





Austrian study provides deep insights into transmission and mutation properties of SARS-CoV-2

Learning from past SARS-CoV-2 outbreaks for future pandemic control

In the COVID-19 pandemic, 57 million people have already been infected worldwide. In the search for vaccines and therapies, a precise understanding of the virus, its mutations and transmission mechanisms is crucial. A recent study by the research group of Principal Investigator Andreas Bergthaler at the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, in the renowned journal *Science Translational Medicine*, makes an important contribution to this. The high quality of epidemiological data in Austria, together with state-of-the-art virus genome sequencing, has supported unprecedented insights of the mutation behaviour and transmission of the SARS-CoV-2 virus.

(Vienna, 23 November 2020) – The project "<u>Mutational dynamics of SARS-CoV-2 in Austria</u>" was launched by CeMM in close cooperation with the Medical University of Vienna at the end of March. Together with the Austrian Agency for Health and Food Safety (AGES) and in cooperation with numerous universities and hospitals all over Austria, scientists are working on drawing a more precise picture of the virus mutations and transmissions that occur by genome sequencing of SARS-CoV-2 viruses. Under the leadership of CeMM Principal Investigators Andreas Bergthaler and Christoph Bock, 750 samples from important SARS-CoV-2 infection clusters in Austria such as the tourist town of Ischgl and Vienna were phylogenetically and epidemiologically reconstructed and their role in transmission and the development of mutations in the SARS-CoV-2 virus.

Mutation analyses revealed correlations between clusters

Based on epidemiological data, the scientists used mutation analyses to reconstruct a SARS-CoV-2 cluster consisting of 76 cases and to uncover a cryptic link between two epidemiological clusters. "This example illustrates how contact tracing and virus mutation analysis together provide a strong pillar of modern pandemic control," says project leader Andreas Bergthaler. Franz Allerberger, Head of the Public Health Division of AGES and co-author of the study, agrees: "The modern techniques of virus genome sequencing support epidemiological contact tracing and offer high-resolution insights of the ongoing pandemic."

Researchers observe the development of new mutations

A special feature of the study is that a chain of eight consecutive transmissions was analysed. "The transmission chain started with a returnee from Italy. Within 24 days, the SARS-CoV-2 virus spread in the greater Vienna region via public and social events in closed rooms", say the CeMM study authors Alexandra Popa and Jakob-Wendelin Genger. The precise breakdown of the transmission chain enabled the scientists to closely observe the development of a new mutation of SARS-CoV-2. "Thanks to excellent epidemiological and our deep virus sequencing data, we could follow how the SARS-CoV-2 virus mutated in one individual and was then transmitted to others," explains Andreas Bergthaler. In addition, the scientists observed the mutation behaviour of the virus during the course of the disease in 31 patients. This may help in the future to assess whether treatments influence the mutation characteristics of the virus.

On average 1,000 virus particles are transmitted during an infection

The results of the current analyses also show that on average 1000 infectious virus particles are transmitted from one infected person to the next. These values are overall considerably higher than for other viruses such as HIV or noroviruses.-Andreas Bergthaler adds: "Yet, occasionally we also found infected people who apparently came into contact with fewer virus particles and still became infected. We suspect that parameters such as the application of protective measures, the transmission route or the immune system may play a decisive role here." These results raise important new questions and hypotheses. Reducing the viral load of infected individuals by a combination of measures such as mouth-nose protection, physical distance and adequate indoor air exchange could play a key role in both preventing the spread of the virus and possibly even influence the course of the disease.

The current study based on data collected during the early phase of the SARS-CoV-2 pandemic in spring 2020, provides important insights into the fundamental dynamics of SARS-CoV-2 mutations within patients and during transmission events. These results support other ongoing research projects aiming at a better understanding and controlling the pandemic.

Find out more about the project: www.sarscov2-austria.org

Attached photos:

Photo 1: Viral genome sequencing helps understanding the mutational behaviour and transmission of the virus (© Bobby Rajesh Malhotra / CeMM (CC BY-NC)).

Photo 2: Austrian study reveals important characteristics of the virus: The analysis of infection clusters and superspreading events in Austria built the foundation to obtain general information on transmission properties between persons and the mutation of the virus in patients (© Andreas Bergthaler's Group / CeMM).

Photo 3: Viral genome data reveal global transmission lines: This graph from the study shows how the reconstruction of the SARS-CoV-2 ancestry provides evidence for the connection of Austrian infection clusters with outbreaks all over the world (© Popa, Genger et al. Science Translational Medicine 2020 (doi:10.1126/scitranslmed.abe2555).

Photo 4: The analysis of epidemiologically-validated chains of infections in Austrian superspreading events found that a relatively large average dose of 1000 infectious viral particles is transmitted (© CeMM).

Photo 5: Last author Andreas Bergthaler with first authors Alexandra Popa and Jakob-Wendelin Genger (© Klaus Pichler / CeMM).

The study "Genomic epidemiology of superspreading events reveals mutational dynamics and transmission properties of SARS-CoV-2" was published in the journal *Science Translational Medicine* on 23 November 2020. DOI: 10.1126/scitranslmed.abe2555

Authors: Alexandra Popa, Jakob-Wendelin Genger, Michael D. Nicholson, Thomas Penz, Daniela Schmid, Stephan W. Aberle, Benedikt Agerer, Alexander Lercher, Lukas Endler, Henrique Colaço, Mark Smyth, Michael Schuster, Miguel L. Grau, Francisco Martínez-Jiménez, Oriol Pich, Wegene Borena, Erich Pawelka, Zsofia Keszei, Martin Senekowitsch, Jan Laine, Judith H. Aberle, Monika Redlberger-Fritz, Mario Karolyi, Alexander Zoufaly, Sabine Maritschnik, Martin Borkovec, Peter Hufnagl, Manfred Nairz, Günter Weiss, Michael T. Wolfinger, Dorothee von Laer, Giulio Superti-Furga, Nuria Lopez-Bigas, Elisabeth Puchhammer-Stöckl, Franz Allerberger, Franziska Michor, Christoph Bock, Andreas Bergthaler

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Andreas Bergthaler studied veterinary medicine in Vienna. After his doctorate under Hans Hengartner and Nobel Prize winner Rolf Zinkernagel at the University of Zurich and the ETH Zurich, he completed postdoctoral research stays at the University of Geneva and the Institute for Systems Biology in Seattle. Since 2011 he has been a research group leader at CeMM and ERC Start Laureate.

CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences is an international, independent and interdisciplinary research institution for molecular medicine under the scientific leadership of Giulio Superti-Furga. CeMM is oriented towards medical requirements and integrates basic research and clinical expertise to develop innovative diagnostic and therapeutic approaches for precision medicine. The main research areas are cancer, inflammation, metabolic and immune disorders as well as rare diseases. The research building of the institute is located on the campus of the Medical University of Vienna and the General Hospital. www.cemm.at

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For further information please contact

Anna Maria Schwendinger Head of PR & Communications

CeMM

Research Center for Molecular Medicine of the Austrian Academy of Sciences Lazarettgasse, AKH BT 25.3 1090 Vienna, Austria Phone: +43-1/40160-70 092 aschwendinger@cemm.oeaw.ac.at http://www.cemm.at/

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