EHC
Empowering the bleeding disorders community

Bleeding Disorder Treatments: Gene Editing

What You Need to Know

for people living with haemophilia and other bleeding disorders

While today's treatments help many people live full lives, the future could bring a world where bleeding disorders are no longer a burden. Thanks to research, science, and advocacy, we are getting closer to that future.[1]

🩸 What Are Bleeding Disorders?

Bleeding disorders, like, for instance, the three most common hereditary bleeding disorders,[2] Haemophilia A and B or von Willebrand Disease (VWD), happen when your blood doesn't clot properly. This is usually caused by a missing or faulty gene that should make important clotting factors like Factor VIII (8), Factor IX (9) or VWF.

✨ What Does the Future Hold?

Scientists around the world — including in Europe — are working on the possibility of a cure for bleeding disorders, not only the treatment of the symptoms. Gene therapy is a treatment where new working genes are introduced into a person's cells to abolish disease. There are different kinds of gene therapy, including gene editing. One of the most promising gene-editing technologies is called CRISPR.

🧬 What is CRISPR?

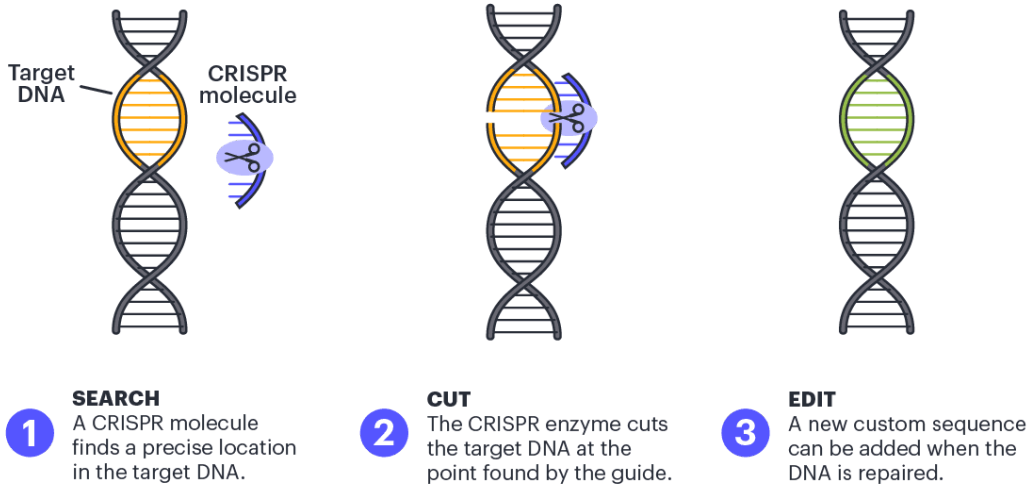
CRISPR (clustered regularly interspaced short palindromic repeats) is a medical technology that scientists use to edit DNA, the genetic code of living beings.[3] Think of it like a pair of molecular scissors that can cut and change specific parts of DNA.[4]

[1]This booklet is for educational purposes only, it does not endorse or promote any specific pharmaceutical organisation, drug or other medical intervention. It is developed, created, and delivered by the EHC independently from the industry.
[2]The exact number of bleeding disorders is unknown because some are rare and newly identified. A wide range of conditions can cause abnormal bleeding, affecting individuals of all ages and genders.
[3]Kessler, Craig M. et al. Development of a novel gene editing lexicon for hemophilia: methodology and results. *Research and Practice in Thrombosis and Haemostasis* 2025; 9(2). DOI: 10.1016/j.rpth.2025.102710
[4]Deoxyribonucleic acid (abbreviated DNA) is the molecule that carries genetic information for the development and functioning of an organism. DNA is made of two linked strands that wind around each other to resemble a twisted ladder — a shape known as a double helix. Each strand has a backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases: adenine (A), cytosine (C), guanine (G) or thymine (T). The two strands are connected by chemical bonds between the bases: adenine bonds with thymine, and cytosine bonds with guanine. The sequence of the bases along DNA's backbone encodes biological information, such as the instructions for making a protein or RNA molecule.

🔧 How Does It Work?[5]

Imagine DNA as a long book with instructions written in a special language (A, T, C, G). Sometimes, there's a "typo" (a mutation) or a part you want to edit. CRISPR helps with that. There are two main components of CRISPR: Cas9 and guide RNA.

CRISPR uses a **guide RNA (gRNA)** - a tiny piece of code - to locate a specific DNA sequence within the patient's cells. It brings along an enzyme called **Cas9**, which works like scissors. It cuts the DNA at the gRNA-targeted location.



Once the DNA is cut, the cell tries to repair it, either by pasting together the ends of the double-stranded break with a small change in the sequence at that break or by integrating a new piece of DNA at the site of the cut. During that process, scientists can:

- **Correct the mutation**: If a corrected DNA sequence is provided, the cell can use it as a template to repair the cut, effectively correcting the mutation.
- **Insert a new gene**: If a functional copy of the gene is provided, it can be inserted into the cut site, replacing the mutated gene.
- **Turn a gene off**.

Various delivery methods,[6] such as viral vectors (like adeno-associated viruses - AAV) and lipid nanoparticles (LNPs), are being explored to deliver CRISPR-Cas9 components to the liver cells.[7]

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[5]CRISPR Explained - a video by Mayo Clinic, US
[6]Taghdiri, M.; Mussolino, C. Viral and Non-Viral Systems to Deliver Gene Therapeutics to Clinical Targets. *International Journal of Molecular Sciences* 2024; 25(13):7333. DOI: 10.3390/ijms25137333
[7]Liver health is crucial for all, and people with bleeding disorders in particular. For the bleeding disorders community, liver health plays an important role in different contexts: from contamination crisis and hepatitis to gene therapy and ageing. Liver disease remains one of the leading causes of death among people with rare bleeding disorders, particularly in Europe. This is especially relevant for individuals with haemophilia and other

🧪 Why Is CRISPR Important?

By editing the mutated gene in patient cells, CRISPR could potentially restore the production of the missing clotting factor, leading to improved blood clotting and reduced bleeding. This could mean fewer bleeds, fewer hospital visits, more freedom and, eventually, significantly improved quality of life:

➔ **Potential** of a cure for genetic bleeding disorders - offering a long-term or permanent solution.

➔ Alleviating the burden of factor replacement therapy (reducing or even ending the need for regular treatment).

➔ Helping the liver produce clotting factor naturally.

⚠️ Are There Risks?

The primary risk associated with CRISPR technology is the potential for off-target genome editing effects. CRISPR technology can induce site-specific DNA mutations in human DNA - unintended gene edits that may occur in other parts of the genome, potentially leading to long-term complications, including cancer.[8]Scientists are studying how to detect, measure, and reduce these risks.

⚠️ Inheritance and follow-up

⚠️ CRISPR-based gene insertion targets specifically liver cells, therefore, **the mutation is not cancelled** in germinal cells, such as oocytes and sperm cells. This means that the usual inheritance patterns still apply to patients with bleeding disorders and their offsprings.

⚠️ Gene-editing is a one-time therapy (it is permanent and irreversible).

⚠️Regular follow-ups are important post-procedure.

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rare coagulation disorders who were historically treated with plasma-derived clotting factors — some of which were contaminated with hepatitis B and C, viruses like HBV, HCV, and HIV, before routine screening and virus inactivation processes were implemented in the 1980s and 1990s. Despite the HCV cure, people who have lived with this infection for decades remain at a higher risk for non-alcoholic fatty liver disease and require further monitoring and care.

[8]Guo C.; Ma X.; Gao F. and Guo Y. Off-target effects in CRISPR/Cas9 gene editing. *Front. Bioeng. Biotechnol* 2023; 11:1143157. DOI: 10.3389/fbioe.2023.1143157

Kalter, N. et al. Off-target effects in CRISPR-Cas genome editing for human therapeutics: Progress and challenges. *Molecular Therapy Nucleic Acids*, 36(3). DOI: 10.1016/j.omtn.2025.102636

⚠️ What You Should Know

- **CRISPR is not a cure today**, but it is one of the most promising options being explored. Before it can be widely used, scientists need to make sure it is both effective and safe. Understanding and controlling off-target effects is an essential step toward making CRISPR therapies available.

- Clinical trials are happening in stages — with more expected in Europe soon.

- Patients will not be left behind — your voice is important in shaping the future of care.

👉 What Can You Do?

- Stay informed — ask your treatment centre or patient group for updates.

- Join conversations — patient voices help guide research and access to new therapies.

- Participate in research if you're interested and eligible — ask your doctor about upcoming trials.

🧹 Want to Learn More?

Reach out to:

- EHC – European Haemophilia Consortium (ehc.eu)

- National patient organisation in your country (ehc.eu/membership/)

- Your treating physician or HTC (Haemophilia Treatment Centre) in your country (https://wfh.org/find-local-support/)

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