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â??CGT is transformative, offering a programmable way to overcome bacterial resistanceâ?•

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The application of cell and gene therapies (CGTs) is moving beyond oncology and rare diseases, with antimicrobial resistance (AMR) being one of the areas. Through its research arm, the Venus Medicine Research Centre (VMRC), Panchkula-based Venus Remedies is utilising CRISPR-based and gene-modulating approaches aimed at selectively disabling high-impact bacterial resistance mechanisms such as metalloâ??betaâ??lactamases, efflux pumps, and membrane porins. Saransh Chaudhary, President, Global Critical Care, Venus Remedies, and CEO, Venus Medicine Research Centre (VMRC) interacted with BioSpectrum to reveal how CGTs can help reduce the global burden of AMR in the near future.

Cell and gene therapies (CGTs) are often associated with oncology and rare diseases. What's the evolving scope of CGT in modern medicine today?

Cell and gene therapies are moving well beyond their original territory of oncology and rare monogenic disorders. We are now seeing serious research into CGT for autoimmune conditions, metabolic disorders, regenerative medicine, and increasingly for infectious diseases. Gene therapies are being investigated for viral infections like HIV and hepatitis, and more recently for multidrug-resistant bacterial pathogens. The clinical relevance of these platforms is broadening significantly.

A big part of this evolution is CRISPR-based precision editing, which allows selective modification of disease pathways at the genomic level with increasingly manageable off-target risks. CGTs are no longer just about replacing a faulty gene. They are enabling immune modulation, cellular reprogramming, and host-directed therapies. As manufacturing improves and regulatory frameworks catch up, these are transitioning from niche interventions to platforms with much wider applicability.

Antimicrobial resistance is increasingly being described as a silent pandemic. Do you believe CGT offers a promising new approach to tackling AMR?

The fundamental problem with conventional small molecule antibiotics is that they are essentially hit and trial. You discover a compound, test it against a panel of pathogens, and hope it works. But resistance evolves through very specific genetic mechanisms, and the pace at which bacteria acquire and share resistance genes far outstrips our ability to discover new molecules through traditional chemistry. We are simply not keeping up.

What makes CGT transformative, if successful, is that it offers a programmable way to overcome resistance. CRISPR-Cas systems, for instance, can be designed to selectively disable specific resistance genes in bacterial genomes, restoring susceptibility to existing drugs. You are no longer screening compound libraries hoping for a hit. You are reading the resistance mechanism and programming a response to it. That is a fundamentally different paradigm.

If, as a community, we are able to crack the science of reliably delivering plasmids, oligonucleotides, mRNAs, and other genetic payloads to bacterial cells in vivo, it would completely change how we develop and treat infections. The potential is enormous. We are not there yet, but the direction is clear and the early science is encouraging.

What are the key translational challenges in applying CGT approaches to infectious diseases particularly around delivery, scalability, and cost?

The single biggest translational challenge is delivery. We can design elegant gene-editing constructs in the lab, but getting oligonucleotides, plasmids, or mRNA payloads to reliably reach bacterial cells inside a living host remains an unsolved problem. That is the bottleneck.

It is important to understand that bacteria are fundamentally different from mammalian cells when it comes to delivery. In mammalian gene therapy, viral vectors such as AAVs and lentiviruses have become reasonably well-established delivery vehicles. But those approaches do not translate to bacteria. You cannot use a mammalian viral vector to deliver a payload into a bacterial cell. The biology is entirely different.

Bacteriophages are likely the more viable delivery route for bacterial targets. Phages naturally infect bacteria and can be engineered to carry gene-editing payloads such as CRISPR constructs. But phage-based delivery comes with its own set of limitations: narrow host range, immune clearance by the patient's own system, difficulty in scaling manufacturing, and the challenge of ensuring the payload reaches bacteria embedded in biofilms or deep tissue infections.

Beyond delivery, scalability and cost remain significant concerns. Manufacturing gene therapies is resource-intensive, and for infectious diseases that disproportionately affect low- and middle-income countries, the economics have to work at a very different price point than oncology CGTs. Long-term safety data are still emerging, and regulatory pathways for these novel modalities are still being defined. But fundamentally, if we solve the in vivo delivery problem, much else follows.

If CGT succeeds in addressing antimicrobial resistance at scale, how could it reshape the future of infectious disease treatment in India and globally?

If CGT-based approaches to AMR are successfully translated at scale, they would represent a genuine shift in how we manage infectious diseases. Instead of relying on broad-spectrum antibiotics that apply blunt selective pressure, gene-editing strategies can selectively eliminate resistance genes, restore susceptibility, and target specific pathogens without disrupting the broader microbiome. That is a fundamentally different model of care.

At the hospital level, integrating rapid pathogen genomics with targeted CGT interventions would allow clinicians to match therapy to the genetic profile of the infecting organism. This could reduce treatment failures, shorten ICU stays, and decrease mortality from multidrug-resistant infections. Critically, because these platforms are programmable, they can be redesigned as new resistance patterns emerge, rather than requiring entirely new drug discovery cycles.

Globally, the impact would go beyond individual patients. Precision microbial control could reduce indiscriminate antibiotic use, preserve microbiome integrity, and shift healthcare systems toward proactive resistance management.

For India, the implications are significant. We face a high AMR burden driven by dense healthcare settings, high infectious disease incidence, and inconsistent antibiotic stewardship. ICMR data shows common infections like pneumonia and bloodstream infections becoming increasingly difficult to treat. CGT-based precision therapies could help tertiary hospitals manage carbapenem-resistant and pan-resistant infections more effectively, while India's large patient base, expanding genomics infrastructure, and strong manufacturing ecosystem position the country to develop cost-optimised CGT therapeutics tailored to the infectious disease burden in low- and middle-income settings.

India has already shown it can innovate in the CGT space, with approvals like NexCAR19 demonstrating that indigenous development of advanced therapies is possible. Extending that capability to antimicrobial applications is a natural next step.

How is Venus Medicine Research Centre leveraging advanced technologies such as CGT, CRISPR, to address complex antimicrobial resistance mechanisms?

Studies show that CRISPR–Cas systems can be programmed to selectively cleave resistance genes within bacterial genomes, thereby re-sensitising pathogens to existing antibiotics. For example, recent reviews highlight the use of CRISPR variants such as Cas9, Cas3, and Cas12 to target resistance determinants in multidrug-resistant pathogens, including genes like blaNDM, oxa23, tetM, and ermB, demonstrating their ability to neutralise resistance pathways and restore antibiotic susceptibility.

Further research published in BMC Medicine explains that CRISPR-Cas systems can introduce precise double-strand breaks in bacterial DNA guided by RNA sequences, disrupting resistance genes, inhibiting quorum sensing, and preventing horizontal gene transfer, all of which are key drivers of antimicrobial resistance. These capabilities are expanding the role of gene editing from theoretical concepts to practical antimicrobial strategies aimed at dismantling resistance at its genetic origin.

Within this evolving landscape, the Venus Medicine Research Centre has been working on CGT-based approaches to antimicrobial resistance for over three years now, with significant milestones achieved at the lab scale. Our focus is on identifying conserved genomic regions associated with high-priority resistance pathways such as metallo-beta-lactamases, efflux pump systems, and outer membrane porins, and designing targeted gene-editing strategies to disable these determinants. It is a long journey, but one that can be hugely fulfilling and meaningful for patients if we get it right.

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