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Japan suggests DNA deletion to treat mitochondrial diseases

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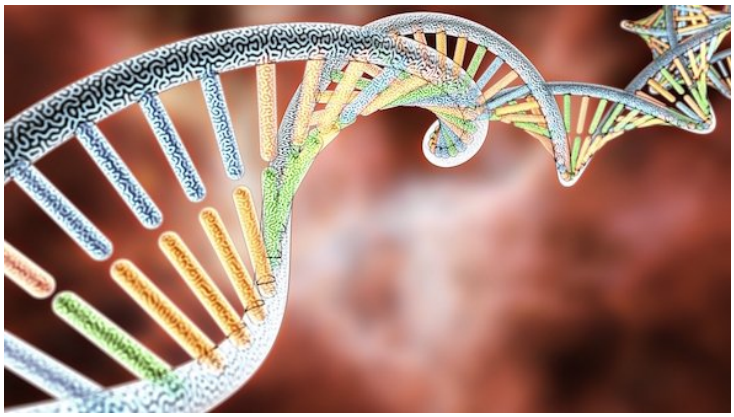
To lead to better treatments



Mutant DNA sequences inside cellular mitochondria can be eliminated using a bespoke chemical compound. The approach, developed by scientists at Kyoto University's Institute for Integrated Cell-Material Science (iCeMS) in Japan, could lead to better treatments for mitochondrial diseases.

In some mitochondrial diseases, mutated DNA and normal DNA co-exist. "This state is called heteroplasmy," explains Kyoto University's Takuya Hidaka, the first author of the study. "To cure mitochondrial diseases, we need to be able to remove mutant mitochondrial DNA from cells."

Current approaches for such mitochondrial diseases are problematic, explains iCeMS bioengineer Ganesh Namasivayam Pandian, who led the study. Some involve injecting genetic material into cells, which could lead to unwanted alterations. In others, antioxidant drugs are administered to reduce the impacts of the mutant DNA, without addressing the core mutation.

Pandian worked with iCeMS chemical biologist Hiroshi Sugiyama, Takuya Hidaka and colleagues to develop a compound made of a mitochondria-penetrating peptide (MPP) bound to a polymer, called a pyrrole-imidazole polyamide (PIP), which can be modified to target a specific DNA sequence. These were then attached to an existing anti-cancer drug, called chlorambucil.

"Our proof-of-concept study can be extended to mitochondrial mutations that cause diseases like Leber's hereditary optic neuropathy, an inherited form of vision loss that currently has no proven treatment," says Pandian.