Prompt initiation of antiretroviral therapy reduces cancer risk in HIV patients

(Vienna, 23 November 2021) HIV patients have an increased risk of developing skin and mucosal cancers, even though HIV is no longer detectable in their blood due to antiretroviral therapy. A new study by MedUni Vienna's Department of Dermatology, the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD) and the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences now shows that the time of starting antiretroviral therapy can influence tumour development. The results have recently been published in the specialist journal "Immunity".

HIV (human immunodeficiency virus) infects and destroys immune cells that carry a specific molecule (CD4 receptor) on their surface. Over the course of the disease, these CD4+ T cells are greatly depleted, and this is associated with an increased risk of infection. Antiretroviral therapy (ART) for HIV-infected patients inhibits viral replication and reduces the viral load to such an extent that HIV is no longer detectable in the blood. This once again increases the number of CD4+ T-cells in the blood, thus normalising the patient's susceptibility to infection. That said, despite years of optimal and suppressive antiretroviral therapy, people with HIV are still at increased risk of developing skin and mucosal cancers. In particular, they have a higher risk of developing those forms of cancer caused by human papillomaviruses (HPV). The risk of HPV-associated anal cancer is as much as 36 times higher in HIV-infected men than in HIV-negative individuals.

Time of starting therapy influences HIV patients' immune response

The research group led by Georg Stary from the Department of Dermatology describes now in the renowned journal "Immunity" a new mechanism for of tissue-specific dysregulation of the immune response in HIV patients. "We found that there are differences in tissue-specific immune responses depending on whether antiretroviral therapy was started promptly after diagnosis of HIV infection or was delayed," summarises Georg Stary, last author of the study. Tissue-resident memory T cells of the skin and mucosa play an important role in this process: these are part of the immunological memory and available for a rapid and effective tissue immune response when an organism has previously had contact with a pathogen.

Major importance of tissue-resident immune cells

In HIV patients who did not start antiretroviral therapy until some time after diagnosis, there was irreversible depletion of tissue-resident memory T cells in the skin and mucosa, despite high numbers of CD4+ T cells in the blood. In contrast, this depletion of memory T cells can be prevented if antiretroviral therapy is started promptly. In addition, it was found that HIV

patients with HPV-induced mucosal cancer have a reduced number of tissue-resident memory T cells in the mucosa. This might explain the greater prevalence and more severe disease progression of HPV-associated tumours in people with HIV.
"The results of the study show the major importance of tissue-resident immune cells in the development of skin and mucosal cancers in HIV patients. Furthermore, the findings may also have implications for other patients at increased risk of developing skin and mucosal cancers and similar phenomena could play a role, for example, in patients who are immunosuppressed following organ transplantation," said Georg Stary.

Service: Immunity
Delayed antiretroviral therapy in HIV-infected individuals leads to irreversible depletion of skin- and mucosa-resident memory T cells. Simona Saluzzo, Ram Vinay Pandey, Laura Marie Gail, Ruth Dingelmaier-Hovorka, Lisa Kleissl, Lisa Shaw, Bärbel Reininger, Denise Atzmüller, Johanna Strobl, Veronique Touzeau-Römer, Andrea Beer, Clement Staud, Armin Rieger, Matthias Farlik, Wolfgang Weninger, Georg Stingl, and Georg Stary. Immunity, DOI: https://doi.org/10.1016/j.immuni.2021.10.021

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Medical University of Vienna - short profile
Medical University of Vienna (MedUni Vienna) is one of the most traditional medical education and research facilities in Europe. With almost 8,000 students, it is currently the largest medical training centre in the German-speaking countries. With 6,000 employees, 30 departments and two clinical institutes, 12 medical theory centres and numerous highly specialised laboratories, it is also one of Europe's leading research establishments in the biomedical sector.

LBI-RUD - Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases
The Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD) was founded in April 2016 by the Ludwig Boltzmann Society together with the Medical University of Vienna, the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences and St. Anna Children's Cancer Research. By harnessing the expertise of its partner organisations, LBI-RUD aims to establish a

coordinated research programme that includes and considers not only the scientific aspects of rare diseases but also social, ethical and economic factors.
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CeMM - Research Center for Molecular Medicine of the Austrian Academy of Sciences
The CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences is an international, independent and interdisciplinary research entity for molecular medicine under the scientific direction of Giulio Superti-Furga. The CeMM is oriented towards medical needs and integrates basic research and clinical expertise to develop innovative diagnostic and therapeutic approaches for precision medicine. The main focuses of its research are cancer, inflammatory diseases and immune disorders, as well as rare diseases. The Center's research building is located on the campus of the Medical University of Vienna and Vienna General Hospital. www.cemm.at