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Mom Genes, Dad Genes

By Jennifer Couzin
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PHILADELPHIA, PENNSYLVANIA--All of us inherit one copy of our genes from mom and one from dad, but these genes can behave differently depending on which parent they came from. The phenomenon, known as imprinting, has long been a source of fascination among geneticists. It's also been linked to some rare genetic diseases, but finding these genes has been a painstaking task. New work presented here today at the American Society of Human Genetics suggests the search is about to become a whole lot easier.

Andrew Sharp, who studies genetics at the University of Geneva in Switzerland, decided that rather than hunt for one gene at a time, as had been done in the past, he would scan entire genomes. Identifying imprinted genes isn't easy, though, because nearly every genome contains a mix of maternal and paternal DNA. So Sharp turned to two exceedingly unusual tissues that don't. One is a tumor called an ovarian teratoma, which develops when an egg is not fertilized but duplicates its chromosomes, leading to all-maternal DNA. The other type of tissue, a hydatidiform mole, results when an egg without a nucleus--and hence without DNA--is fertilized by a sperm. Thus, it contains only paternal DNA.

Sharp first confirmed that known imprinted genes could be detected in these samples. Then, he performed a genome-wide scan on two teratomas and two moles and found that 0.5% of the genome in these samples was methylated, or chemically modified, the first step toward showing they were imprinted. (Imprinted genes are modified by methylation, which in turn influences gene expression.) So far, he's looked more closely at 44 sites, including in human blood samples and placentas, which he used as a control tissue, to see whether one copy of the gene is expressed differently from the other--evidence of imprinting. Fourteen genes so far look promising. "I'm pretty confident some of these are imprinted," Sharp said after his talk, but he also thinks it's likely some will not pan out. Before Sharp's work, researchers had identified 80 imprinted genes in mice and 50 in humans.

Sharp and his colleagues are only beginning to examine the function and behavior of the imprinting genes he found, but so far their functions appear broad--some broadly govern transcription, some metabolism.

"It's the beginning of the story," says Alexandre Reymond of the University of Lausanne in Switzerland, who presented his research on genetic variation as well. Reymond stresses that the imprinting work is very preliminary, and many of the genetic sites Sharp has identified will probably not be imprinted genes. Still, he says, just the notion of a "methylanome"--an unbiased set of genes that can be chemically altered in this way and then modify expression--is valuable, particularly because they may differ between individuals.