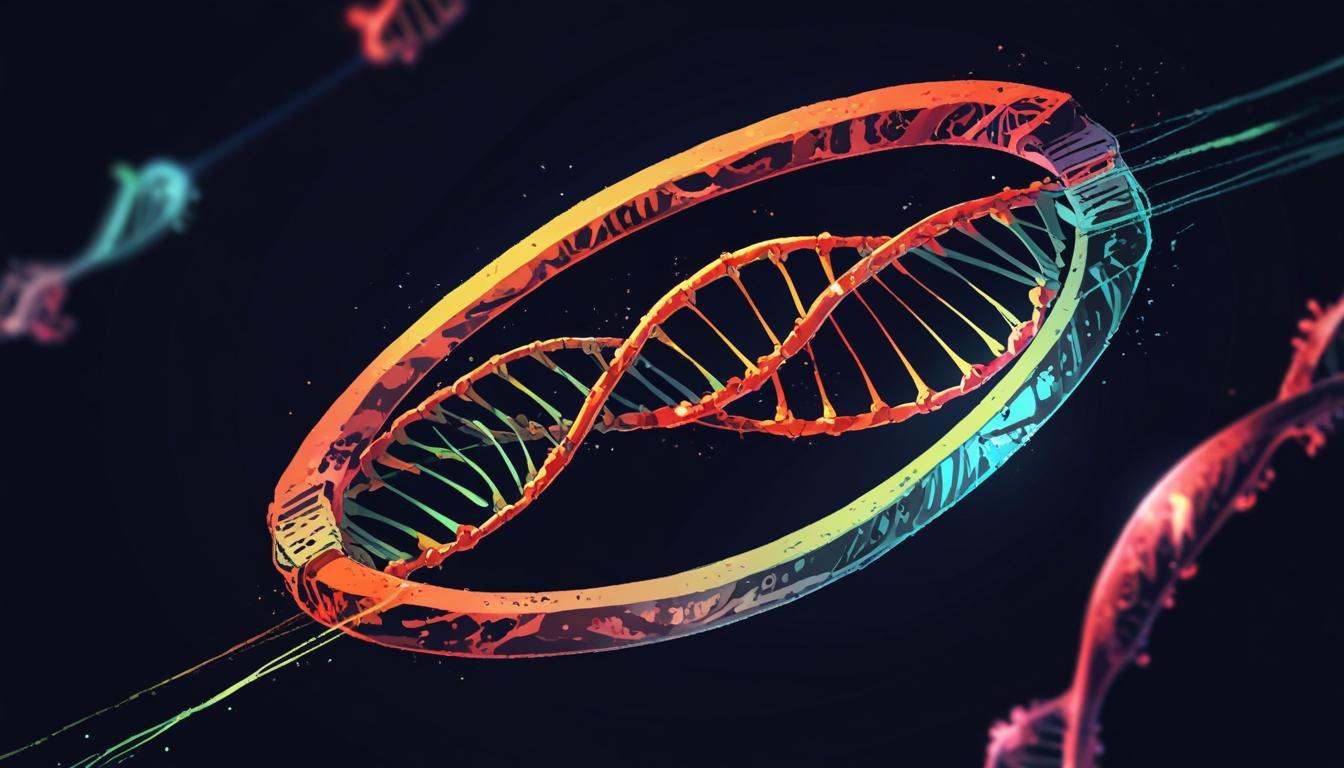
# Birmingham scientists unlock new genetic code advancing antibiotic resistance cure



# Groundbreaking Research in Antibiotic Resistance: Birmingham Scientists Uncover Genetic Code for Plasmid Curing

In a significant advancement in the battle against antibiotic resistance, scientists at Birmingham’s School of Biosciences have made crucial strides in understanding a technique known as plasmid curing. This innovative method aims to ‘displace’ antibiotic resistance genes from bacteria, a pressing concern as these genes pose a growing risk to public health worldwide.

Plasmids, which are small, circular DNA molecules found in many bacteria, facilitate the rapid sharing of crucial genes among bacterial populations. While they can harbour advantageous traits, including those that confer antibiotic resistance, their presence can severely diminish the effectiveness of current treatments. Professor Chris Thomas, leading the research, has been investigating the mechanics of plasmid curing for years. His team has successfully created "multi-copy" plasmids, which allow for the efficient displacement of unwanted plasmids carrying resistance genes. This breakthrough has culminated in a patented process that could reshape approaches to managing antibiotic resistance in bacterial infections.

The complexity of developing a more generalized “probiotic” system capable of spreading through the gut highlighted challenges for Professor Thomas’s group. They discovered that to ensure effective displacement, these systems required higher numbers of plasmid copies, a process termed “potentiation.” This finding underscores the intricate balance between speed and efficiency when designing genetic tools aimed at combating resistance.

In their recent publication in *Nucleic Acids Research*, the researchers identified critical components within the F plasmid, typically found in E. coli, which are essential for effective plasmid displacement. Professor Thomas elaborated on this, stating, “We have identified the part of the plasmid that is absolutely essential for it to work in plasmid displacement, and built a completely new ‘curing cassette’ that does not need to be potentiated.” This advancement not only simplifies the engineering process but also enhances its applicability in diverse contexts.

The implications of this research are profound, especially considering the role of animals as reservoirs for antibiotic resistance genes that can be transmitted to humans. The team’s ongoing work in animal models is promising, with preliminary findings offering insights into how these plasmids can be made to function effectively in realistic biological settings. “We now understand better how to make curing plasmids that work in a real context,” stated Professor Thomas, emphasising the potential for real-world application.

Beyond this groundbreaking work, the study of plasmid curing is gaining momentum in the scientific community. The emergence of novel systems, such as CRISPR-Cas9 technologies, showcases additional promising methodologies. In one recent study, a CRISPR-based system named pCasCure demonstrated over 94% efficiency in eliminating specific resistance genes from clinical isolates, underscoring an exciting avenue for clinical application in treating infections caused by resistant bacteria. Similarly, VADER, a synthetic biology system, aims to address antibiotic resistance in environmental contexts by targeting plasmid-borne resistance genes.

However, the road to effective plasmid curing is fraught with complexities. Researchers caution that while various methods, including the use of intercalating agents and specific antibiotics, have shown some success in lab settings, the potential for promoting further resistance through deployment in clinical settings remains a critical concern. Careful consideration and rigorous testing will be essential to ensure that these strategies do not inadvertently enhance the very problems they seek to address.

As Birmingham scientists collaborate with institutions such as Harper Adams University and Surrey University Veterinary School, the potential for developing innovative, ingestible probiotics to combat both animal and human antibiotic resistance is on the horizon. The imperative need for effective solutions in this fight against antibiotic resistance has never been clearer, and ongoing research in plasmid curing may just hold the key to future breakthroughs.

The promise of these findings could not only revolutionise how we manage antibiotic resistance but also inspire innovative approaches within the broader field of microbial genetics, offering hope in a realm of increasing concern for global health.

## Reference Map:

* Paragraph 1 – [[1]](https://news.google.com/rss/articles/CBMiwAFBVV95cUxPM1BNd0QyRkRZWUh5R3JrSDNocU9lRFUwd1ItRHJKN2Y3VGxDZE02WVp3X0JxeERKaXN1YlBDZEQ5SW4ycDFJT1hMTUUwNWg5czR5UHBzM2U4SFotekgzRWl1ZG5xNnBacmFIaVZNNHFIVUJqbDMwblVxRkk0WE41ejlRUmtqMGRsd2tlX1NyUmtqMzh2WjVuRnBnOFczb0tWQkxYQ2VtMFAtdmpQWWJoSjhIUlRDMUVLb0E4MWs1Zjk?oc=5&hl=en-US&gl=US&ceid=US:en)
* Paragraph 2 – [[1]](https://news.google.com/rss/articles/CBMiwAFBVV95cUxPM1BNd0QyRkRZWUh5R3JrSDNocU9lRFUwd1ItRHJKN2Y3VGxDZE02WVp3X0JxeERKaXN1YlBDZEQ5SW4ycDFJT1hMTUUwNWg5czR5UHBzM2U4SFotekgzRWl1ZG5xNnBacmFIaVZNNHFIVUJqbDMwblVxRkk0WE41ejlRUmtqMGRsd2tlX1NyUmtqMzh2WjVuRnBnOFczb0tWQkxYQ2VtMFAtdmpQWWJoSjhIUlRDMUVLb0E4MWs1Zjk?oc=5&hl=en-US&gl=US&ceid=US:en), [[5]](https://pmc.ncbi.nlm.nih.gov/articles/PMC6199537/)
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* Paragraph 4 – [[3]](https://journals.asm.org/doi/full/10.1128/aem.00053-23), [[2]](https://journals.asm.org/doi/10.1128/aac.00843-20)
* Paragraph 5 – [[1]](https://news.google.com/rss/articles/CBMiwAFBVV95cUxPM1BNd0QyRkRZWUh5R3JrSDNocU9lRFUwd1ItRHJKN2Y3VGxDZE02WVp3X0JxeERKaXN1YlBDZEQ5SW4ycDFJT1hMTUUwNWg5czR5UHBzM2U4SFotekgzRWl1ZG5xNnBacmFIaVZNNHFIVUJqbDMwblVxRkk0WE41ejlRUmtqMGRsd2tlX1NyUmtqMzh2WjVuRnBnOFczb0tWQkxYQ2VtMFAtdmpQWWJoSjhIUlRDMUVLb0E4MWs1Zjk?oc=5&hl=en-US&gl=US&ceid=US:en), [[2]](https://journals.asm.org/doi/10.1128/aac.00843-20)
* Paragraph 6 – [[4]](https://www.mdpi.com/2079-6382/11/6/747)
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2. <https://journals.asm.org/doi/10.1128/aac.00843-20> - This study presents a CRISPR-Cas9-based system, termed pCasCure, designed to eliminate carbapenemase genes and plasmids in clinical Enterobacteriaceae isolates. The system demonstrated high efficiency in curing bla\_KPC, bla\_NDM, and bla\_OXA-48 genes across various species, including Klebsiella pneumoniae and Escherichia coli, with over 94% curing efficiency. Additionally, pCasCure effectively removed several epidemic carbapenem-resistant plasmids by targeting their replication and partitioning genes. The curing of these genes restored antibiotic susceptibility, with a significant reduction in minimum inhibitory concentrations (MICs) observed in all tested isolates. The study underscores the potential of CRISPR-Cas9-mediated plasmid curing as a strategy to combat antibiotic resistance in clinical settings.
3. <https://journals.asm.org/doi/full/10.1128/aem.00053-23> - The article introduces VADER, a synthetic biology system leveraging CRISPR-Cas immunity to degrade antibiotic resistance genes (ARGs) in environmental contexts. VADER employs a one-plasmid system with constitutive functions to target and eliminate ARGs, demonstrated by its ability to degrade plasmid-borne ARGs in Escherichia coli and Pseudomonas aeruginosa. The system utilizes an artificial conjugation machinery, IncP, for delivery via conjugation, showcasing its potential for wastewater treatment processes. The study highlights VADER's promise as an environmentally aimed solution for mitigating the spread of ARGs, offering a novel approach to address antibiotic resistance in environmental settings.
4. <https://www.mdpi.com/2079-6382/11/6/747> - This research investigates the efficacy of non-thermal atmospheric pressure plasmas in degrading antibiotic resistance genes (ARGs) and inactivating antibiotic-resistant bacteria (ARB). The study exposed E. coli strains harboring resistance genes to plasma generated in a sterile saline solution. Results indicated a significant reduction in E. coli levels and a substantial decrease in the presence of ARGs, including tetA, tetR, aphA, and tnpA, after plasma treatment. The findings suggest that non-thermal atmospheric pressure plasmas present a promising alternative for eliminating ARGs and ARB, particularly in wastewater treatment plants and aquatic environments, offering a potential strategy to combat the spread of antibiotic resistance.
5. <https://pmc.ncbi.nlm.nih.gov/articles/PMC6199537/> - This article discusses various strategies to combat antimicrobial resistance, focusing on anti-plasmid approaches and plasmid curing. It highlights the use of aminocoumarin and quinolone antibiotics as laboratory tools for plasmid curing, noting their effectiveness in Gram-positive and certain Gram-negative bacteria. However, the study cautions against the clinical application of these antibiotics for plasmid curing due to potential selection pressures that could maintain or enhance resistance. The article also explores the use of CRISPR/Cas systems for plasmid curing, emphasizing their potential in removing plasmid DNA from bacteria and targeting specific antibiotic resistance genes, offering a promising direction in antimicrobial resistance management.
6. <https://www.frontiersin.org/articles/10.3389/fmicb.2020.00761/full> - This article examines the use of intercalating agents, such as ethidium bromide, acridine orange, and acriflavine, in the removal of resistance plasmids from bacteria. The study demonstrates that these agents can effectively eliminate resistance plasmids in both Gram-positive and Gram-negative bacteria, including Lactobacillus acidophilus, E. coli, and Enterobacter aerogenes. However, the use of intercalating agents is associated with potential mutagenic effects, and their efficiency may be reduced against large plasmids. The article also discusses the use of biocides like triclosan and fusidic acid for plasmid curing, noting their success in removing resistance plasmids in various bacterial species, including E. coli and methicillin-resistant S. aureus.
7. <https://news.google.com/rss/articles/CBMiwAFBVV95cUxPM1BNd0QyRkRZWUh5R3JrSDNocU9lRFUwd1ItRHJKN2Y3VGxDZE02WVp3X0JxeERKaXN1YlBDZEQ5SW4ycDFJT1hMTUUwNWg5czR5UHBzM2U4SFotekgzRWl1ZG5xNnBacmFIaVZNNHFIVUJqbDMwblVxRkk0WE41ejlRUmtqMGRsd2tlX1NyUmtqMzh2WjVuRnBnOFczb0tWQkxYQ2VtMFAtdmpQWWJoSjhIUlRDMUVLb0E4MWs1Zjk?oc=5&hl=en-US&gl=US&ceid=US:en> - This article reports on research conducted by scientists at the University of Birmingham, who have identified essential genetic components for a method known as plasmid curing. Plasmids are small, circular DNA strands that enable bacteria to share beneficial genes, including those conferring antibiotic resistance. Professor Chris Thomas and his team have developed engineered 'multi-copy' plasmids to efficiently displace unwanted resistance-carrying plasmids. Their work has led to a patented method for plasmid displacement. Further research has focused on creating a 'probiotic' system using 'low-copy' plasmids to spread through the gut, necessitating the engineering of plasmids to have a higher number of copies for efficient displacement. The team has identified a critical part of the F plasmid, commonly found in E. coli, essential for effective plasmid displacement. Their findings, published in Nucleic Acids Research, have led to the development of a new 'curing cassette' that does not require potentiation. The research is progressing to investigate the spread of plasmids in animal gut models, with encouraging results. The team is collaborating with institutions like Harper Adams University, Surrey University Veterinary School, and the Animal and Plant Health Agency to develop ingestible probiotics aimed at combating antibiotic resistance in gut bacteria in both animals and humans.