

Researchers identify protein governing platinum resistant ovarian cancer

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The extracellular regulated kinase (ERK) protein is an important mechanism behind platinum-resistance in platinum-resistant ovarian cancer, according to a study from a research team at the George Washington University (GW) Cancer Center. The study, which is the first to provide clinical evidence confirming a link between ERK and hypoxia-inducible factor (HIF-1?), is published in *Clinical Cancer Research*.

Platinum-based chemotherapy drugs, are among the strongest and most widely used against cancer. Up to 80% of [ovarian cancer patients](#) develop platinum-resistance over the course of their treatment. Studies have found that HIF-1?—a subunit of HIF-1, a heterodimeric transcription factor that regulates multiple cellular pathways—is an important mechanism governing platinum resistance. However, the mechanism regulating HIF-1? stability in platinum-resistant ovarian cancer was largely unknown.

"Platinum-based chemotherapy is such a powerful treatment for cancer patients, however so many develop a resistance," said Wenge Zhu, Ph.D., associate professor of biochemistry and [molecular medicine](#) at the GW School of Medicine and Health Sciences and senior author on the study. "We wanted to figure out how that resistance happens for the cancer cells."

The research team evaluated a combination of inhibitors of HIF-1?, ERK, and TGF-?1 with platinum drugs by in vitro and in vivo experiments. They found prolyl hydroxylase domain-containing protein 2 (PHD2) to be an underlying layer of ERK. Zhu and his team observed that from clinical samples the activation of the ERK/PHD2/HIF-1? axis in platinum-resistant ovarian [cancer patients](#), correlated highly with poor prognoses for patients.

"We found that HIF-1? stabilization is regulated by the TGF-?1/ERK/PHD2 axis in platinum-resistant ovarian cancer cell," Zhu said. "Now we can

consider inhibiting any of those components as a potential strategy for treating platinum-resistant patients."

This study also provides insight for further investigation into whether this novel mechanism regulates the development of tumors and future chemotherapy response.

More information: Zhuqing Li et al, ERK Regulates HIF1?-Mediated Platinum Resistance by Directly Targeting PHD2 in Ovarian Cancer, *Clinical Cancer Research* (2019). DOI: [10.1158/1078-0432.CCR-18-4145](https://doi.org/10.1158/1078-0432.CCR-18-4145)

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