Researchers find way to decrease chemoresistance in ovarian cancer

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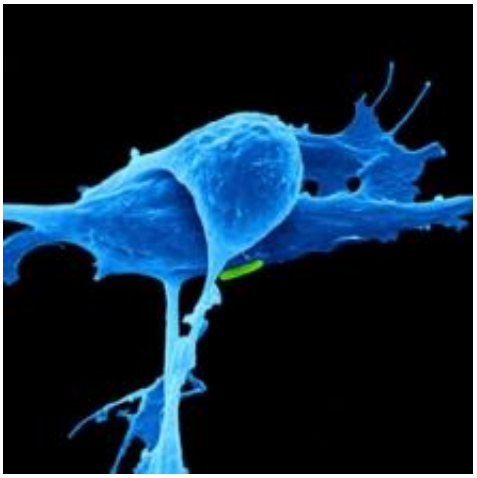

Inhibiting enzymes that cause changes in gene expression could decrease chemotherapy resistance in ovarian cancer patients, researchers at Georgia State University and the University of Georgia say.

Dr. Susanna Greer, associate professor of biology, and research partners at the University of Georgia have identified two enzymes that suppress proteins that are important for regulating cell survival and chemoresistance in ovarian cancer. Their findings are published in the journal, *PLOS ONE.*

Ovarian cancer is one of the deadliest gynecological cancers, with a 60

percent mortality rate and a five-year survival rate for less than 30 percent of women in the advanced stage of the disease. The high mortality rate is largely due to the development of resistance to chemotherapeutic drugs. Understanding the molecular and genetic mechanisms that drive the development of acquired chemoresistance can help improve therapeutic agents for ovarian cancer treatment.

"Ovarian cancer is usually treated by surgery followed by chemotherapy," Greer said, "but because it's typically found fairly late, ovarian cancer is often refractory to chemotherapy. You have tumors that initially respond to chemotherapy and then don't. Ovarian cancer is the 8th most commonly diagnosed cancer in U.S. women, but due to its late diagnosis, causes more deaths than any other cancer of the female reproductive system."

In a previous study, Greer found the expression of the protein RGS10, which regulates ovarian cancer cell growth and survival, is suppressed in ovarian cancer cells that are chemoresistant. The suppression was caused by two important mechanisms that silence genes and contribute to the progression of many cancers - DNA methylation, a biochemical process in which a methyl group is added to specific building blocks of DNA, and histone deacetylation, a process in which enzymes remove functional groups of atoms from proteins associated with DNA.

In their study, the researchers investigate the silencing of RGS10 expression in ovarian cancer cells by epigenetics, which is heritable changes in genes and gene expression that are not caused by changes in the DNA sequence, but rather by reversible and self-perpetuating mechanisms of DNA programming.

They identified two epigenetic regulators, HDAC1, a histone deacetylase, and DNMT1, a DNA methyl transferase. Decreasing the expression of HDAC1 and DNMT1 and blocking their activity

significantly increased RGS10 expression and cell death. This also decreased the binding of HDAC1 to RGS10 in chemoresistant cells.

The research suggests that inhibiting HDAC1 and DNMT1 could be a novel therapeutic approach to overcoming chemoresistance in ovarian cancer.

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