



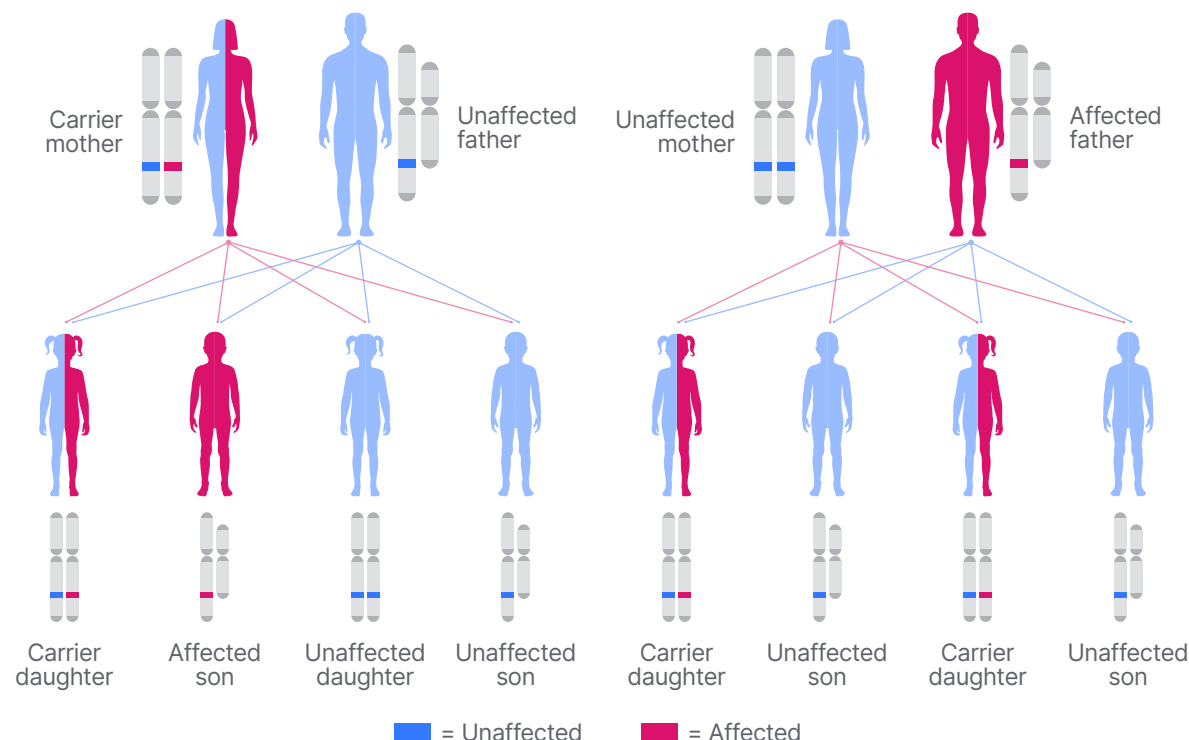
Gene Therapy: The New Frontier in Haemophilia Treatment

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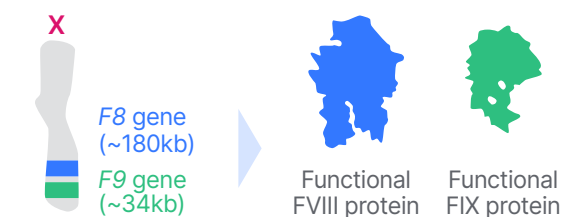
Introduction

Gene therapy is the introduction of an exogenous functional gene into cells to correct genetic disorders.

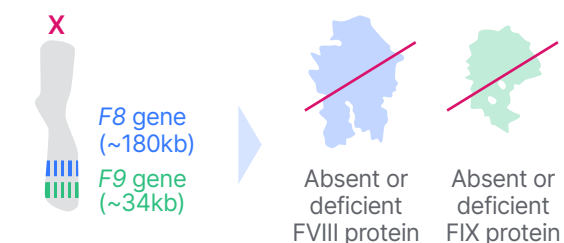
- Haemophilia is a rare, genetic condition caused by a deficiency in clotting factor proteins.¹
- It is an X-linked recessive inheritance, meaning the gene responsible for the disorders are located on the X chromosome.¹
- The main types are haemophilia A and B, caused by a deficiency in FVIII and FIX, respectively.^{2,3}
- Examples of treatment options include replacement clotting factor therapy, desmopressin, emicizumab, and gene therapy.^{3,4,5}
- The most common gene therapy approach for haemophilia is currently based on AAV vectors.⁵
- The goal of all haemophilia treatment is to prevent bleeding, and most bleeding events are joint bleeds that result in crippling arthropathy.



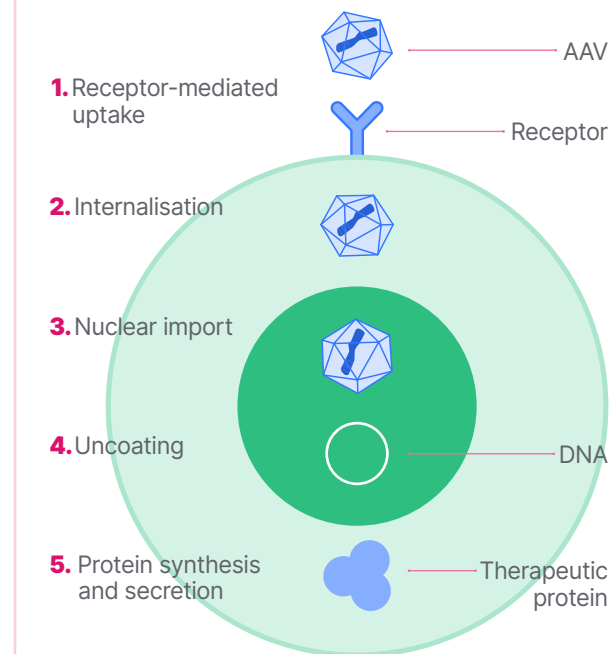
General population



Patients with haemophilia



AAV gene therapy



Significant Milestones

1982

Using **gene sequencing techniques**, researchers clone **FIX** and **FVIII** in 1982 and 1984, respectively.⁶

2011

First trial reporting successful results of **AAV-based gene therapy for haemophilia B**. The six patients treated showed elevated FIX levels after intravenous administration of the therapy.⁷

2017

A Phase I-II trial reports successful results of **valoctocogene roxaparvovec**, an AAV-based gene therapy for severe haemophilia A.⁸

EU UK USA

Valoctocogene roxaparvovec approved in the EU and UK in August 2022⁹ and in the USA in June 2023.¹⁰

2022

AAV

Etranacogene deszaparvovec, an AAV-based gene therapy for haemophilia B, was approved in the USA in November 2022,¹¹ and in the UK and EU in 2023.^{12, 13}

2023

Advantages¹⁴

Reduction of bleeding events.

Reduced burden of prophylactic infusion therapy.

Improved quality of life by reducing joint bleeding, pain and arthropathy is a major impact quality of life.

Disadvantages¹⁴

Little is known on the suitability of AAV-based gene therapy for children and infants with haemophilia, or its use in symptomatic female carriers.

Liver toxicity has been reported as a side effect from gene therapy. Additionally, side effects from corticosteroids often given to treat transaminitis have a negative impact.

Pre-existing anti-AAV antibodies limit eligibility, while treatment effects vary and long-term durability remains uncertain.

Abbreviations

AAV: adeno-associated virus; FIX: factor IX; FVIII: factor VIII.

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