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Researcher finds potential new use for old drugs

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A class of drugs used to treat parasitic infections such as malaria may also be useful in treating cancers and immune-related diseases, a new WSU-led study has found.

Researchers discovered that simple modifications to the drug furamidine have a major impact on its ability to affect specific human proteins involved in the on-off switches of certain genes.

"This was rather unexpected, given how relatively simple the molecules are that we modified and how difficult it has been to affect these proteins," said Gregory Poon, pharmaceutical scientist at Washington State University.

The proteins – known as transcription factors – regulate the expression of genes in a highly coordinated and intricate manner, making them attractive targets for therapeutic drugs. But it has proven difficult to design drugs to affect them, Poon said.

"For this reason, they have been called undruggable," he said. "Recently, however, scientists have been making headway in targeting these transcription factors with drugs, and now our results suggest this class of drugs can be a useful addition to the arsenal."

Furamidine belongs to a family of drugs known as heterocyclic dications. The drug has a long history of use in serious parasitic diseases such as malaria, African sleeping sickness and PCP, a common infection

in HIV/AIDS.

"There is tremendous knowledge and experience with using furamidine and related drugs in humans, so these drugs have an important advantage over other classes of drugs that are relatively behind in clinical experience," Poon said.

Poon collaborated with researchers at Georgia State University. The team found that derivatives of furamidine can target a specific transcription factor known as PU.1.

PU.1 is a major factor in development and function of the human immune system, and it plays important roles in diseases such as some leukemias, multiple sclerosis and diabetes. PU.1 is also a member of a large family of related transcription factors, known as ETS, that is involved in a broader range of cancers and other diseases.

"I am fortunate to be working with some of the best people in this area," Poon said, referring to his collaborators, Dave Boykin and David Wilson of Georgia State University. "The challenge now is to fine-tune this class of drugs to make them as specific as possible to other ETS-family transcription factors as well."

More information: The findings were published in *Nucleic Acids Research* journal at nar.oxfordjournals.org/content … 0/23/nar.gkt955.full

Provided by Washington State University