

Jumping genes discovery 'challenges current assumptions'

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Jumping genes do most of their jumping, not during the development of sperm and egg cells, but during the development of the embryo itself. The research, published this month in *Genes and Development*, "challenges standard assumptions on the timing of when mobile DNA, so-called jumping genes, insert into the human genome," says senior author Haig H. Kazazian Jr., MD, Seymour Gray Professor of Molecular Medicine in Genetics at the University of Pennsylvania School of Medicine.

Jumping genes - also called transposons - are sequences of DNA that can move or jump to different areas of the genome within the same cell. Jumping gene insertions do cause disease; however, it's not known how frequently diseases due to insertions can be inherited in the next generation. They are a rare cause of several [genetic diseases](#), such as hemophilia and Duchenne muscular dystrophy. In addition, transposon insertion into the genome could play a role in the development of cancer.

The current work alters thinking in the field of jumping genes, challenging standard assumptions that mobile DNA inserts only in eggs and sperm during their respective early development. In this study, the researchers found that insertions took place during embryogenesis after fertilization, at a time when nearly all of the changes can't be inherited. The researchers now purport, based on the study's findings, that many of those insertions occur in the early embryo, perhaps in the 4- or 8-cell stage.

The study looked at retrotransposons, one class of [jumping genes](#), with the L1 family the most abundant type of retrotransposon in the human genome. Retrotransposons move by having their DNA sequence transcribed or copied to RNA, and then instead of the genetic code being translated directly into a protein sequence, the RNA is copied back to DNA by the retrotransposon's own enzyme called reverse transcriptase. This new DNA is then inserted back into the genome. The process of copying is similar to that of retroviruses, such as HIV, leading scientists to speculate that retroviruses were derived from retrotransposons.

The L1 family of retrotransposons comprises about 17 percent of the human genome. Eventually, continuous jumping by retrotransposons expands the size of the [human genome](#) and may cause shuffling of genome content. For example, when retrotransposons jump, they may take portions of nearby gene sequences with them, inserting these where they land, and thereby allowing for the creation of new genes. Even otherwise unremarkable insertions of L1 may cause significant effects on nearby genes, such as lowering their expression.

Insertions can come from an L1 retrotransposon that is in the genome of the embryo or it can arise from an L1 that was in a parent and is not in the embryo. In the latter case, the L1 RNA from that parent is carried over through fertilization and inserts in the embryo. Insertions in the latter case are much less frequent than when the L1 itself is present in the genome of the embryo.

Despite L1 abundance in the genomes of mammals, relatively little is understood about L1 retrotransposition outside of the test tube. Using transgenic mice and rats containing human or mouse L1 elements, the team demonstrated abundant L1 RNA in both egg and sperm cells and embryos. However, the integration events usually occur during the development of the embryo rather than in egg or sperm cells and are not heritable.

They also demonstrated that L1 RNA transcribed in egg or sperm cells can be carried over through fertilization and integrate during embryogenesis, an interesting example of heritability of RNA independent of its encoding [DNA](#), creating somatic mosaicism during mammalian development. Soma are all cells other than egg or [sperm cells](#). A cell mosaic is an insertion that occurs after fertilization in which some cells have the insertion and others don't within the same tissue type. The mosaicism suggests a role for L1 in carcinogenesis and other diseases; for example cancerous growth may be initiated if insertions happen near an oncogene.

Source: University of Pennsylvania School of Medicine ([news](#) : [web](#))

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