

"Junk DNA" Creates Novel Proteins

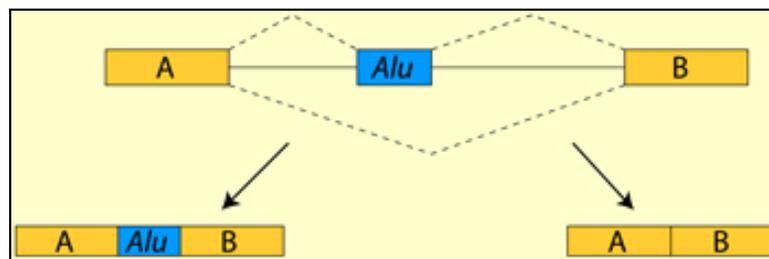
By [Nancy Touchette](#)

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DNA sequences long considered genomic garbage are finally getting a little respect. Researchers have figured out how short stretches of DNA that do not normally code for proteins worm their way into genes.

This can result in the production of abnormal proteins and lead to genetic diseases, such as Alport Syndrome, a rare kidney disease. But the sequences, sometimes called "junk DNA," have also allowed humans and other species to create new proteins in a process that has dramatically influenced evolution.

Gil Ast and his colleagues at Tel Aviv University in Israel have figured out how the sequences, known as *Alu* elements, are incorporated into genes to create novel proteins. More than 300,000 sequences are poised for insertion into genes—all that's needed is a single mutation.



Alu sequences lying between coding regions of genes can be spliced in (left) or out (right) during RNA processing to create many versions of the same gene.

Through a process called alternative splicing, humans create multiple versions of a gene and, consequently, multiple proteins. It's a way of constructing a new protein, while keeping a backup copy of the original version.

"This is a way to experiment with new structures," says Wojciech Makalowski of the Pennsylvania State University in University Park. "We create two versions of a protein and check which is better."

For example, the researchers found that the ADAR2 enzyme contains 40 amino acids in its active site that are derived from an *Alu* element. The addition changes the activity of the enzyme.

"Without this enzyme, we would die," says Ast. "The incorporation of an *Alu* into the enzyme changed its function, and we have evolved to rely on it."

One of the biggest surprises to come from the sequencing of the human genome was that we have about 30,000 genes but produce approximately 90,000 proteins. And 99 percent of our DNA codes for no protein at all. The new research provides a clue as to why we have so much "junk DNA." It also suggests an explanation of how so few genes can produce so many

proteins.

Alu elements are short sequences of DNA that are peppered throughout the genome. They comprise approximately ten percent of the entire genome—ten times more than all the genes put together. Until recently, their function had remained a mystery.

But a few years ago, researchers studying splicing—a process by which pieces of RNA are cut and pasted together—discovered that many *Alu* sequences get inserted into existing coding sequences.

In the new study, published in *Science*, Ast and his colleagues discovered a unique sequence within most *Alu* elements that can be mutated at a single base to create a new splice site. Splice sites are special sequences recognized by the cellular machinery that cuts and pastes together RNA.

Although mice and human have the same number of genes, and many genes share the same functions, only primates have *Alu* sequences. Ast speculates that these sequences have played a key role in our evolution.

“We believe that *Alus* allowed the shuffling of genetic information that may have led to the evolution of primates,” says Ast. “They may contribute to a lot of disorders we don’t even know about yet. But they have also created genetic diversity.”

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[Lev-Maor, G. *et al.* The birth of an alternatively spliced exon: 3' splice-site selection in *Alu* exons. *Science* **300**, 1288-1291 \(May 23, 2003\).](#)

[W. Makalowski. Not junk after all. *Science* **300**, 1246-1247 \(May 23, 2003\).](#)

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