires submitted.

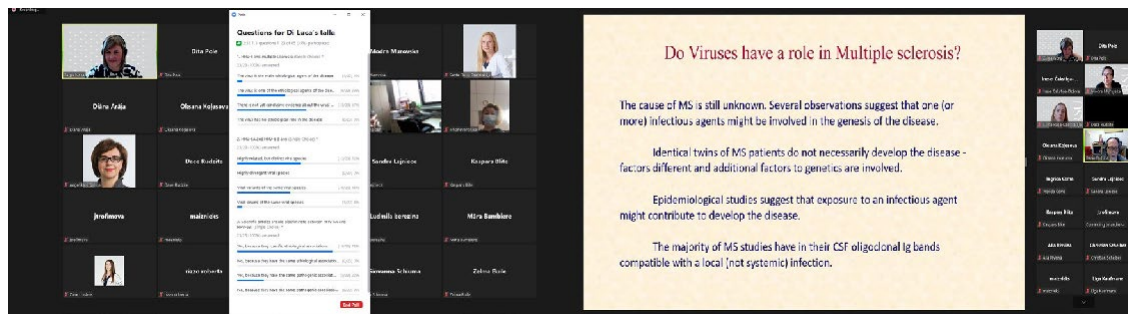
The workshop started with a short welcome address by the director of Research Department, RSU, Latvia - Liene Ņikitina-Zaķe and coordinator of VirA project Assoc Prof, Lead Researcher and Director of the Institute of Microbiology and Virology, RSU – Modra Murovska. Subsequently Lead Researcher Zaiga Nora-Krūkle - the Leader of WP3 Virology platform, organizer and moderator of the workshop, introduced participants with a workshop agenda and technical issues related to discussion sessions and questions.

Overview of the presentations

In order to meaningfully structure the 20 lectures that were given on both days of the workshop, we split the talks in 4 sessions:

Session 1 was devoted to viral infections as initiators in autoimmune diseases.

In this session, a lecture “HHV-6 and Multiple Sclerosis” was given by **Dario Di Luca**, Professor, Department of Medical Sciences, Microbiology and Clinical Microbiology, University of Ferrara, Italy. The speech was followed by a Q&A session. Prof Di Luca reviewed the evidence associating HHV-6 with multiple sclerosis (MS). Several observations associate MS to virus infection. Several candidates have been proposed, on the basis of sound experimental observations: Epstein Barr virus, endogenous retroviruses, etc. Several evidences suggest that also HHV-6 might have a role in MS development. However, not all data agree. Several papers describe the epidemiological association between HHV-6 and MS, the presence of viral footprints (nucleic acids, antigens) in lesions and/or patients, specific immunologic reactivity, etc. However, several other papers report negative results. Prof Di Luca reported the results obtained by the research group at University of Ferrara, pointing to the importance of the patient's genetic background, especially in relation to the innate response to viral infection. This genetic variability could be one of several explanations (for example, different stages of the disease) for the discrepancy among published results.



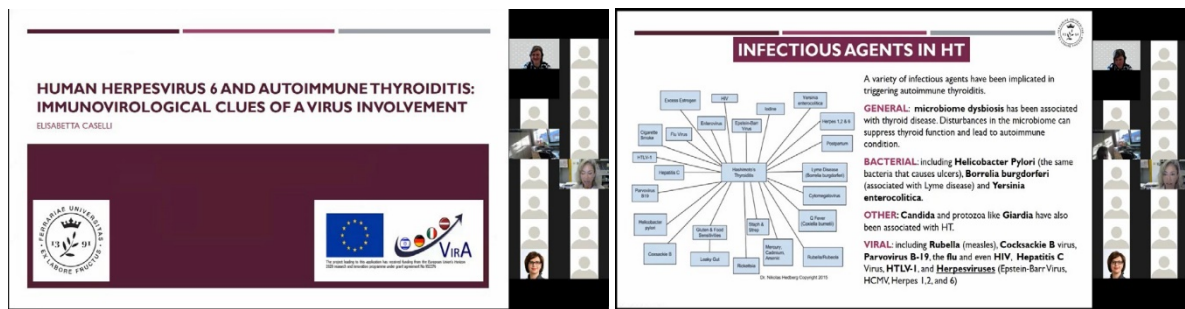
The next speaker was **Daria Bortolotti**, PhD, Assistant Professor, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy who gave a lecture “Role of Herpesvirus proteins in neurological disorders”. Neurological disorders present several risk factors which could participate to disease outcome and progression, including herpesvirus infections. Among herpesviruses, Human Herpesvirus (HHV)-6 infection has been described as peculiarly involved in MS pathogenesis. In particular, specific HHV-6 proteins, such as U24 and dUTPase, are able to affect host immune system activation and microglia migration, participating to MS pathogenetic process.

The third lecturer in the first session was **Hans Klein**, MD, PhD Department of Nuclear Medicine and Molecular Imaging, University of Groningen, The Netherlands with the lecture “Treatment of hippocampal neuroinflammation with valaciclovir: A placebo-controlled PET imaging study”. He presented an idea that herpes simplex virus (HSV)-1 is a tract tracing instrument in neuroanatomy via facial and visceral routes and that the virus might be involved in the development of schizophrenia. There is a hypothesis that microglia activation is a surrogate marker for psychosis: “fever of the mind”. Upon HSV-1 infection of the brain inflamed hippocampus on PET image degenerates/disappears on MRI 6 months later. Hans Klein told more about their study where the reduction of the fever of the mind by cessation of the viral DNA synthesis was done by high dose of valaciclovir. To confirm the hypothesis, it is important to detect viral replication in the brain during the activation of schizophrenia, but since viral activation has to be detected in tissues, the work is very complicated because studies have to be performed *ex vivo* or post-mortem.

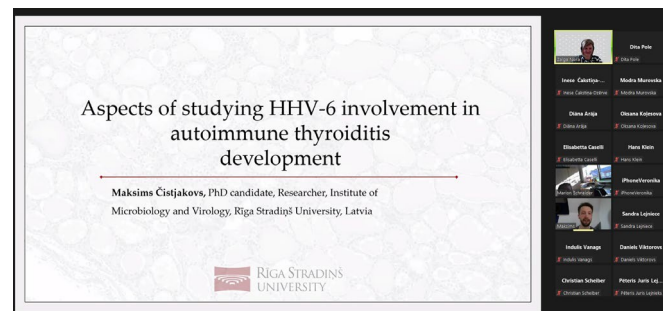


Session 2 was the continuation of the first session on autoimmune diseases and viruses.

The first speaker in this session was **Elisabetta Caselli**, Professor, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy. She in her presentation “Human herpesvirus 6 and autoimmune thyroiditis: immunovirological clues of a virus involvement” talked about Hashimoto’s thyroiditis (HT) that is a very common autoimmune thyroid diseases characterized by abundant lymphocyte infiltrate and thyroid impairment, and human herpesvirus 6 (HHV-6) that has been suggested as possible environmental trigger. They found transcriptionally active HHV-6A in 82% of thyrocytes from fine needle aspirates of HT patients, compared to 10% of controls, and showed that HHV-6A infection of thyroid cells induced *de novo* expression of HLA-II antigens, higher killing by natural killer (NK) cells from HT patients, and increased expression of miRNAs associated with HT *in vivo*. Notably, HT patients also showed increased antibody and T-cell responses toward HHV-6 U94 protein, and higher CD3-CD56brightNK cells, whose activation correlates with anti-TPO (thyroid peroxidase) and anti-Tg (thyroglobulin) antibody levels. Taken together, these observations support a potential role of HHV-6A in HT, suggesting that multiple uncontrolled HHV6A reactivations might trigger the development of the autoimmune responses against thyroid antigens observed in HT subjects.

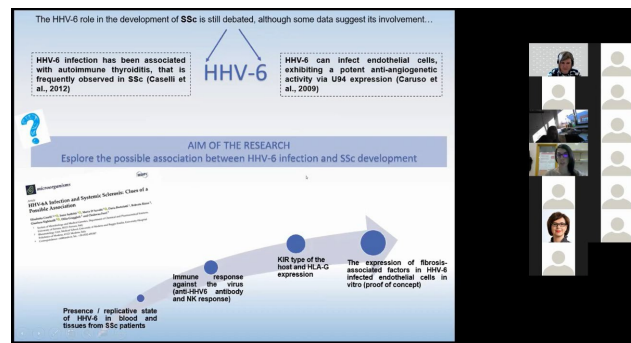


The next lecture was given by a PhD candidate, a researcher from the Institute of Microbiology and Virology, RSU - **Maksims Čistjakovs**, who continued the topic of research on autoimmune thyroiditis. His presentation title was “Aspects of studying HHV-6 involvement in autoimmune thyroiditis development”. As HHV-6 is able to establish latency and reactivate, the infection can have long-lasting effect on its host’s health and can contribute to the development of several autoimmune disorders, including autoimmune thyroiditis. HHV-6 possesses a number of immunomodulating properties for immune evasion and viral distribution. These include the ability to alter the repertoire of molecules expressed on infected cell surfaces, as well as chemokine and cytokine expression and secretion modulation. Another immunomodulation strategy utilized by herpesviruses, including HHV-6, is the ability to encode viral chemokines (HHV-6 U83) and chemokine receptors (HHV-6 U12/U51). In current presentation main aspects of studying HHV-6 involvement in autoimmune thyroiditis were analysed and discussed.



Next lecture “Etiologies of fibromyalgia in times of COVID-19” was prerecorded and given by **Howard Amital**, Professor, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; Head of the Department of Medicine and The Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Hashomer, Israel. He was talking about the characteristic clinical features of fibromyalgia stressing out that there is not only widespread body aches, pains and tenderness, but also cognitive problems, depressive and anxiety symptoms. Prof Amital explained the difference in pain compensation mechanisms between healthy individuals and patients with fibromyalgia. This was followed by information (compilation of patient telephone interview results) on the development of fibromyalgia in patients hospitalized for COVID-19 based on the professor's experience during the first wave of COVID-19 in Israel.

The workshop was continued by **Maria D'Accolti**, PhD, postdoc, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy. She gave the lecture “Beta-herpesviruses HCMV and HHV-6 as potential triggers of systemic sclerosis”. Systemic sclerosis (SSc) is a severe autoimmune system disease characterized by vasculopathy and fibrosis, which is often fatal. Beta-herpesviruses, including HHV-6 and Human Cytomegalovirus (HCMV), have been long hypothesized as SSc triggers, thus they aimed to clarify their potential association with the disease. The results showed that HHV-6 was present with higher frequency in the blood and skin tissue of SSc patients, who also displayed higher titer of antibodies directed against the HHV-6 U94 protein, compared to controls. Of note, the more-tissue tropic HHV-6A species was present and actively replicating in SSc skin biopsies, whereas no controls harbored active virus. Similarly, HCMV and its transcripts were detected in endothelial cells from a SSc skin biopsy. Last, she showed that both viruses significantly altered the expression of pro-fibrotic and pro- apoptotic factors, associated with SSc pathogenesis *in vivo* and *in vitro* infected human primary fibroblasts, supporting their potential direct role in the onset and/or progression of tissue fibrosis.



Session 3 on autoimmune viruses, NK cells and autoimmune diseases was started by Professor **Roberta Rizzo** from department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy. She gave a lecture “Role of KIR receptors in autoimmune diseases” and after this presentation, the workshop participants had the opportunity to participate in a Q&A session.

Innate host immune system plays a crucial role in autoimmune diseases outcome, particularly in presence of herpetic infections. NK represent the first line of defense against viral infections and their activity is regulated by a specific inhibitory and activating receptor repertoire, such as killer immunoglobuline-like receptors (KIR). In particular the inhibitory KIR2DL2 receptor has been reported to be associated to an increased susceptibility to herpetic infection associated to neurodegeneration in both MS and Alzheimer's diseases.

Questions for Rizzo's talk:

3 questions / 23 participants

1. KIR in Chronic Cholest *

07/12/2020 answered

killer cell immunoglobulin-like receptor

killer cell receptor

killer cell receptor

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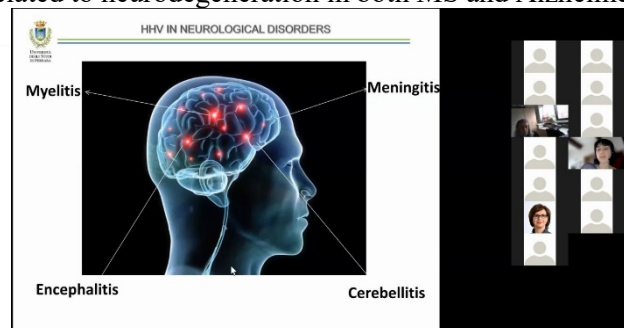
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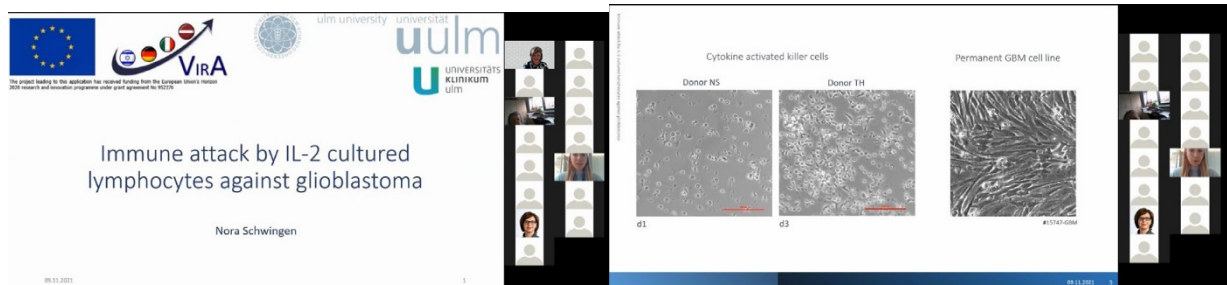
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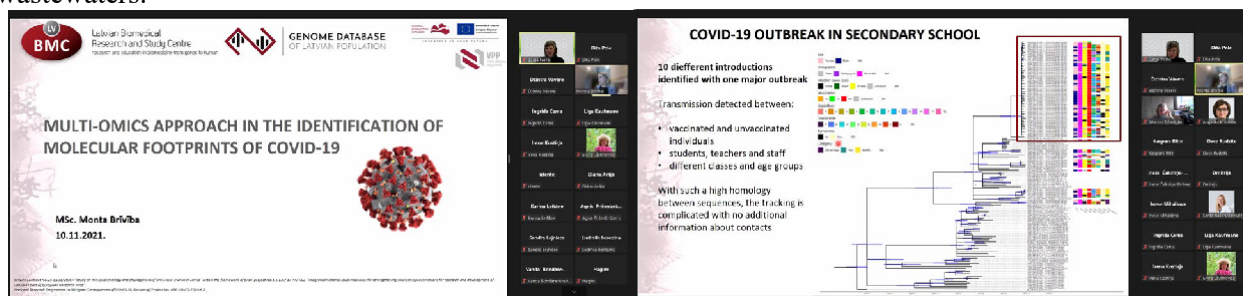


Next speaker was master student **Nora Schwingen** from Division of Experimental Anesthesiology, Ulm University Hospital, Department of Anesthesiology and Intensive Care, Ulm University, Germany. She presented study results on “Immune attack by IL-2 cultured lymphocytes against glioblastoma”. NK cells were isolated from healthy donors PBMCs and activated by IL-2/IL-15. Then cells were cultured and screened for surface receptor expression by flow cytometry, co-cultured and live monitored, next the HLA and KIR genotypes were identified. Nora Schwingen concluded that kinetics of cellular cytolysis may change during long-term co-incubation, which may result from attenuation of TIGIT (inhibitory immune checkpoint receptor) expression or may indicate physical inactivation of cytotoxic cells by laminin filaments derived from lysed target cells.



Second day of the workshop (10th of November, 2021) started with the continuation of Session 3. And the first speaker was **Monta Brīvība** – Researcher from Latvian Biomedical Research and Study Centre. Monta Brīvība presented study results “Multi-omics approach in the identification of molecular footprints of COVID-19”. She focused on two aspects in her presentation: firstly, she told about establishment of COVID-19 related biobank and integrated platform for research data in Latvia and after she shared finding

of SARS-CoV-2 genome analysis in Latvia. The goal of the project was to establish an open biobank and data exchange resource to facilitate the research on COVID-19, create a framework for its integration with health care initiatives, and ensure international cooperativity. As a result, there is created COVID-19 data platform that is available for research community in Latvia. Regarding sequencing of SARS-CoV-2, so far there are 6656 isolates sequenced. Monta Brīvība also showed how variants of the virus appeared and how quickly they spread in Latvia, also analyzed outbreaks in different hospital units and schools. At the end of the presentation she stressed out how important is to monitor the spread of virus variants by analyzing the wastewaters.



Next lecture “SARS-CoV-2 as an autoimmune virus” was prerecorded by **Yehuda Shoenfeld**, President of Ariel University, Professor, Medical Research Infrastructure Development and Health Services Fund by the Sheba Medical Center, Israel. Professor talked about genetic predictors of severe COVID-19 and recalled that interaction of SARS-CoV-2 with ACE2 is the key to understand the molecular mechanisms at the basis of the virus infection. He also described the COVID-19 mechanism of autoimmunity: hyper stimulation of the immune system in a genetically prone subject and molecular mimicry.

Kunal Garg, PhD student, Division Experimental Anesthesiology, Ulm University Hospital, Department of Anesthesiology and Intensive Care, Ulm, Germany continued with the lecture “EBV and COVID-19”. He presented study results on EBV and SARS-CoV-2 as autoimmune viruses. EBV derived extracellular vesicles (EVs) can suppress dendritic cells in patients with gastric carcinoma, increase inflammation through autoreactive T and B cells in Type I diabetes and inhibit polarization of T helper (Th-17) cells in MS. But EVs role in emerging autoimmune diseases is unclear. There is a hypothesis that EVs may trigger molecular mimicry in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). In conclusion Kunal Garg pointed out that deep immune profiling and machine learning approach is important to investigate autoimmunity and differential diagnosis.

Session 4 was the last session in the workshop dedicated to virus infected cells and tissues. And the first speaker in this session was **Irene Sofritti**, PhD student, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy with the lecture “Modulation of miRNome of human fibroblasts by HCMV and HHV-6 infection: possible significance in the induction of fibrosis in systemic sclerosis”. HCMV and HHV-6 have been suggested as triggers of the onset and/or progression of SSc, a severe autoimmune disorder characterized by vasculopathy and multi-organ fibrosis. Since in SSc patients miRNA expression has been found deregulated at the tissue or blood level, their study was aimed to investigate the impact of HCMV and HHV-6 infection on the miRNome of *in vitro* infected primary human dermal fibroblasts, which represent one of the main SSc target cells. The analysis, allowing the detection and quantification of 754 miRNAs, showed that both viruses significantly modulated miRNA expression in infected cells, with evident early and late effects. The correlation between these *in vitro* results with *in vivo* observations is strongly suggestive of a role of HCMV and HHV-6 in the multistep pathogenesis of fibrosis in SSc.

Next lecturer was Assist Prof **Valentina Gentili** from the Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy with lecture “HLA-G and viral infections in pregnancy disorders”. Pregnancy is a condition characterized by a tollerogenic environment to preserve the semi-allogenic fetus from the maternal immune system attack characterized by high expression of the tollerogenic Human Leukocyte Antigen (HLA)-G molecule. HLA-G immunosuppressive properties are also exploited by viruses as immune-escape mechanism and consequently, viral infection during pregnancy (e.g. herpesvirus infections) could take advantage by HLA-G expression, affecting pregnancy outcome.

HLA-G and viral infections in pregnancy disorders

Dr. Valentina Gentili

Università degli Studi di Ferrara

HHV-6A infection alters the immunological status of the endometrium

Th1/Th2 balance

Endometrial eNK Cell Immune-Phenotype

Endometrial receptivity

Fetal site: EVT, HLA-G, KIR2DL4

Maternal site: eNK cell, KIR2DL4, Cytokine secretion (IFN- γ , GM-CSF), Inhibition of eNK cytotoxicity, Generation of Tregs

➤ eNK cells: reduced cytotoxicity

➤ Allow trophoblast invasion thanks to peculiar cytokine secretion

➤ HHV-6A-positive infertile women presented a different immune-phenotype of eNK

Giovanna Schiuma, PhD student, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy talked about “HLA-G and viral infections during transplantation”.

This study investigated the role of the tolerogenic molecule HLA-G in infection episodes after transplantation, obtaining that soluble HLA-G (sHLA-G) level is directly related to infections in heart transplant (HT) recipients. Hence, sHLA-G pre-transplant level is predictive for identifying HT patients at risk to develop serious infections. Moreover, in the specific case of HCMV infection, HT rejection is strongly associated to virus reactivation. Both soluble and tissue HLA-G levels, are lower in case of rejection and are associated to high HCMV DNAemia, suggesting the down-regulation of the molecule mediated by the virus as the cause of rejection in HT.

Next speaker was **Christian Scheiber**, PhD student, Ulm University, Germany who talked about “Data on ICP (infected cell protein) inducible miRNA in Exosomes”. He focused on the explanation of miRNA networks which might be of interest when investigating the HSV1 impact in psychiatric diseases. HSV1 genome includes latency-associated transcript which is the only one abundantly transcribed during latency. In association with that there are 4 miRNAs described. Christian Scheiber concluded that extracellular vesicle- derived miRNA profiles may serve as stratification tools.

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Data on ICP (infected cell protein) inducible miRNA in Exosomes

Christian Scheiber, Hans Klein, Karl Bechter and E. Marion Schneider

Division of Experimental Anaesthesiology, Ulm University Hospital

Viral workshop – Viral infections as aetiological or trigger factors of autoimmune diseases

What cells want to tell us (and other cells) ...

Diameter: ~ 100 nm - 1 μ m, ~ 50 - 100 nm, > 1 μ m

Microvesicles, Exosomes, Apoptotic bodies

Release: Shedding, Budding, Blebbing

Contents: Surface proteins, Cytosolic proteins, Genomic DNA, miRNA

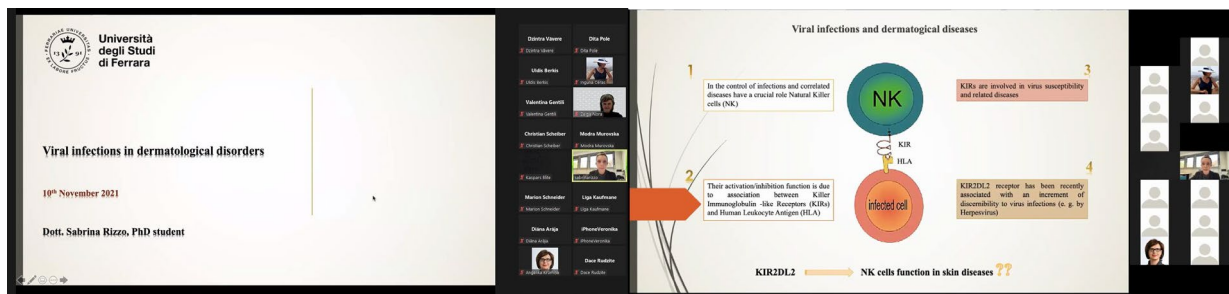
Uptake: Endocytosis, Early Endosome, Late Endosome, Lysosome

Effects: Surface proteins, Cytosolic proteins, Genomic DNA, miRNA

(Modified from Lässer, 2017)

Lecture “Rheumatological disorders and herpesvirus infections” was given by **Silvia Beltrami**, PhD student, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy. Several evidences demonstrate the implication of HHV infections in the immune system activation, that can lead to the development of autoimmune disorders like rheumatological diseases, including Systemic Lupus Erythematosus (SLE). Patients with the most prevalent manifestation of SLE, the Neuro Psychiatric Systemic Lupus Erythematosus (NPSLE), evidenced a role of HHV infections in the modulation of immune system involving the expression of inhibitory receptor KIR2DL2 a crucial for NK cells modulation, and the levels of IgG against HHV, in correlation with the state of the disease.

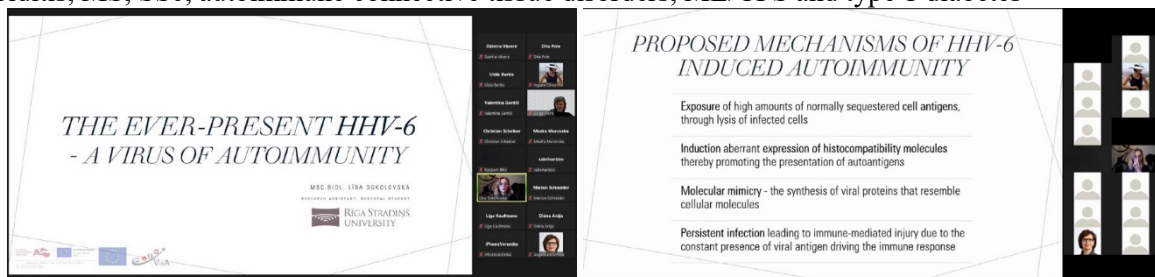
Next was **Sabrina Rizzo**, PhD student, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy with the lecture “Viral infections in dermatological disorders”. HHV-8 infection is known to be associated to cutaneous lesions, including Kaposi’s Sarcoma (KS), in which the presence of KIR2DL2, an inhibitory NK cell receptor, has been identified as a risk factor. The comparison between patients with HIV-negative classical-KS and HIV-positive endemic-KS showed that even if HHV-8 infection was reported in all subjects of both populations, classical-KS subjects showed a higher KIR2DL2 genotype frequency. This result supported an impairment of NK-mediated immunity, due to KIR2DL2, as a risk cofactor in the developing of classical-KS in HHV-8 positive subjects.



Then **Liba Sokolovska** Research Assistant, PhD student, Institute of Microbiology and Virology, Rīga Stradiņš University, Riga, Latvia summarized on HHV-6 “The ever-present HHV-6 - a virus of autoimmunity”. The talk briefly summarized the characteristics of HHV-6 (HHV-6A and B) and the autoimmune disorders it has been linked to.

The talk emphasized some of the characteristics of HHV-6 that could be the reason why this human pathogen has been extensively studied in the context of autoimmune disorder development: firstly, the high worldwide prevalence and the early primary infection; secondly, the establishment of latency with the potential of reactivation and thirdly, the broad cell tropism, and lastly the myriad of immunomodulatory properties the viruses possess.

The autoimmune disorders linked to HHV-6 infection summarized in this talk included autoimmune thyroiditis, MS, SSc, autoimmune connective tissue disorders, ME/CFS and type 1 diabetes



The last lecture of the two-day workshop was given by Prof. Dr. rer. nat., Head of the Division of Experimental Anesthesiology, **Marion Schneider** from Ulm University Hospital, Department of Anesthesiology and Intensive Care, Ulm, Germany. She was talking about “Structural features of ZIKA-V infected glioblastoma” and after the talk there was an online Q&A session with multi-choice answers.

They investigated ZIKA-V infected glioblastoma cell lines. Can we develop the vaccination protocol against glioblastoma (GBM) by increasing the antigenicity that was the main question of the study. Is there a role of neurotropic viruses in oncolytic therapy of GBM? The professor showed and explained the process of obtaining a cell line. Applying visualization techniques showed what these cell lines look like as well as demonstrated the results of antigen expression in these glioblastoma cell lines. The results of the cell line experiments showed that ZIKA-V is not a good choice for further development of the vaccination protocol for GBM.

Marion Schneider (Q&A)

Questions: 1. Report a question

1. Where are ZIKA viruses associated in GBM? (Marion Schneider)

1.0/1.0 (100%) answered

Correct Answer	Wrong Answer
Extracellular	10/100 (10%)
Intracellular	10/100 (10%)
Both	10/100 (10%)
None	10/100 (10%)

2. What are the characteristics of Glioblastoma Cell lines? (Marion Schneider)

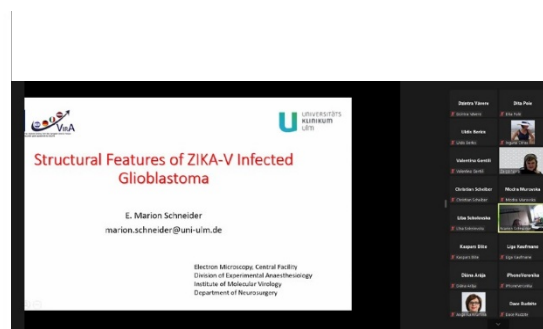
1.0/1.0 (100%) answered

Correct Answer	Wrong Answer
High expression of HIF1A	10/100 (10%)
High expression of CD133	10/100 (10%)
High expression of CD133	10/100 (10%)
High expression of CD133	10/100 (10%)

3. Which type of cell death is induced by ZIKA virus in GBM? (Marion Schneider)

1.0/1.0 (100%) answered

Correct Answer	Wrong Answer
Apoptosis	10/100 (10%)
Autophagy	10/100 (10%)
Pyroptosis	10/100 (10%)
Necrosis	10/100 (10%)



On the first and second day of the workshop, the lectures were followed by a discussion section with experts from Italy, Germany and Israel, as well as participants and speakers from Latvia.

Conclusions

The International Workshop on viral infections as aetiological or trigger factors of autoimmune diseases provided state-of-the-art knowledge on viral involvement, mechanisms of involvement and the body's response to autoimmunity.

Importantly, in several reports, experts from Italy and Germany also described and demonstrated different methodological approaches to study the mechanisms of action of viruses.

Current research on SARS-CoV-2 was also presented, covering both long-COVID, fibromyalgia, and various autoimmune processes that may be induced by the virus.

This workshop is definitely a success, given the high attendance and the feedback from the participants, where most indicate that the information and knowledge gained at the event will be useful in future work.

Annex 1 – Workshop agenda



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



EU Horizon 2020 Twinning project

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

Workshop by online Zoom meeting platform

VIRAL INFECTIONS AS AETIOLOGICAL OR TRIGGER FACTORS OF AUTOIMMUNE DISEASES

9-10 th November, 2021

Workshop leader Dr.med., Lead Researcher Zaiga Nora-Krūkle

AGENDA

November 09, 2021	
10.00 – 10.10 <i>CET 9.00 – 9.10</i>	Welcome and opening Liene Ņikitina-Zaķe , Director of Research Department, RSU, Latvia Modra Murovska , Assoc. Professor, Project Coordinator, Institute of Microbiology and Virology, RSU, Latvia
Session 1 - Virus Infections as Initiators in Autoimmune Diseases: Neurological Diseases, Thyroiditis, Scleroderma	
10.10 – 10.45	HHV-6 and Multiple Sclerosis (Q&A) Dario Di Luca , Professor, Department of Medical Sciences, Microbiology and Clinical Microbiology, University of Ferrara, Italy
10.45 – 11.15	Role of Herpesvirus proteins in neurological disorders Daria Bortolotti , PhD, Assistant Professor, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
11.15 – 12.00	Treatment of hippocampal neuroinflammation with valaciclovir. A placebo-controlled PET imaging study Hans Klein , MD, PhD Department of Nuclear Medicine and Molecular Imaging, University of Groningen, The Netherlands
12.00 – 12.15	<i>Break</i>
Session 2 - Virus Infections as Initiators in Autoimmune Diseases: Thyroiditis, Scleroderma, Fibromyalgia	
12.15 – 12.45	Human herpesvirus 6 and autoimmune thyroiditis: immunovirological clues of a virus involvement



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RĪGA STRADIŅŠ
UNIVERSITY

	Elisabetta Caselli , Professor, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
12.45 – 13.05	Aspects of studying HHV-6 involvement in autoimmune thyroiditis development Maksims Čistjakovs , PhD candidate, Researcher, Institute of Microbiology and Virology, Rīga Stradiņš University, Latvia
13.05 – 13.30	Etiologies of fibromyalgia in times of COVID-19 Howard Amital , Professor, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; Head of the Department of Medicine B and The Zabudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Hashomer, Israel
13.30 – 14.15	Break
14.15 – 14.30	Beta-herpesviruses HCMV and HHV-6 as potential triggers of systemic sclerosis Maria D'Accolti , PhD., postdoc., Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
Session 3 - NK cells and autoimmune diseases, Autoimmune Viruses	
14.30 – 15.05	Role of KIR receptors in autoimmune diseases (Q&A) Roberta Rizzo , Professor, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
15.05 – 15.40	Discussion

November 10, 2021

Session 3 - NK cells and autoimmune diseases, Autoimmune Viruses (continuation)	
10.00 – 10.35 <i>CET 9.00 – 9.35</i>	Multi-omics approach in the identification of molecular footprints of COVID-19 Monta Brīvība , MSc. biol, Researcher, Latvian Biomedical Research and Study Centre
10.35 – 11.10	SARS-CoV-2 as an autoimmune virus Yehuda Shoenfeld , President of Ariel University, Professor, Zabudowicz Center for Autoimmune Diseases, Sheba Medical Center, Israel
11.10 – 11.30	EBV and COVID-19



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	Kunal Garg , PhD student, Division Experimental Anesthesiology, Ulm University Hospital, Department of Anaesthesiology and Intensive Care, Ulm, Germany
Session 4 - Virus infected cells and tissues	
11.30 – 11.50	Modulation of miRNome of human fibroblasts by HCMV and HHV-6 infection: possible significance in the induction of fibrosis in systemic sclerosis Irene Soffritti , PhD student, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
11.50 – 12.05	Break
12.05 – 12.35	HLA-G and viral infections in pregnancy disorders Valentina Gentili , Assistant Professor, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
12.35 – 12.55	HLA-G and viral infections during transplantation Giovanna Schiuma , PhD student, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
12.55 – 13.15	Data on ICP (infected cell protein) inducible miRNA in Exosomes Christian Scheiber , PhD student, Ulm University, Germany
13.15 – 13.35	Rheumatological disorders and herpesvirus infections. Silvia Beltrami , PhD student, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
13.35 – 14.10	Break
14.10 – 14.30	Viral infections in dermatological disorders Sabrina Rizzo , PhD student, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
14.30 – 14.50	The ever-present HHV-6 - a virus of autoimmunity Lība Sokolovska , Research Asistant, PhD student, Institute of Microbiology and Virology, Rīga Stradiņš University, Riga, Latvia
14.50 – 15.25	Structural features of ZIKA-V infected glioblastoma (Q&A) Marion Schneider , Prof., Dr. rer. nat., Head of the Division Experimental Anesthesiology, Ulm University Hospital, Department of Anaesthesiology and Intensive Care, Ulm, Germany
15.25 – 16.00	Discussion and closing remarks

Annex 2 – List of participants

09.11.2021

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Annex 3 – Evaluation form results

No.	What is your overall assessment of the event? (1 = insufficient - 5 = excellent)	Which topics or aspects of the workshop did you find most interesting or useful?	Did the workshop achieve the programme objectives?	If no, why?	Knowledge and information gained from participation at this event. -Met your expectations?	Knowledge and information gained from participation at this event. -Will be useful/applicable in my work?	Please comment on the organization of the event (from 1 = insufficient to 5= excellent)	Comments and suggestions (including activities or initiatives you think would be useful, for the future)	Further comments or suggestions
1	3	Hhv-6 and neuroinflammatory reaction	Yes		Yes	Definitely	4		
2	5	All topics are good	Yes		Yes	Mostly	5	no comments yet	
3	5	To be able to identify viral infections as possible triggers for autoimmune diseases	Yes		Yes	Definitely	5	-	Thank you!
4	5	Basic information about HHV6 (A and B), Autoimmune diseases and SARS-CoV2	Yes		Yes	Somehow	5	Good job!	
5	5	Autoimmune thyroiditis	Yes		Yes	Somehow	5	ok	about different arthritis
6	5	Covid-19 vaccine	Yes		Somehow	Somehow	5		
7	5	HHV6	Yes		Yes	Definitely	5		
8	5	I very enjoyed all the lectures of Italian colleagues, specially prof Bortolotti about the role of herpesvirus proteins in neurological disorders.	Yes		Yes	Mostly	5		

9	5	Human herpesvirus 6 and autoimmune thyroiditis, structural features of ZIKA-V infected glioblastoma, current understanding of fibromyalgia	Yes	Yes	Definitely	5	
10	5	COVID-19	Yes	Yes	Definitely	5	
11	4	Structural features of ZIKA-V infected glioblastoma	Yes	Somehow	Somehow	4	
12	5	HHV-6	Yes	Yes	Definitely	5	
13	5	Viruss and autoimmunity	Yes	Yes	Mostly	5	good, that there were those questions after some presentations!!!
14	5	About CMV	Yes	Yes	Definitely	5	
15	5	Covid-19.	Yes	Yes	Mostly	5	
16	4	Autoimmunity and neurological diseases	Yes	Yes	Somehow	4	
17	4	Neurological conditions due to viruses	Yes	Yes	Definitely	4	
18	5	About Covid-19	Yes	Yes	Definitely	5	
19	4	All topics	Yes	Yes	Mostly	5	Q&A after each or 2-3 presentations.
20	5	HHV6 and Covid-19	Yes	Yes	Mostly	5	

Annex 4 – Pool reports

Correct answers:

1. There is not yet conclusive evidence about the virus' role in the disease
2. Highly related, but distinct viral species
3. Yes, because they specific ethiological associations

Questions for Di Luca's talk:

3 questions | 23 participated

1. HHV-6 and multiple sclerosis: (Single Choice) *

23/23 (100%) answered

The virus is the main ethiological agent of the disease	(1/23) 4%
The virus is one of the ethiological agents of the disease	(9/23) 39%
There is not yet conclusive evidence about the virus' role in the disease	(13/23) 57%
The virus has no ethiological role in the disease	(0/23) 0%

2. HHV-6A and HHV-6 B are: (Single Choice) *

23/23 (100%) answered

Highly related, but distinct viral species	(12/23) 52%
Highly divergent viral species	(0/23) 0%
Viral variants of the same viral species	(10/23) 43%
Viral strains of the same viral species	(1/23) 4%

3. Scientific articles should discriminate between HHV-6A and HHV-6B: (Single Choice) *

23/23 (100%) answered

Yes, because they specific ethiological associations	(18/23) 78%
No, because they have the same ethiological associations	(0/23) 0%
Yes, because they have the same pathogenic associations but with different virulence	(5/23) 22%
No, because they have the same pathogenic association and virulence	(0/23) 0%

Correct answers:

1. Killer cell immunoglobulin-like receptor
2. Are part of the cells responsible for the innate immune response
3. An inhibitory receptor

Questions for Rizzo's talk:

3 questions | 23 participated

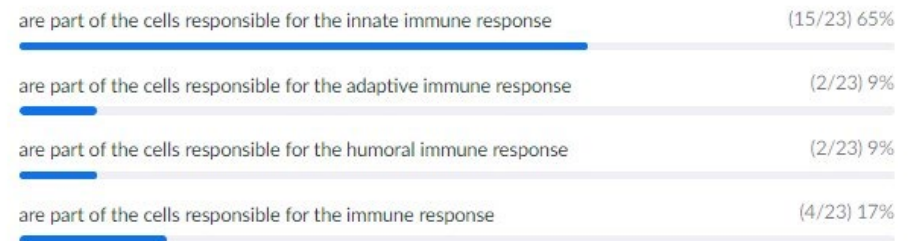
1. KIR is: (Single Choice) *

23/23 (100%) answered



2. NK cells: (Single Choice) *

23/23 (100%) answered



3. KIR2DL2 is: (Single Choice) *

23/23 (100%) answered

