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Biological and Clinical Implications of the Vascular Endothelial Growth Factor Coreceptor Neuropilin-1 in Human Immunodeficiency Virus

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[Published in OFID, 2023](#)

Background

People with HIV (PWH) have an increased risk of heart disease and cancer compared to the general population. It is not fully understood why this risk is higher. One method to help us better understand this increased risk is to study the proteins in the body which may be involved in inflammation (the body's response to infection).

Participants in this study were either enrolled in the Mechanistic Substudy of REPRIEVE or were part of the Center for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort. The REPRIEVE Trial is a global clinical research study which showed that treatment with a statin medication (cholesterol-lowering medication) reduces heart disease events among PWH. U.S. REPRIEVE participants in the substudy underwent all REPRIEVE trial procedures, as well as CT scans of the blood vessels surrounding the heart and blood tests to measure levels of immune and inflammation markers and other proteins in the blood. CNICS is a longitudinal observational cohort of PWH across the US that researchers use to better understand the effects of HIV treatments to improve the care of PWH.

Goals of the Study

This study aimed to explore the protein NRP-1 and its role in heart disease and cancers among PWH. NRP-1 is a protein that is involved in the formation of new blood vessels and the immune system. In an earlier study by REPRIEVE Investigators, NRP-1 was found to have a strong relationship with plaque, or fatty build up, the arteries around the heart. This study builds on these findings by studying NRP-1 in more detail.

➤ The participants:

<u>REPRIEVE</u>	<u>CNICS</u>
○ 734 REPRIEVE participants	○ 968 CNICS participants
● Average age: 51	● Average age: 47
● 119 (16%) female	● 169 (17%) female
○ Current/former smoker: 56%	○ Current/former smoker: 46%
○ Body mass index: 27.0 kg/m ²	○ Body mass index: 26.1 kg/m ²

➤ The findings:

- NRP-1 was associated with groups of other proteins that are involved in forming new blood vessels, cell communication, regulating the immune system, and the movement of cells. But, NRP-1 was less strongly associated with markers of inflammation that are typically higher in PWH.
- A higher level of NRP-1 was common in people who were older, male, and/or had a history of HCV or lower CD4 level.
- NRP-1 was associated with many types of cancers, all-cause death, and type 2 heart attack (caused when the supply or demand of oxygen to the heart is not balanced).

In Summary: Among PWH in the U.S., NRP-1 may be an important marker of many different diseases, including heart disease and cancers. Future studies could help us understand how NRP-1 impacts the health of PWH.

REPRIEVE Trial Website: reprivetrial.org

The findings shared in this summary are from the REPRIEVE population at a specific point in time. These findings are descriptive and not intended to change clinical care. If you have questions about what you've read, please talk to members of the REPRIEVE study team at your local site or a health care provider