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Two repressor genes identified as essential for placental development

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Two particular repressor genes in a family of regulatory genes are vital for controlling cell proliferation during development of the placenta, according to a new study by researchers with the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

The two genes are called E2f7 and E2f8. Their absence in stem cells results in a placenta made up of overcrowded and poorly organized cells that cannot properly transport oxygen and nutrients or support normal embryonic development.

When placental stem cells were also missing a third gene, the activating gene called E2f3a, the placental defects were corrected and embryos carried to birth.

The findings, published in the journal *Developmental Cell*, shows at the molecular level how these E2Fs control cell proliferation in intact animals, the researchers say.

"The findings provide insight into the role of these two repressor genes," says principal investigators Gustavo Leone, associate professor of Medicine and associate director of Basic Research.

The two genes belong to a family of regulatory genes that, in humans, has eight members. They are all believed to activate or suppress other genes to control cell division and proliferation in both normal and cancer

cells. But which genes they regulate and how they interact with one another in living animals is poorly understood.

"E2F regulatory genes have been thought to be important for a long time, but with so many of them, it's been hard to tell which one is doing what," Leone says.

"Here, we show that the repressors E2f7 and E2f8 are essential for the development of an intact, functional, placenta, and that they balance out the effects of the activating gene E2f3a," Leone says. "Because these two repressors are important for proliferation, they may also play an important role in suppressing tumor development."

For this study, Leone and his colleagues used animal models that lacked one or more of the three E2F genes in trophoblast stem cells, which give rise to the placenta.

Earlier work led by Leone has shown that in some cases, an E2F gene can be an activator in some tissues and a repressor in others.

Provided by Ohio State University Medical Center

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