Earliest embryonic lethality gene identified

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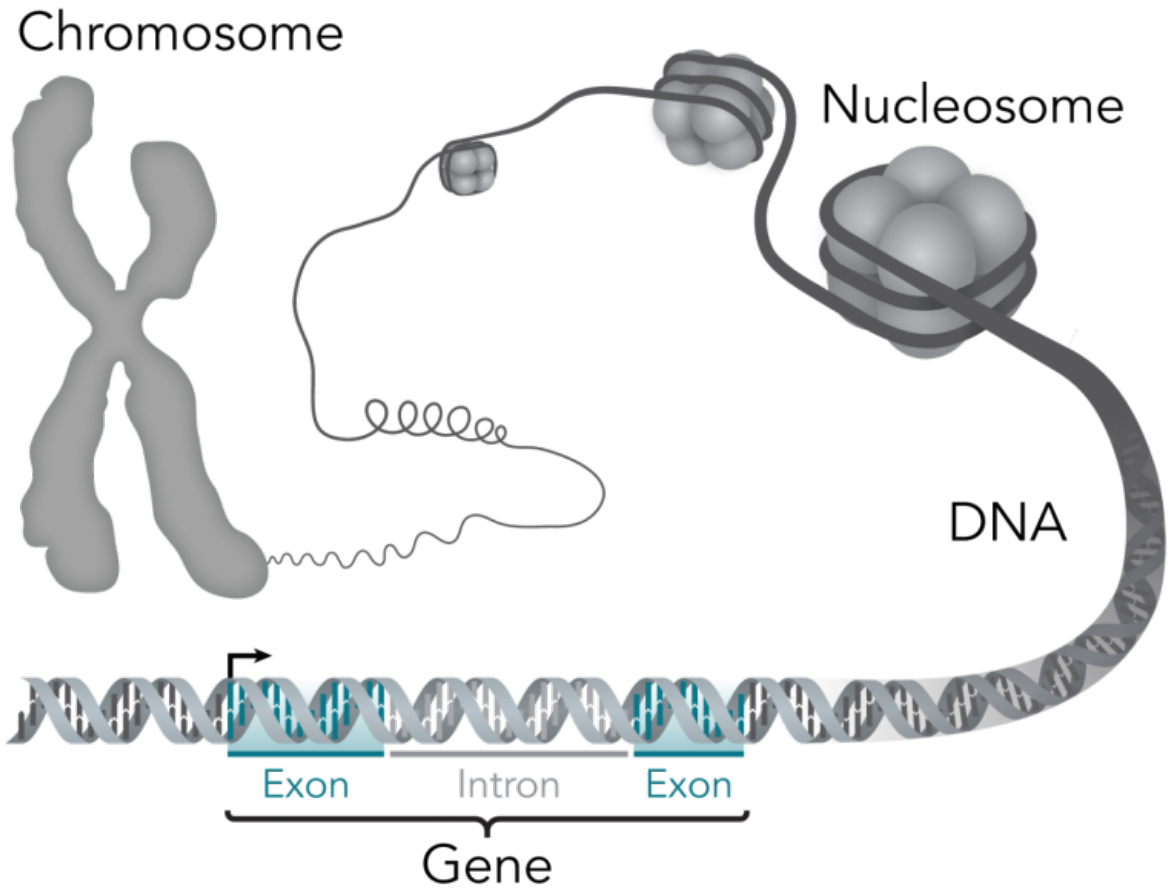

This stylistic diagram shows a gene in relation to the double helix structure of DNA and to a chromosome (right). The chromosome is X-shaped because it is dividing. Introns are regions often found in eukaryote genes that are removed in the splicing process (after the DNA is transcribed into RNA): Only 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 Splettstoesser/Wikipedia/CC BY-SA 4.0

A new study, published in the open access journal *Genome Biology*, has identified a single gene (TLE6) which, when mutated, is responsible for human embryonic lethality at an earlier stage of development than has ever previously been documented.

Many genetic mutations exist which are fatal to developing embryos, but identifying them can be difficult, especially in the earliest stages of embryonic development. Identifying the genetic mutations responsible for embryo lethality provides new insights into the biological processes underlying embryonic development, and could also potentially lead to improved fertility treatments, by allowing scientists to screen and identify unviable embryos before implantation as part of IVF treatment.

Researchers from Alfaisal University, Saudi Arabia worked with two consanguineous families, where a marriage has taken place within the same family, in which several women were having persistent difficulties conceiving after IVF treatment. Using gene sequencing to study the embryos conceived by these women, the researchers found that a mutation in a single gene (TLE6) was halting the development of embryos at a very early stage.

Around one in seven people worldwide live in communities with consanguineous marriages, which is particularly common in North Africa, the Middle East and West Asia. In consanguineous marriages, there is often an increased prevalence of homozygous recessive genotypes. This makes the effects and characteristics of these genotypes much easier to identify and study, allowing researchers to gain new insights into genetic development.

Although previous studies have worked with consanguineous families to identify genes responsible for embryonic lethality in the late first

trimester and beyond, this is the first study to pinpoint a gene which works in the earliest stages of embryonic development at the pre-implantation stage. Although the mechanism by which mutation in TLE6 stops embryonic development is not clear, the results show that it is a maternal effect gene. TLE6 encodes a protein that forms a part of the sub-cortical maternal complex, which is vital to very early embryo development. It is likely that the observed embryonic lethal effects are linked to aberrant activity of this protein.

More information: Anas M. Alazami et al. TLE6 mutation causes the earliest known human embryonic lethality, *Genome Biology* (2015). DOI: 10.1186/s13059-015-0792-0

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