

## A hidden code in our DNA explains how new pieces of genes are made

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Credit: AI-generated image (disclaimer)

We're all here because of mutations. Random changes in genes are what creates variety in a species, and this is what allows it to adapt to new environments and eventually evolve into completely new species. But most random mutations actually disrupt the functions of our genes and so are a common source of genetic diseases.



This ambiguity creates a great challenge. On the one hand, <u>mutations</u> are needed for biological innovation, and on the other hand they cause diseases. How does nature resolve this conflict? Recent research by me and my colleagues suggests that one answer could lie in a genetic code that allows evolution to innovate while minimising the disruption this can create.

This code is hidden within a part of <u>our genome</u> (the complete set of our genetic material) known as <u>repetitive genetic elements</u>, which we now know plays a key role in evolution. These elements are sequences within our DNA that can make many copies of themselves. In order to build the proteins that our bodies need, our cells <u>take instructions</u> from our DNA by transcribing it into a similar molecule called RNA. But in rare cases, instead of building a protein, some RNA molecules convert back into DNA and insert themselves at new locations in our genome.

In this way, the repetitive elements can continually create new copies of themselves. As a result, the <u>human genome</u> contains <u>thousands of</u> <u>repetitive elements</u> that are not present in any other species because they have copied themselves since humans evolved.

But repetitive elements aren't just useless copies. Barbara McClintock, the scientist who discovered them in 1948, showed <u>they can act as</u> <u>switches</u> that switch genes on and off in maize. This was initially thought to be an obscure phenomenon with no relevance for humans. Yet now it has become clear that repetitive elements are an important toolkit for evolution. By turning genes on and off, the repetitive elements can influence what characteristics a species evolves. They have been useful for biological innovations, such as evolution of <u>pregnancy in mammals</u>.

Perhaps the most elegant example of this is in the <u>evolution of the</u> <u>peppered moth</u>. This moth normally has light-coloured wings, but during Britain's industrial revolution a repetitive element inserted itself into the



gene that controls the colour pattern of the wings. As a result, a black strain of the peppered moth evolved and this allowed it to blend in and escape its predators amid the polluted environment.



Credit: Dan Cristian Pădureț from Pexels

So what does all this have to do with managing the disruption of mutations? Our research looks at the repetitive elements that were copied within the genome of the ancestors of modern primates. There are over 1.6m of these "<u>Alu elements</u>" dispersed all over the human genome, and some of them have accumulated <u>random mutations</u> that



enabled them to become functional parts of our genes.

We have <u>found a code</u> in the RNA that controls Alu elements hiding inside <u>human genes</u>. This code combines competing positive and negative molecular forces, like a ying and yang in our cells. It is well known that <u>competing molecular forces</u> control many aspects of our genes. In our case, the positive force (acting through the protein called U2AF65) allows the Alu elements to remain part of RNA and the resulting protein. The negative force (acting through the protein called hnRNPC) opposes this and removes the elements from the RNA.

We've known for decades that evolution <u>needs to tinker</u> with genetic elements so they can accumulate mutations while minimising disruption to the fitness of a species. Our most recent research, <u>published in the</u> <u>journal eLife</u>, looked at over 6,000 Alu elements to show that our code does exactly this.

The two forces are tightly coupled in evolution, so that as soon as any mutations make the ying stronger, the yang catches up and stops them. This allows the Alu elements to remain in a harmless state in our DNA over long evolutionary periods, during which they accumulate a lot of change via mutations. As a result, they become less harmful and gradually start escaping the repressive force. Eventually, some of them take on an important function and became indispensable pieces of human genes.

To put it another way, the balanced forces buy the time needed for mutations to make beneficial changes, rather than disruptive ones, to a species. And this is why evolution proceeds in such small steps – it only works if the two forces remain balanced by complementary mutations, which takes time. Eventually, important new molecular functions can emerge from randomness.



These findings tell us that humans are not a fixed pinnacle of evolution. Our genomes are like those of any other species: a fluid landscape of DNA sequences that keep changing. This explains how our genome can host its ever-changing repetitive elements despite their potential to disrupt the existing order in our cells.

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