Researchers find gene that increases rate of maternal aneuploidy

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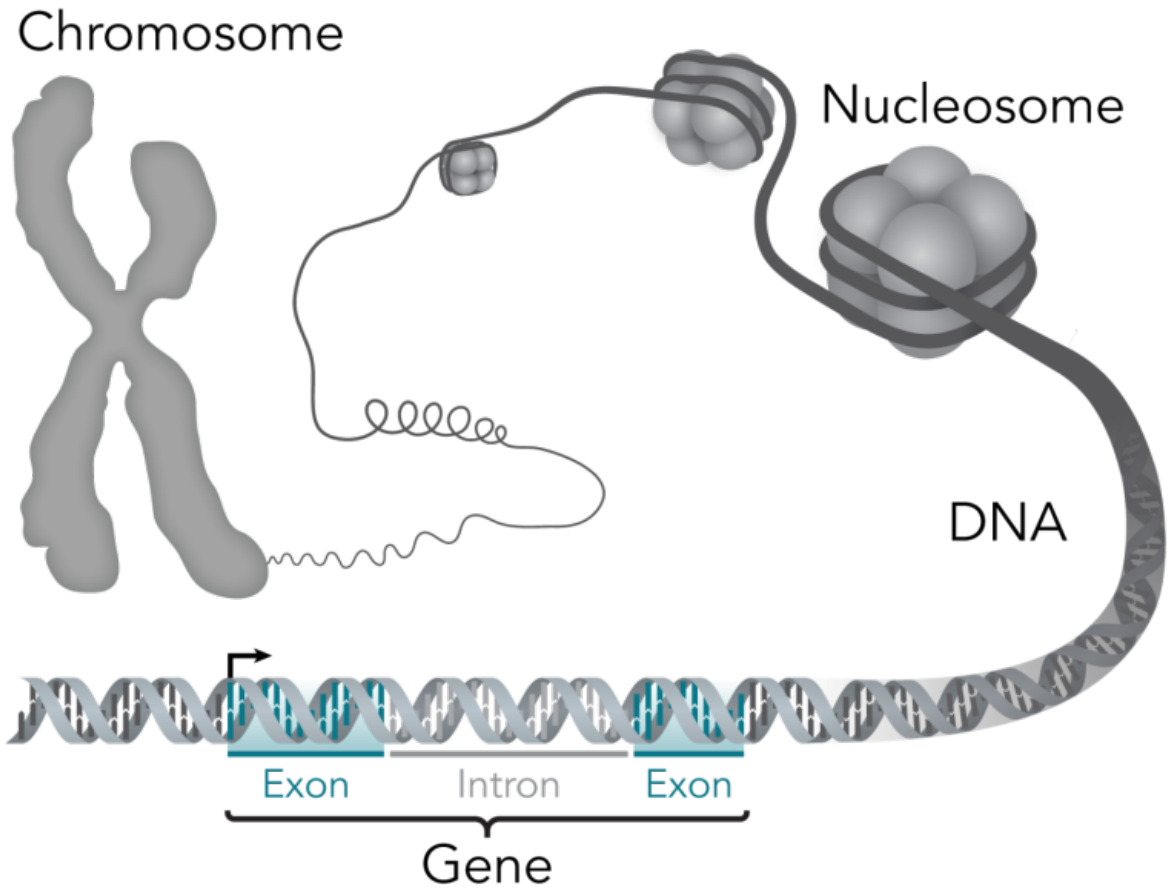

This stylistic diagram shows a gene in relation to the double helix structure of DNA and to a chromosome (right). The chromosome is X-shaped because it is dividing. Introns are regions often found in eukaryote genes that are removed in the splicing process (after the DNA is transcribed into RNA): Only the exons encode the protein. The diagram labels a region of only 55 or so bases as a gene. In reality, most genes are hundreds of times longer. Credit: Thomas

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(Medical Xpress)—A team of researchers at Stanford University has found a gene that increases the rate of maternal aneuploidy in embryos. In their paper published in the journal *Science*, the team describes how they used material from in vitro fertilization procedures to conduct pre-implantation genetic screening which allowed them to learn more about aneuploidy—how it comes about, its frequency and what it may have to do with human evolution. Samuel Vohr and Richard Green with the University of California offer a Perspectives piece on the work done by the team in the same journal issue.

Scientists know that on average only 70 percent of conceptions result in delivery of a baby—of the 30 percent that do not survive, a large number are due to aneuploidy—but why this occurs has remained somewhat of a mystery. In this new research, the team at Stanford has found a gene that actually increases the rate of aneuploidy in humans, though why we have such a gene remains up for debate.

Aneuploidy is the primary cause of miscarriage, which has led to a great detail of research into its cause—in this new effort, the researchers were able to conduct genetic studies on human embryos as part of the routine analysis conducted by fertility specialists during in vitro procedures. Using the material they were able to sequence the genomes of three-day old embryos and both parents. Doing so allowed them to zero in on a particular genome region that appeared to be involved in causing defects in chromosome numbers. Prior research has shown that a particular gene, Polo-like kinase 4, (PLK4) exists in that region—the researchers gave it a closer look and found a particular mutation that increased the rate of maternal aneuploidy. Additional study showed that the mutation is actually quite prevalent in human populations the world over.

The findings by the team lead to questions about why such mutations would be so prevalent, and whether it has been a positive selection in our evolutionary history. The team wonders if perhaps it might have something to do with paternity confusion—where it might have been beneficial for early populations to not be able to identify the father of children. But the discovery has also opened the door to other questions, Vohr and Green note, such as the ethics involved in genetic screening for the gene.

More information: Common variants spanning PLK4 are associated with mitotic-origin aneuploidy in human embryos, *Science* 10 April 2015: Vol. 348 no. 6231 pp. 235-238. DOI: 10.1126/science.aaa3337

ABSTRACT
Aneuploidy, the inheritance of an atypical chromosome complement, is common in early human development and is the primary cause of pregnancy loss. By screening day-3 embryos during in vitro fertilization cycles, we identified an association between aneuploidy of putative mitotic origin and linked genetic variants on chromosome 4 of maternal genomes. This associated region contains a candidate gene, Polo-like kinase 4 (PLK4), that plays a well-characterized role in centriole duplication and has the ability to alter mitotic fidelity upon minor dysregulation. Mothers with the high-risk genotypes contributed fewer embryos for testing at day 5, suggesting that their embryos are less likely to survive to blastocyst formation. The associated region coincides with a signature of a selective sweep in ancient humans, suggesting that the causal variant was either the target of selection or hitchhiked to substantial frequency.