Finding may explain anti-cancer activity of thiazole antibiotics

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University of Illinois at Chicago College of Medicine researchers have discovered how some recently approved drugs act against cancer cells. The finding may lead to a more effectively targeted anti-cancer strategy.

In a new study reported in the journal PLoS ONE online, UIC researchers show how a class of drugs inhibits a protein called FoxM1 and suggest that the drugs' ability to inhibit FoxM1 may account for their anti-cancer activity.

FoxM1 is one of the most highly over-produced proteins in cancer cells and is believed to play an important role is causing cells to become cancerous. Because production of the protein is not usually switched on in non-dividing cells, the protein may present a promising target for anti-cancer treatments.

Andrei Gartel, UIC associate professor of molecular genetics, and his colleagues had previously shown that antibiotics called thiazoles kill cancer cells and inhibit FoxM1. When they went on to investigate whether the antibiotics attacked other proteins involved in cancer, they got a surprising result.

"We found that these thiazole antibiotics actually stabilized other cancer-causing proteins," Gartel said.

It was an unexpected hint suggesting that thiazole antibiotics may act as inhibitors of the proteasome, a molecular complex that acts as a trash

collector in cells, degrading old proteins that the cell has marked for destruction. This inhibition of the proteasome was confirmed in later experiments, Gartel said.

Recently, a number of proteasome inhibitors have shown promise against cancer, but no one understands why they have anti-cancer effects.

"We decided to see if these proteasome inhibitors, including Velcade, were, like our antibiotics, targeting FoxM1," he said.

The researchers found that the proteasome inhibitors did inhibit FoxM1 and that they also caused cells to self-destruct in the same concentrations.

It's possible, Gartel suggested, that by using thiazole antibiotics in combination with well-known proteasome inhibitors, "we may see a synergy that allows us to markedly reduce the dose of any one of these drugs and still effectively kill the cancer cells."

Source: University of Illinois at Chicago (news : web)