

## **Multiomics investigation revealing the characteristics of HIV-1-infected cells in vivo**

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By using the samples obtained from HIV1-GFP-infection in a humanized mouse model, a series of omics analyses were performed. Credit: SATO Kei

For eradication of HIV-1 infection, it is important to elucidate the detailed features and heterogeneity of HIV-1-infected cells in vivo. In this study, a hematopoietic stem cell-transplanted humanized mouse model infected with a gene-modified HIV-1 was used to reveal multiple characteristics of HIV-1-producing cells in vivo.

A research group at The Institute of Medical Science, The University of Tokyo (IMSUT) using HIV-1-infected <u>cells</u> performed "multiomics" analyses, which are technologies recently developed to comprehensively investigate the features of biological samples.

"Our findings describe multiple characteristics of HIV-1-producing cells in vivo, which could provide clues for the development of an HIV-1 cure," said the lead scientist, Kei Sato, Associate Professor (Principal Investigator) in the Division of Systems Virology, Department of Infectious Disease Control, IMSUT. The results of this research were published in *Cell Reports* on July 14, 2020.

### Study for 'HIV-1 cure'

For eradication of HIV-1 infection, it is important to gain an in-depth understanding of the wide-ranging characteristics of HIV-1-infected cells in vivo.

Recently developed 'omics' analyses can be a powerful tool to identify the characteristics of HIV-1-infected cells. However, it should be noted that a large majority of the CD4+ T cells in infected individuals are uninfected, and therefore, the transcriptional profiles of 'bulk' CD4+ T



cells in vivo do not reflect those of 'pure' HIV-1-producing cells.

# Multiomics analysis to comprehensively reveal the features of HIV-1-infected cells in vivo

In this study, the research group used a human <u>hematopoietic stem cell</u> -transplanted humanized <u>mouse model</u> that maintains human leukopoiesis under relatively stable immunological conditions in vivo and a replication-competent reporter HIV-1, and used four recently developed techniques to investigate viral genomics and transcriptomics.

According to the research group, this study consisted of the four following analyses:

First, droplet digital PCR revealed the presence of potential reservoirs in infected humanized mice. Second, ligation-mediated PCR showed the preference of HIV-1 to integrate into open chromatin regions, as suggested by the association of the epigenetic modifications of integration sites with viral production. Third, digital RNA-sequencing quantified the absolute copy number of viral transcripts in the HIV-1-producing cells in vivo and further identified the differentially expressed genes between virus-infected and uninfected cells. Finally, single-cell RNA-sequencing revealed and characterized the heterogeneity of the HIV-1-producing cells in vivo.

Associate Professor Sato emphasized "To our knowledge, this study is the first investigation to describe multiple aspects of HIV-1-producing cells and also the first comprehensive investigation of the characteristics of HIV-1-infected cells in vivo."

**More information:** Hirofumi Aso et al, Multiomics Investigation Revealing the Characteristics of HIV-1-Infected Cells In Vivo, *Cell* 



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