MEDIA RELEASE

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New route into cells could make gene therapies safer

Scientists from the Centenary Institute and the University of Sydney have made a landmark discovery that could lead to safer and more effective gene therapies for a range of serious genetic disorders including Duchenne muscular dystrophy, Pompe disease and haemophilia.

Published in the leading journal *Cell*, the study identifies a previously unknown gateway into human cells, a receptor called AAVR2, that gene therapy viruses use to deliver therapeutic genes. This newly uncovered pathway could allow lower doses of virus to be used in treatment, helping to reduce side effects and treatment costs, while improving patient outcomes.

Gene therapies typically use modified viruses, known as adeno-associated viruses (AAVs), to deliver healthy genes into the body. These treatments have the potential to be life-changing for patients, their families and caregivers. However, they frequently require high vector doses to achieve therapeutic effects which in some cases can trigger severe immune responses, lead to serious complications, or even death.

“We found that certain AAV types can use this newly identified receptor, AAVR2, to enter cells, providing an alternative to the previously known entry route,” said Dr Bijay Dhungel, lead author of the study and researcher at the Centenary Institute’s Centre for Rare Diseases & Gene Therapy and the University of Sydney.

“This discovery uncovers a completely new pathway for delivering genes into cells. Modulating this pathway can potentially make gene therapies safer, cheaper and more precise,” he said.

Using advanced genetic, biochemistry and molecular biology techniques, the researchers showed that AAVR2 plays a crucial role in helping several AAV types, including those widely used in patients, enter cells more efficiently.

“We not only identified this new receptor AAVR2 but also discovered how it binds to the viruses that deliver the genes,” said co-senior author Dr Charles (Chuck) Bailey, Head of the Centre for Rare Diseases & Gene Therapy at the Centenary Institute and researcher at the University of Sydney.

“We then went a step further and engineered a miniature version of the receptor and demonstrated that this significantly enhances how efficiently the gene therapy is taken up in human cells and tissues. We believe this knowledge will ultimately improve the accessibility of gene therapies to patients.”

The researchers say the findings have important implications for the future of gene therapy, offering new strategies to tailor treatments, lower required doses and potentially avoid immune-related complications that have limited some current approaches.

The discovery also advances scientific understanding of how therapeutic viruses interact with human cells. This is essential knowledge for developing the next-generation of safe, effective and precision-guided gene therapies.

The study was supported by funding from NSW Health, National Health and Medical Research Council (NHMRC), Therapeutic Innovation Australia, Tour de Cure, Cure the Future and Brandon Capital CUREator.

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Images:
Dr Chuck (Charles) Bailey and Dr Bijay Dhungel
https://drive.google.com/file/d/1FjkvTn1QvQNOsI8gNpbZj07D5KxvLwPa/view?usp=sharing

Publication:
An alternate receptor for adeno-associated viruses
https://www.cell.com/cell/fulltext/S0092-8674(25)00692-0

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The Centenary Institute is a world-leading independent medical research institute, closely affiliated to the University of Sydney and the Royal Prince Alfred Hospital. Our research spans the critical areas of cancer, cardiovascular disease, rare diseases, inflammation, infectious diseases, healthy ageing and biomedical AI. Our strength lies in uncovering disease mechanisms and applying this knowledge to improve diagnostics and treatments for patients.
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