Finding could lead to reduced side effects in anti-cancer antibiotics

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Most of us have had a doctor prescribe an antibiotic for a stubborn bacterial infection, or for a cut that gets infected. However, prescribing an antibiotic to fight cancer? In fact, anti-cancer antibiotics have been used since the 1950s to successfully treat several forms of cancer, but often the side effects limit the duration they can be given to a patient.

One particularly promising anti-cancer antibiotic is Geldanamycin and a modified form of this drug known as 17AAG. Despite its proven ability to selectively kill many different forms of cancer in laboratory studies, the use of these drugs is limited due to side effects, mainly liver failure, in patients.

Newly published results from Van Andel Research Institute (VARI) researchers have determined how the anti-cancer antibiotic Geldanamycin and its derivative 17AAG work in more detail and have uncovered a possible explanation for side effects observed in clinical trials of the drug.

"The article provides novel and significant information about the clinical potential of these compounds in cancer therapy," said Yale School of Medicine Professor and Chair of Pharmacology Joseph Schlessinger, Ph.D.

Although there was much preclinical interest in the antibiotic Geldanamycin as an anti-cancer drug, it turned out to be a poor candidate for clinical trials because of its toxicity. Derivatives such as

17AAG were developed to decrease toxicity and are still being evaluated in clinical trials.

VARI researchers determined how Geldanamycin and 17AAG work in more detail in a study published in Proceedings of the National Academy of Sciences U.S.A., which could inform future drug design, and also found a way to potentially decrease the antibiotics' toxicity.

"There was so much interest early on in Geldanamycin because it resulted in the degradation of oncoproteins, important protein targets in tumor cells," said VARI Research Scientist and lead author of the paper Qian Xie, M.D., Ph.D.

"If there is a chance of decreasing the toxicity of Geldanamycin and 17AAG, it would be a boon in the treatment of cancer," said George Vande Woude, Ph.D., head of the Laboratory of Molecular Oncology at VARI that published the study.

Provided by Van Andel Research Institute