Most people think of cancer and HIV as diseases with little in common. But the two are strongly connected, said Daniel DiMaio, MD, PhD, Waldemar Von Zedtwitz Professor of Genetics and Deputy Director of Yale Cancer Center. “That’s why HIV studies have always been an important part of our portfolio at the Cancer Center.”

So it can be frustrating when asked why a cancer center is studying HIV. “It’s mostly a matter of educating people,” explained Dr. DiMaio.

That begins by understanding that HIV is a virus, and that some viruses cause cancer. Viruses cause about 15 percent of all cancers. Hepatitis B and C viruses account for most of the world’s liver cancer. The human papillomavirus accounts for all of the world’s cervical cancer and approximately 30% of head and neck cancers in the United States. Though a direct link between HIV and cancer hasn’t yet been found, researchers have started to suspect that one exists.

The indirect links between HIV and cancer are well established. “There are at least three connections,” said Walther Mothes, PhD, Associate Professor of Microbial Pathogenesis and newly appointed Co-Director of the Cancer Center’s Molecular Virology program, who studies HIV.

First, notes Dr. Mothes, if HIV is left untreated, AIDS quickly weakens the immune system, opening the door to cancer viruses such as Kaposi sarcoma-associated human herpes virus-8 (HHV8), Epstein-Barr virus, and human papillomavirus. Second, even people whose HIV infection is controlled with antiretroviral therapy are more susceptible to cancer than the general population because their immune system remains compromised by the infection. Unsurprisingly, they have a higher incidence of cancers typical of AIDS, such as Kaposi sarcoma, but HIV also seems to amplify the activity of other virus-induced cancers, including anal, liver, and cervical cancers. “Cancer remains a leading cause of death among AIDS patients,” said Dr. Mothes.

A possible third connection between HIV and cancer is also emerging. In HIV-infected patients who have been on antiretroviral therapy for many years, researchers are finding indications that the virus integrates into chromosomal DNA and causes clonal expansion of T-cells. “That’s a precursor to the development of cancer,” explained Dr. Mothes. There’s a possibility that over time, in addition to HIV’s indirect role as an immunosuppressant, the virus may become recognized as a direct carcinogen.

All of this is why new research has excited HIV scientists. To elude attack by the immune system, the virus mutates constantly and changes its shape. That makes it very difficult to develop vaccines. Researchers have been working on many different strategies to try to break HIV’s ability to change shape, including using drugs that prevent the virus from changing shape or using antibodies that are able to keep the virus in a closed position.

To escape detection, HIV protein 1 usually stays closed as much as possible, opening briefly to change shape and infiltrate another cell. “To infect a cell,” described Dr. Mothes, “the virus needs to open up.”

If researchers can devise a drug that keeps the viral protein closed, the virus can’t infect. Scientists have discovered that some AIDS patients have developed “broadly neutralizing antibodies” that offer protection against the disease, but no one knew how the antibodies worked. It now appears as if these antibodies block infection by keeping the spike protein in the closed position.

This gives researchers a target for a vaccine. “T’s a major advance,” said Dr. Mothes. “If we can generate a vaccine that can protect the population against HIV, and if patients no longer have to take antiretroviral medications, we would also relieve many people from the burden of cancer. That is one reason that it is important for a cancer center to include the study of HIV.”