Outside influence: Genes outside nucleus have disproportionate effect

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Studies on *Arabidopsis* plants like this six-week-old lab-grown specimen show that the genes of mitochondria and chloroplasts have a disproportionate effect on cellular metabolism compared to the far more numerous nuclear genes. Credit: Baohua Li, UC Davis

New research from the University of California, Davis, shows that the tiny proportion of a cell's DNA that is located outside the cell nucleus has a disproportionately large effect on a cell's metabolism. The work, with the model plant *Arabidopsis*, may have implications for future

treatments for inherited diseases in humans.

Plant and animal cells carry most of their genes on chromosomes in the nucleus, separated from the rest of the cell. However, they also contain a small number of genes in organelles that lie outside the nucleus. These are the mitochondria, which generate energy for animal and plant cells, and chloroplasts, which carry out photosynthesis in plant cells.

The influence of genes outside the nucleus was known to an earlier generation of field ecologists and crop breeders, said Dan Kliebenstein, professor in the UC Davis Department of Plant Sciences and Genome Center and senior author on the paper published Oct. 8 in the online journal *eLife*. This is the first time that the effect has been quantified with a genomic approach, he said.

Bindu Joseph, a postdoctoral researcher in Kliebenstein's lab, and Kliebenstein studied how variation in 25,000 nuclear genes and 200 organellar genes affected the levels of thousands of individual chemicals, or metabolites, in leaf tissue from 316 individual *Arabidopsis* plants.

They found that 80 percent of the metabolites measured were directly affected by variation in the organellar genes—about the same proportion that were affected by variation among the much larger number of nuclear genes. There were also indirect effects, where organellar genes regulated the activity of nuclear genes that in turn affected metabolism.

"At first it's surprising, but at another level you almost expect it," Kliebenstein said. "These organelles produce energy and sugar for cells, so they are very important."

Similar effects could also occur in mammalian cells, Kliebenstein said. That has implications for in vitro fertilization therapies aimed at preventing diseases caused by faulty mitochondria being passed from

mother to child. The British government recently proposed draft regulations for "three-parent embryos," created by taking a the nucleus from a fertilized egg and putting it into an egg cell from a third donor with its own set of mitochondria. The technique has so far only been tested in animals.

"From what we can see in plants, there might be an issue, but it needs testing," Kliebenstein said.

Large population surveys that aim to link conditions such as obesity to specific genes should also take more account of organellar genes, he said.

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