The importance of soluble CD14 and inflammation

Research suggests that one of the body’s sensors to help detect invading bacteria is called soluble CD14, written as sCD14. Levels of this protein are elevated in HIV-negative people who are experiencing severe bacterial infections. Research suggests that sCD14 is released by a group of cells called monocytes. These are cells of the immune system that play multiple roles in helping to detect and fight infections.

Since the 1990s, researchers have found that sCD14 levels are higher than normal in HIV-positive people, including those with severe bacterial infections.

However, interest in sCD14 has resurfaced in recent years as scientists study HIV-related inflammation and its effect on the immune system and survival. Here is a summary of some findings related to sCD14 and HIV:

- Treatment with the HIV integrase inhibitor raltegravir (Isentress) as part of combination therapy can modestly reduce levels of sCD14 in the blood, particularly in HIV-positive women. However, note that levels of sCD14 even in raltegravir users remain relatively high compared to those in healthy HIV-negative people.
- High sCD14 levels in the blood are associated with an increased risk of death among HIV-positive people.
- In one study, HIV-positive women with elevated levels of sCD14 were at increased risk for cardiovascular disease.

Disagreement about lingering inflammation

Some researchers think that bacteria cause elevated levels of sCD14 in the blood. This seems to make sense because the initial work on understanding sCD14 in HIV-negative people linked this protein to bacterial infections.

The gut (or intestines) plays an important role in human health. The intestines not only absorb food but are surrounded by lymphatic tissues and lymph nodes that intercept any germs that get into our intestines. These parts of the immune system also contain many CD4+ cells. When HIV infection occurs, the immune system surrounding the gut loses many of its CD4+ cells. As a result, some scientists say that the intestines become immunologically weaker and are less able to fend off germs. A weakened intestine may allow more germs to pass through and get into the body. The intestines and their surrounding lymphatic tissue and lymph nodes may also produce more chemical signals that favour inflammation.

The leakage of bacteria from the gut into the blood is called “bacterial translocation” by researchers. Clinical trials are planned or underway to test supplements of gut-friendly bacteria (probiotics) to try to reduce HIV-related inflammation.

Beyond bacteria

Researchers in San Francisco have conducted elegant and sophisticated experiments to try to understand why monocytes produce sCD14 even in HIV-positive people who do not have bacterial infections. As part of this work, they took blood samples from both HIV-positive and HIV-negative people for analysis.

They found that monocytes from HIV-positive people seem to be activated because of exposure to interferon-alpha and not bacteria or bacterial proteins. Furthermore, activation of monocytes in their experiments resulted in the release of sCD14. The activation of monocytes in their experiments stemmed from exposure to HIV.

Other researchers in London, UK, have found that persistent activation of another group of cells—natural killer (NK) cells, which can help fight HIV-infected cells and cancers—occurs in people with HIV. This activation did not occur because of bacterial infections.

Back to the lymph nodes
What all of these studies of sCD14 have in common is that they have assessed blood for this protein. Most HIV (and most of the body’s CD4+ cells) is not in the blood. Instead, most HIV and CD4+ cells are inside lymph nodes, lymphoid organs (such as the spleen and thymus) and lymphatic tissues around the gut, mouth, nose, anus and rectum.

Recently, researchers in the U.S. found that HIV-infected cells continue to produce HIV in the lymph nodes of ART users who are highly adherent and who had viral loads in their blood less than 50 copies/ml.

This discovery will likely stimulate much research to explore the impact of HIV and related inflammation. Such research may provide more clues about how to reduce HIV-related inflammation, including levels of sCD14.

—Sean R. Hosein

REFERENCES:


Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

CATIE provides information resources to help people living with HIV and/or hepatitis C who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

CATIE endeavours to provide the most up-to-date and accurate information at the time of publication. However, information changes and users are encouraged to ensure they have the most current information. Users relying solely on this information do so entirely at their own risk. Neither CATIE nor any of its partners or funders, nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. Any opinions expressed herein or in any article or publication accessed or published or provided by CATIE may not reflect the policies or opinions of CATIE or any partners or funders.

Information on safer drug use is presented as a public health service to help people make healthier choices to reduce the spread of HIV, viral hepatitis and other infections. It is not intended to encourage or promote the use or possession of illegal drugs.

Permission to Reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: This information was provided by CATIE (the Canadian AIDS Treatment Information Exchange). For more information, contact CATIE at 1.800.263.1638.

© CATIE

Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

Available online at: