# Development of new protein may lead to novel treatment options for cancer, birth defects

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Researchers have engineered an artificial protein that may block malignant properties of cancer cells as well as correct certain birth defects.

The findings, which appear in the journal *Proceedings of the National Academy of Sciences*, may lead to identifying new molecular targets suitable for therapeutic intervention.

Cells in the human body need to communicate with each other to function properly. This is accomplished by a molecular mechanism called signal transduction and its dysregulation leads to human disease. A group of molecules called G proteins act as a signaling mechanism that enables cells to change their behavior when they are activated by surface receptors.

According to the researchers, the G proteins can be activated via alternative mechanisms independent of surface receptors that also impact normal cell behavior and pathogenesis. Unfortunately, there are no efficient tools to investigate these alternative G protein activators and learn how to tackle their aberrant behavior in disease, until now.

"We have engineered an artificial protein that when expressed in cells can specifically blunt receptor-independent G protein activation and subsequent changes in cell behavior. We implemented this to block

malignant properties of cancer cells and to correct birth defects associated with the aberrant dysregulation of cellular communication," explained corresponding author Mikel Garcia-Marcos, PhD, associate professor of biochemistry at Boston University School of Medicine (BUSM).

The researchers started with a natural G protein, removed some parts and changed some others to create a new protein that binds very tightly to a family of G protein activators while losing the ability to bind to any other known partner. Using this approach they created a protein that specifically inhibits a family of G protein activators without affecting any other component of the cellular machinery. Then they introduced it in cancer cells and observed that it can prevent their malignant properties by selectively inhibiting G protein activators. Similarly, when they introduced the engineered protein in an experimental model, it blunted developmental defects induced by a G protein activator.

"Our findings provide the proof of principle to target a novel family of G protein regulators that are known to contribute to the development of cancer and the appearance of birth defects.

Although the clinical implications for this discovery are indirect—since the engineered protein cannot be delivered to patients—it does represent a significant advance in the identification of a new class of molecular targets in cancer or neonatal malformations" said Garcia-Marcos.

**More information:** Anthony Leyme el al., "Specific inhibition of GPCR-independent G protein signaling by a rationally engineered protein," *PNAS* (2017). www.pnas.org/cgi/doi/10.1073/pnas.1707992114