Sticky Notes in Our DNA and the Implications for Human Health

Until the 1980s, researchers thought they had a decent grasp of what made us human, that is, DNA, genes, and chromosomes[1]. We knew DNA carried biological instructions, that genes could switch on or off, and that certain sequences coded for the traits that are passed down generations.

You probably already know that DNA is a code made up of four letters, A, T, C, and G, arranged in a specific sequence across approximately three billion base pairs. These sequences form genes, which tell cells how to build proteins. Proteins, in turn, do the heavy lifting in the body: building tissue, carrying signals, and regulating just about everything.

But not all genes are active at all times in all locations. A gene responsible for making insulin, for example, should be active in the pancreas but not in your hair. Similarly, our blood cells are different from our brain cells even though they carry the same DNA. So, how does your body know when and where to use which gene?

Methylation is one part of a larger system of gene regulation called epigenetics, that is, the changes that affect how genes work without altering the DNA code itself. It involves adding a small chemical tag, a methyl group, to DNA[1]. This tag often attaches to a C base (cytosine) when it precedes a G base (guanine) in a pairing known as CpG.

If DNA is a movie script with thousands of pages, the methylation tag is the director's sticky notes in the margins. "Don't say this line too loud," "let your voice drift in and out", or "skip this scene entirely." In this context, the note might say, "ignore this gene." And just like that, the gene remains quiet.

This *quieting* isn't always bad. In fact, it is necessary. Methylation helps shape development in the womb, determines which genes are active in different tissues, and keeps potentially harmful sequences (like ancient viruses hiding in our genome) turned off. It also plays a role in a process called X-chromosome inactivation, which is how female cells silence one of their two X chromosomes to maintain balance with male cells[1,2].

But things get murky when methylation doesn't go as planned.

In recent years, scientists have linked faulty methylation to many diseases. One of the most well-known is cancer. In many tumours, excess methylation silences genes that normally suppress abnormal growth, while genes that promote abnormal cell division go unchecked[3].

What's remarkable is how subtle these chemical tags are, how their effects vary depending on their location in the DNA and in different cells, and how difficult they are to study. Traditional methods of studying DNA, called sequencing technologies, read short snippets of the massive script at a time and require a separate technique to read the sticky notes or methylation tags before even attempting to interpret whatever message may be present. On the other hand, emerging methods read long stretches, sometimes tens of thousands of letters at once, and can detect methylation patterns directly, without needing extra steps[4].

This means researchers can now study methylation across entire genes or regions, track how its patterns differ between healthy and diseased tissue, and even begin to ask questions about how methylation changes over time.

Why does it change with age? Can lifestyle or environment alter it in meaningful ways? How reversible is it? Can we "edit" methylation the way we are now able to edit genes? It is one thing to know a note has been left on a page; it's another to know who wrote it, when, and why, and how long that note is meant to exist.

So, what controls methylation?

There is no definite answer yet. Some research has reported that environmental factors like diet and stress may influence methylation. Other growing evidence suggests that genetic variants, that is, misspellings or omissions in the expected order of ATCG of the DNA, can affect the spread of methylation[5,6]. These variants may be inherited from a parent or acquired during a person's life, and if any of them can nudge methylation in a peculiar or dangerous direction, it might determine what disease a person is likely to get, how severely they might be affected, and what kind of treatment would work.

Why should any of this matter? Because understanding methylation could reshape how we diagnose and treat genetic diseases. Already, researchers are developing "epigenetic clocks" that use methylation to estimate biological age, offering clues about health beyond what's written in your birth certificate. In cancer, identifying methylation patterns unique to tumour cells could lead to earlier detection or more personalised treatment approaches. Some "epigenetic therapies" even aim to reverse harmful methylation, essentially peeling off the sticky notes that silence important genes.

We're not there yet, but the potential for human health that could result from learning to read, and perhaps "write" methylation, is extensive.

References

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