Research suggests HIV causes rapid aging in key infection-fighting cells

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In the early years of the AIDS epidemic, being infected with the virus that causes the disease was considered a virtual death sentence. But with the development of antiretroviral therapy, many with HIV are now living much longer. In fact, it is estimated that by 2015, about half of all HIV-positive individuals will be older than 50.

Yet those over 50 also progress to AIDS faster than adults in their 20s or 30s. And those in the younger age bracket — even those responding well to antiretroviral therapy — still exhibit illnesses and clinical conditions commonly associated with older people, such as certain cancers and liver diseases. For the most part, the reasons for this have remained a mystery.

But a UCLA AIDS Institute study published today in the online journal *PLoS ONE* suggests a partial explanation, showing that HIV causes a specific subset of CD4+ "helper" T-cells — which play an important role in the body's response to infection — to age rapidly, by as much as 20 to 30 years over a three-year period.

In the study, researchers witnessed a decline in CD4+ T-cell numbers and, most strikingly, found that in the surviving T-cells, the HIV virus caused rapid and drastic shortening of the ends of chromosomes, called telomeres, which protect the chromosomes and prevent them from fusing together, much like plastic tips keep shoelaces from unraveling. Telomeres become progressively shorter during natural cell division; when they become too short, cells do not function properly.

"Our findings have important implications for the health of both young and old HIV-1–infected adults," said lead investigator Tammy M. Rickabaugh, an assistant research immunologist in the division of hematology and oncology at the David Geffen School of Medicine at UCLA. "They underscore the importance of developing new approaches to boost immune function to complement current treatments, which are exclusively directed against the virus."

The researchers examined two subsets of CD4+ T-cells (CD45RA+ CD31+ and CD45RA+ CD31-) in two groups of individuals — those aged 20–32 and those aged 39–58 — who had been infected with HIV for one to three years and who had not been treated with antiretroviral therapy. They compared these two groups with samples from age-matched controls who were HIV seronegative.

The researchers specifically focused on "naive" T-cells — those that had not previously encountered any pathogens and thus act as a reserve against future infections and cancers. They found that in individuals infected with HIV-1, these cells underwent unexpectedly rapid aging — the equivalent of 20 to 30 years of aging within three years of infection. They also found that the number of CD31- T-cells, which are more quickly pulled into the fight against new pathogens, had fallen drastically.

The researchers also investigated whether appropriate treatment could reverse this aging effect. They examined cells from HIV-positive individuals who had been on antiretroviral therapy for two years and whose therapy had successfully kept HIV-1 under control. They found that while the therapy kept their viral loads at undetectable levels, it did not entirely restore their immune systems, suggesting a reason why younger HIV-positive people still become ill with conditions more common to older people.

"Taken together, our results help to explain some of the clinical observations that have been documented in HIV-infected people and emphasize the need for developing therapeutic approaches directed at improving the naive immune cell compartment," said senior investigator Beth D. Jamieson, an associate professor of medicine in the division of hematology and oncology at the David Geffen School of Medicine at UCLA. "This is critically important in light of the demographic shift of HIV-infected persons."

More information: dx.plos.org/10.1371/journal.pone.0016459

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