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**Press release N° 23/2021**

**HIV, the immune response to Tat determines the recovery of CD4+ T-cells and controls residual viraemia in patients on long-term therapy**

The observational study published today in [The Lancet EBioMedicine](https://www.sciencedirect.com/science/article/pii/S2352396421000992) conducted in HIV + patients on long-term antiretroviral therapy (cART), indicates the fundamental role of the immune response against the HIV-1 Tat protein in ensuring a continuous recovery of CD4+ lymphocytes, and in reducing the residual viremia that cART is unable to abolish. The study, conducted by the National Center for Research on HIV/AIDS (CNAIDS) of the Istituto Superiore di Sanità (ISS) in Italy, strengthens the scientific rationale behind the studies already published by the ISS on the importance of an anti-Tat vaccine to enhance the immune system reconstitution, which cART alone, although very effective in blocking viral replication, often achieves only partially even after years of therapy.

“The suppression of viral replication caused by the onset of cART leads to a strong and fast recovery of the number of CD4+ lymphocytes, the cells that "orchestrate" the immune response and are "attacked" by HIV – explains Barbara Ensoli, Director of CNAIDS at ISS and coordinator of the study – However, after a few years of therapy, the increase in CD4+ lymphocytes slows down and eventually vanishes before reaching the optimal levels, especially in patients who start treatment late. Furthermore, low-levels of intermittent “residual” viremia persist even in fully virologically suppressed patients, triggering progression and non-AIDS associated co-morbidities. Our study, conducted in patients on long-term therapy and followed for 3 years, identified the immune response to Tat as the determining factor for long-lasting CD4+ T-cell increases even after years of cART, and for the control of residual viremia.”

On the other hand, "Anti-Tat antibodies are infrequent in infected patients (20-30%) but, when present, they are associated with greater control of residual viremia, and higher CD4+ T cell levels, with dynamics of CD4 increases over time higher than that observed in patients who do not have anti-Tat immune responses". - adds Dr. Ensoli "In these patients there is also an improvement in the functioning of the immune system (immunoreconstitution) compared to patients who do not have the immune response to Tat. These data confirm the results with the Tat vaccine, which has completed the Phase II trial in humans both in Italy and in South Africa, with positive effects that persist even after 8 years from vaccination" ([Ensoli et al, Retrovirology 2015](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4414440/pdf/12977_2015_Article_151.pdf); [Ensoli et al, Retrovirology 2016](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4899930/pdf/12977_2016_Article_261.pdf); [Sgadari et al, Frontiers in Immunology 2019](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6381398/pdf/fimmu-10-00233.pdf)).

The study involved 10 Clinical Centers in Italy: University Hospital of Ferrara, San Gallicano Institute of Rome, S. Maria Goretti Hospital of Latina, S.M. Annunziata of Florence, University Division of Infectious and Tropical Diseases - University of Brescia and ASST Spedali Civili, Hospital "Policlinico Consorziale" Hospital of Bari, University Hospital of Modena Polyclinic, Amedeo di Savoia Hospital of Turin, Luigi Sacco Hospital of Milan, IRCCS Ospedale San Raffaele.