MedicalXpress

Drugs may shut down several Epstein-Barr virus-induced diseases

January 25 2010

(PhysOrg.com) -- Using a class of drugs being clinically tested to treat other kinds of cancer, researchers at the University of Wisconsin School of Medicine and Public Health found that the drugs were the first to stop the latent form of EBV infection from causing disease.

The same virus that causes relatively mild mononucleosis, the "kissing disease," can also cause severe mono as well as several potentially deadly kinds of cancer.

Now researchers think they can kiss a stealthy form of Epstein-Barr virus (EBV) goodbye - or at least shut it down enough to successfully treat several of the dangerous diseases it causes.

Using a class of drugs being clinically tested to treat other kinds of cancer, researchers at the University of Wisconsin School of Medicine and Public Health found that the drugs were the first to stop the latent form of EBV infection from causing disease.

The drugs, Hsp90 inhibitors, prevented human EBV-related tumors from growing in mice, protected immune cells from transforming into tumors and killed established tumor cells at low, non-toxic doses.

Until now, there have been no effective drugs for treating latent EBV infection in any of the EBV-associated diseases, which in addition to mono include a subset of stomach cancers, certain types of nose-throat cancer and lymph node cancers such as lymphoproliferative disease, says

lead author Shannon C. Kenney, MD.

"This discovery suggests a new way of treating patients with severe mononucleosis, which in rare circumstances can be fatal, and patients with EBV-driven cancers, particularly immuno-compromised AIDS and transplant patients," says Kenney, an infectious disease expert at UW Hospital and Clinics.

The study appears in the current (Jan. 25, 2010) Proceedings of the National Academy of Sciences.

Kenney, also a professor of oncology at the McArdle Laboratory for Cancer Research and of medicine, has studied EBV for nearly 30 years. Most of her work has focused on the form of EBV that actively produces infection, but recently she turned to the so-called latent form.

"The latent infection form actually is not so latent," says Kenney, a member of the UW Carbone Cancer Center. "This is the form of EBV that is most closely associated with cancer development."

Latently infected cells express transforming viral proteins that can change normal cells into cancer cells. One key viral protein, EBNA-1, is required for EBV to live long-term in host cells. Many scientists and drug companies are looking for ways to block this viral protein, expressed in every EBV-infected cell.

Kenney and her team had been using Hsp90 (heat shock protein 90) inhibitors as they studied the infectious form of EBV.

"Normal cells can survive when treated with Hsp90 inhibitors," Kenney says. "In contrast, Hsp90 inhibitors are toxic to certain types of cancer cells, which often are more dependent upon high levels of Hsp90."

After they discovered that EBNA-1 itself must have Hsp90 in order to function in cells, the Wisconsin researchers conducted three different experiments to see what the effect of exposing EBV-infected cells to Hsp90 inhibitors would be.

In all three experiments, the results showed a dramatic reduction in EBNA-1-related activity. The drugs killed EBV-induced tumor cells in one experiment, halted the growth of EBV-induced tumors in mice in another and protected normal immune cells from becoming transformed to tumor cells in the third.

And while the drugs were highly toxic to EBV-infected cells, they had very little effect on normal cells at the doses used in the experiments.

The researchers found the underlying explanation to be that EBNA-1 could not be processed - synthesized and translated - to any degree when Hsp90 inhibitors were present.

Kenney expects the inhibitors-geldanamycin, 17-AAG and 17-DMAG-may be useful for most but not all kinds of EBV-induced cancers as well as severe mono.

In fact, the drugs may be even more widely useful, says Kenney, because clinicians are seeing that people older than age 70 are getting certain forms of EBV-induced cancers more frequently.

"There also is tantalizing early evidence that EBV may contribute to auto-immune diseases such as lupus and multiple sclerosis," she says.

And what about the possibilities for standard mono?

"The majority of healthy humans will get over mono with no treatment after a month or two," says Kenney. "But Hsp90 inhibitors could

potentially help, in terms of getting people back to school or work sooner. Clinical trials will need to be performed in patients to determine if these drugs are useful in severe mononucleosis."

Provided by University of Wisconsin-Madison