MedicalXpress

Scientists identify possible key in virus, cancer research

August 27 2015

Florida State University researchers have taken a big step forward in the fight against cancer with a discovery that could open up the door for new research and treatment options.

Fanxiu Zhu, the FSU Margaret and Mary Pfeiffer Endowed Professor for Cancer Research, and his team uncovered a viral protein in the cell that inhibits the major DNA sensor and thus the body's response to viral infection, suggesting that this cellular pathway could be manipulated to help a person fight infection, cancer or autoimmune diseases.

They named the protein KicGas.

"We can manipulate the protein and/or the sensor to boost or tune down the immune response in order to fight infectious and autoimmune diseases, as well as cancers," Zhu said.

The study was published today in the journal *Cell Host and Microbe*.

Zhu leads a research team investigating how DNA viruses can cause cancer, a major focus of researchers worldwide. About 15 percent of human cancer cases are caused by viruses, so scientists have been seeking answers about how the body responds to viral infection and how some viruses maintain life-long infections.

In the past few years, researchers finally identified the major DNA sensor in cells, known as cGas. That spurred researchers to further

examine this sensor in the context of human disease because ideally that sensor should have been alerting the body to fight disease brought by a DNA virus.

Essentially, a DNA virus is an intracellular parasite that contains genetic material. Several notable diseases including smallpox, herpes, and chickenpox are caused by DNA viruses. One of the reasons these diseases are so difficult to cure is because they take over the cellular machinery of their human host, often making it impossible to kill the virus without also harming the person.

Although people are equipped with sophisticated immune systems to cope with viral infection, many viruses have co-evolved mechanisms to evade or suppress the body's immune responses.

So the discovery of this protein is critical to further exploration of how these DNA viruses work and how they can be thwarted.

To uncover this protein, Zhu's team studies Kaposi's sarcoma-associated herpesvirus (KSHV), a human herpesvirus that causes some forms of lymphoma and Kaposi's sarcoma, a cancer commonly occurring in AIDS patients and other immunocompromised individuals.

In this study, researchers screened every protein in a KSHV cell—90 in total—and ultimately found that one of them directly inhibited the DNA sensor called cGAS. They infected human cell lines with the Kaposi's sarcoma virus to mimic natural infection, and found when they eliminated the inhibitor protein—KicGas—the cells produced a much stronger immune response.

To do this work, Zhu collaborated with several scientists both in the U.S. and Germany, including FSU Professor of Chemistry and Biochemistry Hong Li.

Li, whose focuses are molecular biology and molecular biophysics, specifically examined how the protein inhibited the cGAS activity in test tubes. For the next phase of research, she is building a three-dimensional model of the interactions to help them better understand how the inhibitor functions.

"These are hard problems to solve, and there is still much to learn here," Li said.

Learning how the inhibitor functions is a big next step, though.

"Once we figure that out, we can hopefully design something to fight the disease," Zhu said.

Provided by Florida State University