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IIT-B designs DNA-based strategy to make drug-resistant bacteria responsive to antibiotics again

27 March 2026 | News

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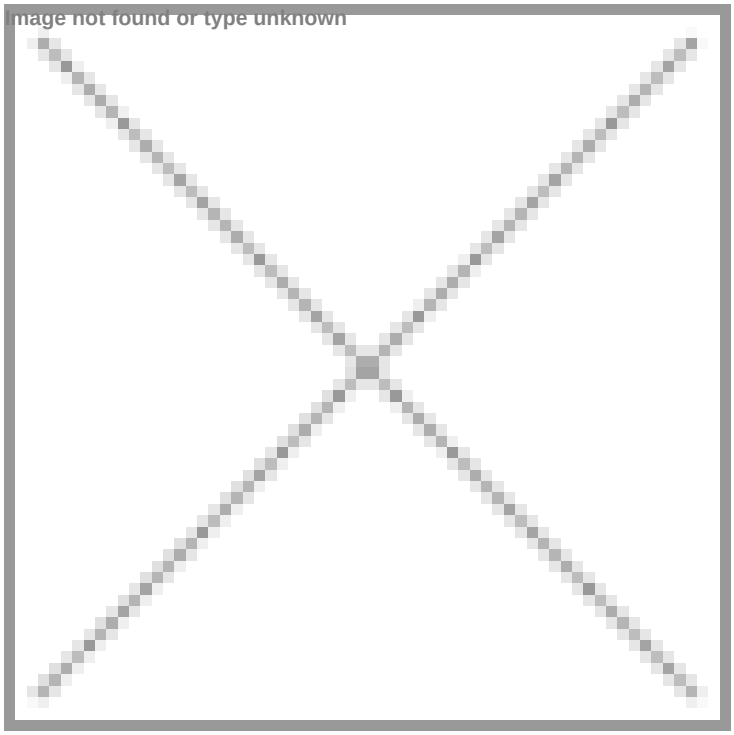

When new drugs are introduced, microbes continue to adapt, and resistance can emerge quickly. This reality has pushed scientists to rethink not only how antibiotics kill microbes, but how to stop bacteria from disarming them in the first place.

Two recent studies from the Indian Institute of Technology Bombay (IIT-B), from the Department of Chemistry, have presented a different strategy. Instead of developing yet another antibiotic, the team focused on protecting the ones that already exist. Their work, published across two complementary papers, uses short DNA sequences that can bind to and block the enzymes that bacteria use to resist antibiotics. By stopping these enzymes from working, the researchers were able to make resistant bacteria respond once again to common antibiotics.

The researchers have focused on specially identified short strands of DNA known as aptamers. Unlike the conventional drugs, aptamers are made up of nucleic acids, synthetically produced, relatively stable, and easier to modify. Thus, they make attractive candidates for therapeutic applications. To generate DNA aptamers that bind to a specific Erm enzyme known as Erm42, the researchers used a laboratory method called SELEX. This process allows researchers to sift through millions of random DNA sequences and isolate the ones that bind most strongly to a specific target. After multiple rounds of selection and testing with techniques like gel-monitoring assays and surface plasmon resonance, the team identified two aptamers that attached tightly to the enzyme Erm42.

While the DNA aptamers worked well in laboratory assays, another challenge remained. It is known that DNA molecules, when administered alone, are vulnerable to nuclease degradation and often struggle to cross bacterial membranes. This makes it difficult for them to enter inside the bacteria.

To address this, in the second study, the researchers explored a liposome-based delivery system. The researchers conducted studies that confirmed that the aptamer-loaded liposomes were stable and appropriately sized for biological applications.

In the future, if developed for therapeutic use, the aptamer could be given alongside existing antibiotics. By blocking the resistance mechanism, the engineered aptamer could help restore the antibiotic’s effectiveness.