Researchers discover cellular 'doorway' exploited by cancer-causing virus

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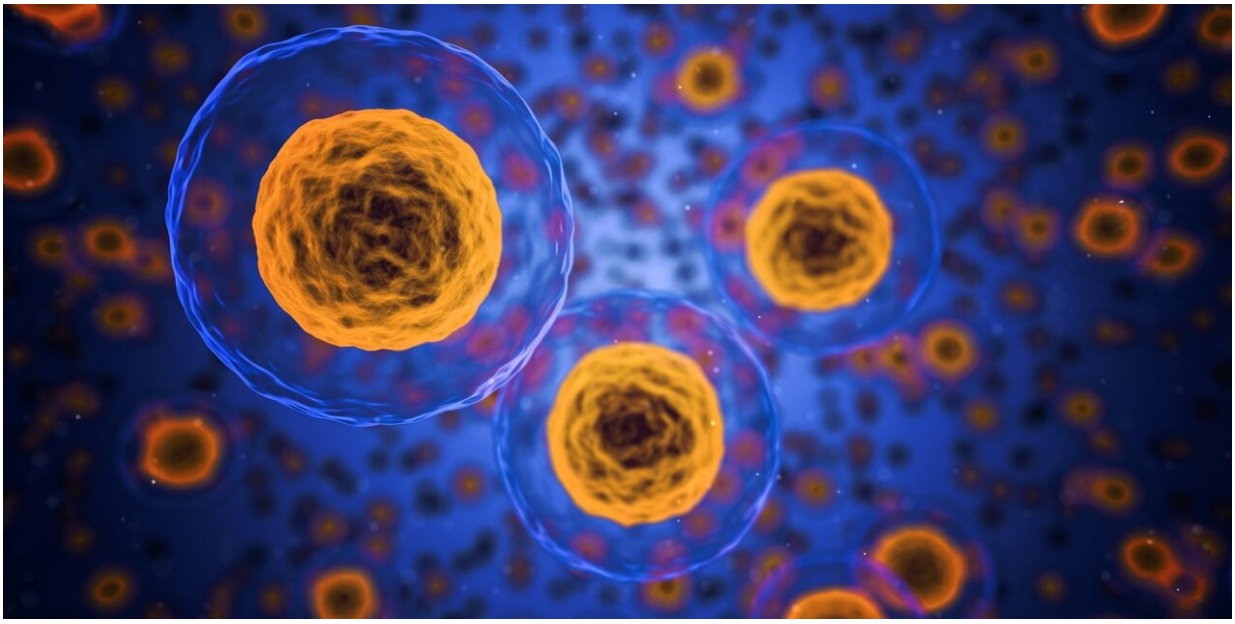

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Researchers at the University of Reading have contributed to a study that could lead to new treatments for a deadly cancer caused by a herpesvirus.

The study, published in *Science Signaling*, found that a protein called Kv1.3 acts as a crucial "doorway" allowing Kaposi's sarcoma-associated herpesvirus (KSHV) to replicate and spread. KSHV causes Kaposi's

sarcoma, a cancer that commonly affects people with weakened immune systems, including those with HIV/AIDS.

Dr. Mark Dallas from the University of Reading's School of Pharmacy was part of the international team that made the discovery. The research was led by Professor Adrian Whitehouse at the University of Leeds.

"Imagine Kv1.3 as a gateway into the cell that KSHV uses to override our body's defenses," explained Dr. Dallas. "By understanding how this cellular doorway works, we've uncovered a potential new way to lock out the virus and prevent cancer development."

The researchers found that Kv1.3 acts like a cellular "dimmer switch," adjusting the electrical charge across cell membranes. KSHV hijacks this mechanism, using it to create an environment that's ideal for virus replication while simultaneously dampening the immune system's alarm bells.

"It's as if KSHV is turning down the lights and suppressing the cell's alarm system," said Dr. Dallas. "This allows the virus to replicate unchecked, giving it a head start before the immune system realizes there's an intruder."

By blocking Kv1.3, the team significantly reduced KSHV's ability to replicate in laboratory tests. This suggests that drugs targeting Kv1.3 could potentially stop the virus from spreading and causing cancer.

Kv1.3 inhibitors, which could be thought of as keys to locking this cellular doorway, are already being investigated as treatments for other conditions, including psoriasis. Some have shown early promise in clinical trials for KSHV-associated cancers.

KSHV-associated tumors account for about 2% of all infection-

attributed cancers globally. This rises to 14% in countries ranked with a lower life expectancy. People living with HIV/AIDS have a higher risk, with KSHV causing cancer in approximately 1 in 20 individuals.

"For individuals with weakened immune systems, KSHV is like a thief that strikes when the security system is down," Dr. Dallas added. "Our findings suggest Kv1.3 inhibitors could prevent the virus taking control of our cells' machinery to replicate and cause harm."

More information: Holli Carden et al, K v 1.3-induced hyperpolarization is required for efficient Kaposi's sarcoma–associated herpesvirus lytic replication, *Science Signaling* (2024). DOI: 10.1126/scisignal.adg4124

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