'Jumping genes' could make for safer gene delivery system

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To move a gene from point A to point B, scientists and gene therapists have two proven options: a virus, which can effectively ferry genes of interest into cells, and a plasmid, an engineered loop of DNA that can do the same thing, albeit usually only on a short-term basis.

The catch is that viruses can be infectious and some types of viruses occasionally land in a target genome near an oncogene and raise the risk of cancer. Plasmids don't carry that risk, but they are not nearly as efficient at reproducing in cells, which is important when the goal is to integrate an introduced gene into the targeted cells of the organism or patient.

Now, however, the advent of new nonviral gene delivery systems using transposons, or "jumping genes," provides a safer alternative than viruses and more efficient delivery than plasmids, according to a publication by a University of Wisconsin-Madison molecular biologist and biological safety expert.

In an article in the current issue (September) of the journal *Applied Biosafety*, UW-Madison molecular biologist and associate biological safety officer Margy Lambert describes the gene delivery potential of transposons, stretches of DNA capable of jumping from one DNA molecule to another.

"Almost any application where you use viral vectors, you could use this technique," explains Lambert. "You can do a lot with it, and it is safer.

Problems with viral vectors are extremely rare, but the consequences can be severe."

Gene therapy, says Lambert, is one area where the new technology could make a name for itself. At present, there are an estimated 140 gene therapy trials under way in the United States. Most are aimed at treating fatal conditions such as cancer. Many use the less efficient plasmids as expression vectors, but some utilize viruses and no gene therapy treatment has been deemed safe or effective enough to merit Food and Drug Administration (FDA) approval as a routine therapy.

And sometimes unanticipated outcomes that belie the safety of current gene therapy strategies manifest themselves in tragedy. In July, for example, a 36-year-old Illinois woman died after experimental gene therapy treatment in which an engineered virus was injected into her knee to treat rheumatoid arthritis. The viruses used were engineered to suppress the immune system only in the knee. In the case of rheumatoid arthritis, the immune system is out of whack and is responsible for the painful inflammation characteristic of the condition. The FDA has placed the trial on hold while the cause of death is investigated.

Transposons, or jumping genes, argues Lambert, are a potentially safer way to go. "You lose the infectivity component and you minimize the insertional mutagenesis risk."

Techniques for targeting transposon vectors to regions of the genome devoid of cancer genes are being refined. Meanwhile, a key advantage over simple plasmids is that jumping gene technology is more effective at achieving stable expression of genes introduced into animal cells.

To harness jumping genes, researchers use an enzyme to ferry a desired DNA sequence from one DNA molecule to another inside a cell. The enzyme can then be turned off to stop genes from jumping.

Lambert acknowledged there are both technical and safety issues to be worked out in the development of transposon vectors before they could be tried in human therapy. But the use of such new vectors "offers a great opportunity to maximize the advantages and minimize the drawbacks of existing delivery systems."

Source: University of Wisconsin-Madison