MEDIA RELEASE

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New discovery could improve treatment for people with haemophilia A

Researchers from the Centenary Institute have uncovered a reason why some people with haemophilia A develop resistance to their critical treatment, paving the way for the development of more effective therapies.

Haemophilia A is a genetic disorder that impairs the blood's ability to clot, caused by a deficiency in a clotting protein called factor VIII (FVIII). Individuals with the condition are typically treated with regular FVIII infusions to aid clotting and prevent dangerous bleeding episodes. However, in some cases, the body's immune system recognises the infused protein as foreign and produces antibodies that block the treatment's effectiveness.

In a new study, researchers found that FVIII doesn't always form all of its stabilising chemical links, called disulfide bonds. These bonds help maintain the protein's proper shape. When some are missing, FVIII can take on slightly different shapes, making it more likely to trigger an immune response.

"Our research showed that antibodies from patients prefer to bind to these alternate forms of FVIII, interfering with how the treatment works," said lead study author Dr Diego Butera from the Centenary Institute's Centre for Cancer Innovations.

"This helps explain why some people develop resistance to treatment and opens the door to designing more stable forms of FVIII that are less likely to be targeted by the immune system," he said.

Senior study author, Professor Philip Hogg, researcher at the Centenary Institute's Centre for Cancer Innovations and the University of Technology Sydney said the findings were significant and could also have broader relevance beyond haemophilia A.

"By engineering FVIII to include more stable disulfide bonds that help better maintain its structure, we could potentially create versions of the protein that last longer and work more effectively for patients," said Professor Hogg.

"Additionally, our research highlights a broader principle—that therapeutic proteins can exist in multiple structural forms and understanding these variations is key to improving the safety and effectiveness of protein-based treatments."

The study was published in the medical journal *Blood Advances*.

[ENDS]

Image:
Professor Philip Hogg and Dr Diego Butera:
https://drive.google.com/file/d/1mYW-lQmo3VYDn8A-9qKW2FCblqESr78b/view?usp=sharing

Publication:
Patient anti-FVIII drug antibodies bind preferentially to a subset of FVIII covalent states
https://ashpublications.org/bloodadvances/article/doi/10.1182/bloodadvances.2025016474/536666/Patient-anti-FVIII-drug-antibodies-bind

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About the Centenary Institute
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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