

Orphan receptor proteins deliver 2 knock-out punches to glioblastoma cells

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Two related proteins exert a lethal double whammy effect against glioblastoma cells when activated with a small molecule, say researchers at Georgetown Lombardi Comprehensive Cancer Center.

The scientists say when activated, one [protein](#), called the short form, stops glioblastoma cells from replicating their DNA, and the other, called the long form, prevents cell division if the DNA has already been replicated, explains Rebecca Riggins, PhD, assistant professor of oncology at Georgetown Lombardi. The study was posted online Dec. 12 in the journal *Cell Cycle*.

Both proteins are produced by the estrogen-related receptor beta (ERR β) gene. They are known as "orphan receptors" because they don't bind to any substances naturally produced by the body. ERR β proteins are similar in shape to the receptor that binds the hormone estrogen—hence their name—but they do not bind estrogen and are not otherwise related. Both men and women have ERR β genes.

In this study, Riggins and her co-author, postdoctoral fellow Mary Heckler, PhD, examined glioblastoma cells in the laboratory for the presence of ERR β and found both long and short forms. To understand what these proteins were doing, they used a laboratory chemical, DY131, which had been designed to bind and activate these proteins.

To their surprise, the researchers discovered that DY131 exerted a strong, but distinct, effect on both the short and long forms of ERR β .

The short form had been known to act as a tumor suppressor in prostate cancer, and a similar anti-cancer action was found by the researchers in glioblastoma. The study, however, is the first to find a function for the long form in cancer.

"While much work remains to understand the clinical potential of this finding, it may ultimately be possible to directly target the long and [short](#) forms of ERR β in combination with other therapies to improve outcomes in [glioblastoma](#)," Riggins says.

Riggins, a member of the breast cancer program at Georgetown Lombardi, is now studying the behavior of the same proteins when activated by DY131 in triple negative breast cancer, for which there is no therapeutic target.

Provided by Georgetown University Medical Center

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