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NTU scientists map key part of human DNA associated with ageing and cancer

Their work paves the way for a deeper understanding of longevity, and the development of better anti-cancer drugs. ST PHOTO: LIM YAOHUI

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SINGAPORE - In a world first, scientists from Nanyang Technological University (NTU) have mapped out the molecular structure of a key part of human chromosomes called telomeres.

Their work paves the way for a deeper understanding of longevity, and the development of better anti-cancer drugs.

Telomeres are protective caps at the ends of chromosomes, which are made of DNA and proteins.

Like the plastic tips on the ends of shoelaces, the telomeres cap and protect the ends of the chromosome from damage. Telomeres also shorten every time a cell divides, till they no longer can - and the process is linked to ageing and cancer.

The researchers' advance in genetic research was published in September in the journal Nature, after eight years of work.

The research team found that telomeres are not structured in the zig-zag formation as depicted in textbooks, but rather in columns and a spring formation.

This leaves a part of the DNA exposed and unprotected, making it more susceptible to damage than previously thought, Professor Lars Nordenskiold, the chair of NTU's School of Biological Sciences who led the team of 11 in the study, told a media briefing on Thursday.

The discovery will help researchers understand how telomeres, despite their essential role in preventing damage to DNA, are themselves hotspots for DNA damage, said Prof Nordenskiold.

Dr Aghil Soman, an NTU research fellow who co-authored the study, emphasised that the genetic model had been derived from organic human DNA, instead of artificial DNA commonly used in such studies for its more stable properties.

"It is the first insight of the telomeric chromatin structure which has been missing for decades. It is a kind of a black box for a long, long time.

"It also provided the first insight into how telomeric DNA is being packaged in our body," said Dr Soman.

The researchers added that previous studies into the structure of telomeric DNA stalled due to the challenges of replicating it, owing to its chemical instability and repetitive nature.

However, they overcame this by improving on the existing method of replicating DNA in Escherichia coli (E. coli) bacteria so that it would work for human telomeres and create chains of telomeric DNA long enough for a full picture of its structure, they said.

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Dr Soman said with the molecular structure mapped, scientists can unlock, for instance, more secrets to longevity.

"One example of this is a protein, Sirt6, which can extend the lifespan of certain living things by around 30 per cent, but nobody knows how this mechanism happens. Our work gives a template to study the structural mechanism by which this extends the lifespan."

Another potential application is to design anti-cancer drugs that solely target telomeres with high affinity, said Dr Soman, explaining that cancer cells escape death by finding ways to elongate their telomeres.

"This would help overcome the limitation of drugs like cisplatin, which, although kills cancer cells in humans, also causes damage to the kidneys, liver and brain."

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