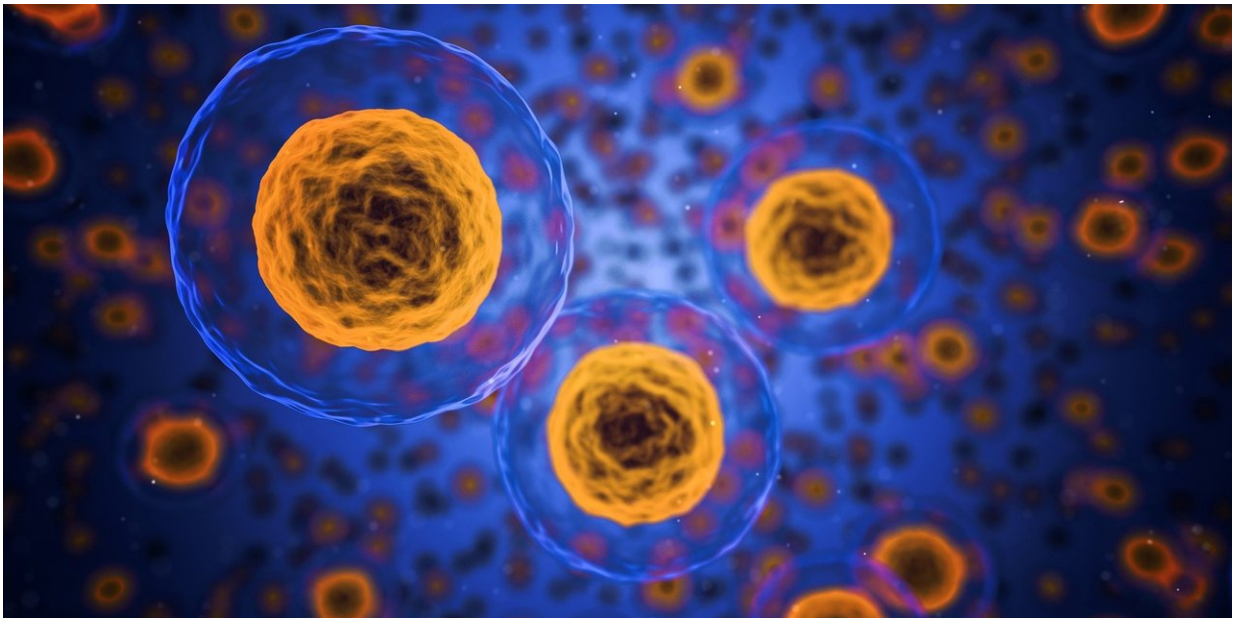


Potential target for treating many cancers found within GLI1 gene

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Scientists from the Stanley Manne Children's Research Institute at Ann & Robert H. Lurie Children's Hospital of Chicago found that a region within the DNA of the cancer-promoting GLI1 gene is directly responsible for regulating this gene's expression. These findings, published in the journal *Stem Cells*, imply that this region within GLI1 could potentially be targeted as cancer treatment, since turning off GLI1 would interrupt excessive cell division characteristic of cancer.

"From previous research, we know that GLI1 drives the unrelenting cell proliferation that is responsible for many cancers, and that this gene also stimulates its own expression," says co-senior author Philip Iannaccone, MD, Ph.D., Professor Emeritus at the Manne Research Institute at Lurie Children's and Northwestern University Feinberg School of Medicine.

"We established in living [human embryonic stem cells](#) that removing the GLI1 regulatory region eliminated GLI1 expression and halted its activity. These findings are promising and could point to a therapeutic target for [cancer](#)."

Dr. Iannaccone and colleagues used CRISPR gene editing technology to delete the binding region of the GLI1 DNA in human embryonic stem [cells](#). They found that without this region, GLI1 remained turned off, which interfered with the gene's normal activity of driving embryonic development of blood, bone, and nerve cells.

"A surprising aspect of this work was that turning GLI1 off affected stem cell differentiation to all three embryonic lineages," says first author Yekaterina Galat, BS, Research Associate at the Manne Research Institute at Lurie Children's.

"The developmental function of GLI1 ends after birth, so if we manage to stop its expression in the context of cancer, it should not have [negative consequences](#) to normal biology," explains Dr. Iannaccone.

GLI1 expression is associated with about a third of all human cancers. In addition to promoting cell proliferation, GLI1 expression increases tumor cell migration and is associated with resistance to chemotherapy drugs.

"Our team plans to study GLI1 associated proteins that assist in regulation of GLI1 expression through its binding [region](#)," says Dr. Iannaccone. "Targeting these proteins as a means to stop GLI1 activity

could prove to be a fruitful treatment strategy for cancer."

More information: Yekaterina Galat et al, CRISPR editing of the GLI1 first intron abrogates GLI1 expression and differentially alters lineage commitment, *Stem Cells*

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Provided by Ann & Robert H. Lurie Children's Hospital of Chicago

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