Gene Therapy for SCD: Webinar program for patients

webinar

PATIENTS

Session 1: Introduction to Sickle Cell Disease (SCD) and Gene therapy

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Imagine Institute / Assistance Publique Hopitaux de Paris (APHP)

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EDITSCD

ERN | EuroBloodNet

Disclosure for conflict of interest

Annarita Miccio: *no conflict of interest*

Michaela Semeraro: *no conflict of interest*

What we will talk about today

1

Past & Present of Sickle Cell Disease

An overview on the history of SCD and the current worldwide distribution of the disease.

2

What Causes Sickle Cell Disease

Understanding what hemoglobin is, how it works and how genetic mutations in hemoglobin genes cause SCD.

3

Current Therapies for Sickle Cell Disease

Advantages and drawbacks of current therapeutic options for SCD.

4

Genetic Therapies for SCD

Gene therapy approaches to treat SCD. Advantages and limitations of new therapeutic approaches.

5

Introduction to Future Webinars

SCD-related topics of the next webinars in this 7-part series.

01

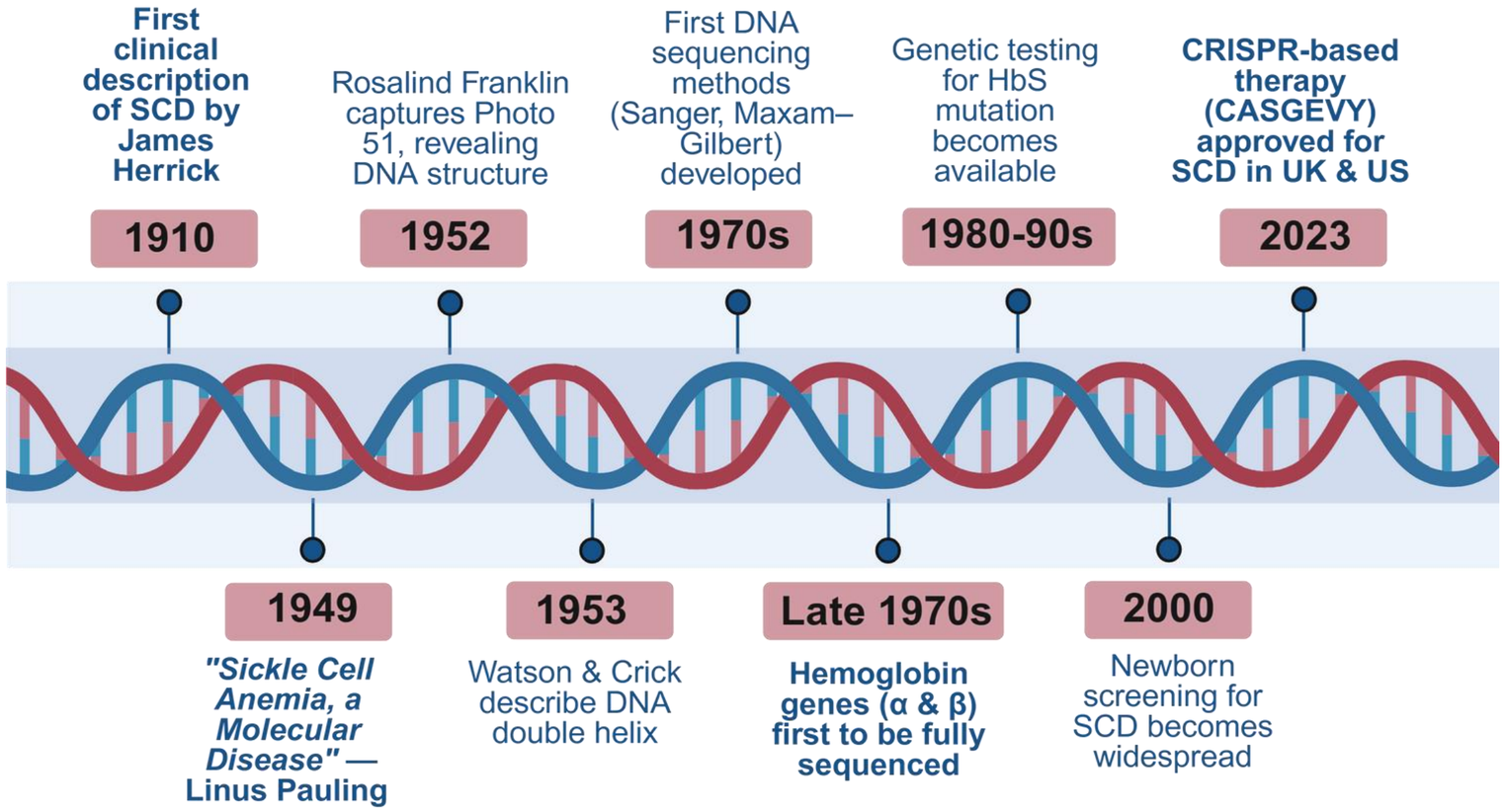
PAST AND PRESENT OF SICKLE CELL DISEASE

An overview on the history of Sickle Cell Disease and the current worldwide distribution of the disease.

Michaela Semeraro
APHP

Past & Present of Sickle Cell Disease (SCD)

Sickle Cell Disease was the first genetic disease studied by science, and the first with an approved gene therapy.



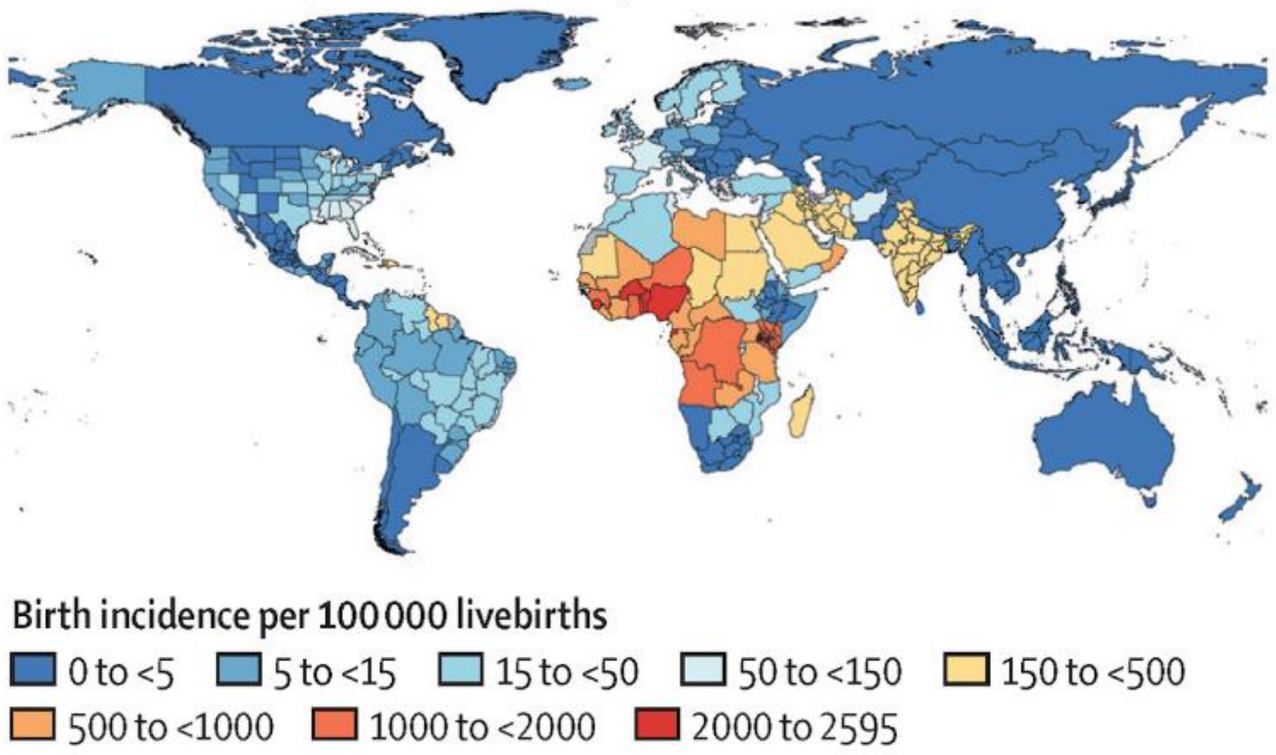
Adapted from: https://www.nature.com/articles/s12276-025-01514-0

Geography and Distribution of Sickle Cell Disease

Sickle Cell Disease affects more than 8 million people worldwide

Sickle cell disease is most prevalent in sub-Saharan Africa, India, the Middle East and some South American countries.

52,000 people in Europe and 100,000 in the United States suffer from Sickle Cell Disease. In the United States, 9 of 10 people who have sickle cell disease are of African ancestry or identify as Black, and about 1 in 13 Black babies are born with sickle cell trait, meaning that they inherited a sickle cell gene from one parent.

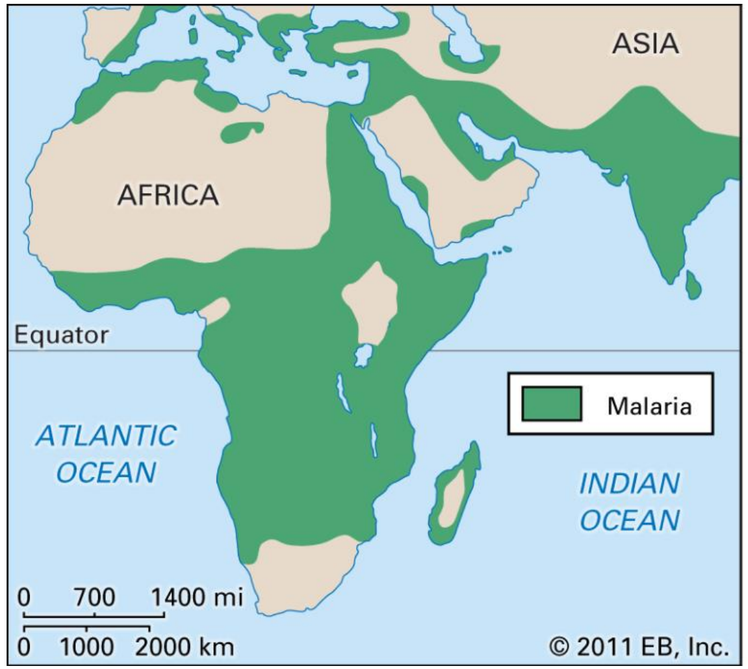


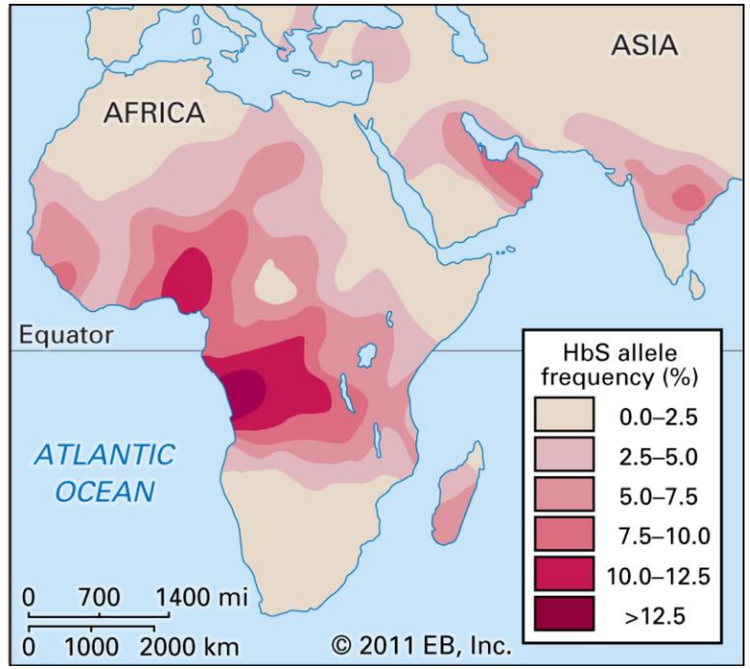
Geography and Distribution of Sickle Cell Disease

Sickle Cell Disease can affect people of any race

However, it is more common in populations exposed to malaria because carrying one copy of the sickle cell gene confers malaria resistance.

Migration from sub-Saharan Africa, the Middle East, and India, where SCD is most prevalent, has resulted in higher incidence rates in Europe and North America, creating new public health challenges and necessitating expanded screening and management programs.





From: https://www.britannica.com/science/malaria

02

THE MOLECULAR BASIS OF SICKLE CELL DISEASE

Understanding what hemoglobin is, how it works and how genetic mutations in hemoglobin genes cause SCD.

Michaela Semeraro
APHP

The Biology of Red Blood Cells – Hemoglobin

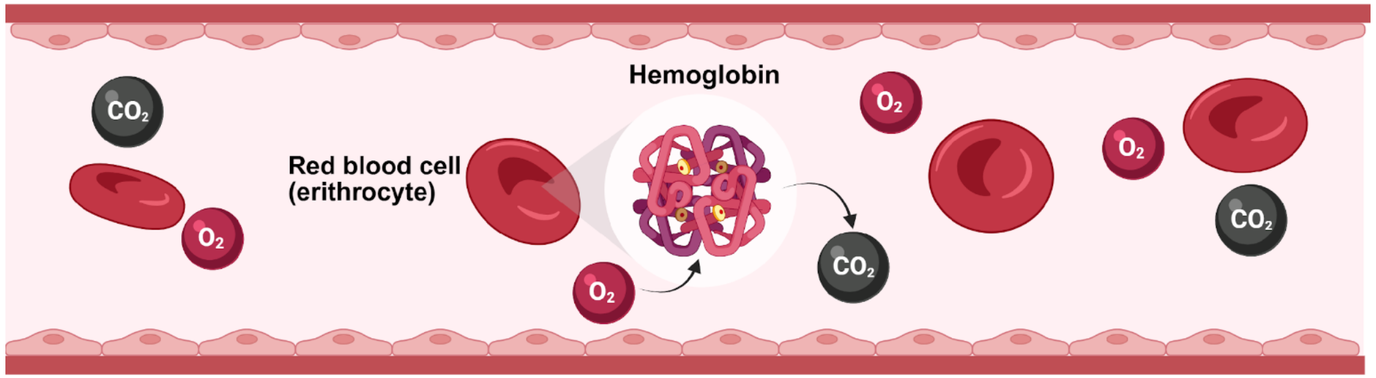
Hemoglobin binds oxygen and carbon dioxide in our blood

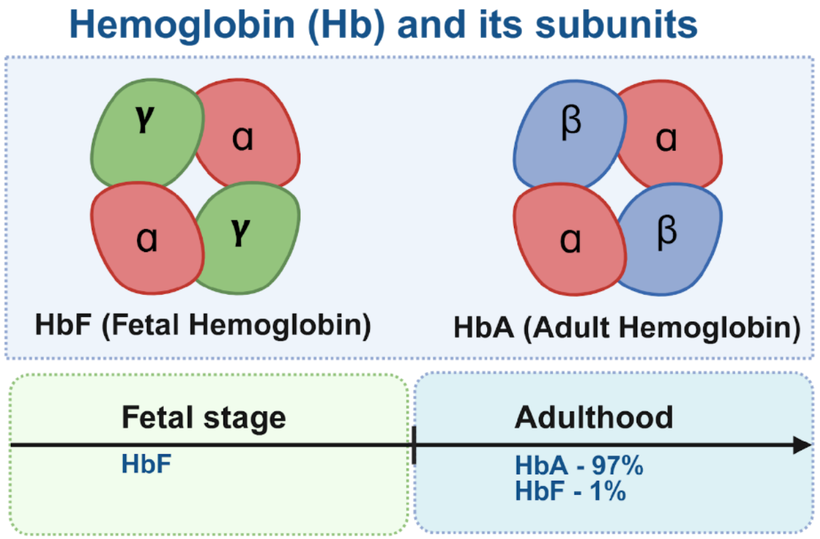
Red blood cells use hemoglobin to carry oxygen from the lungs to the tissues, and carbon dioxide back to the lungs.

Hemoglobin is formed by two pairs of proteins called “globins”. All hemoglobin forms have an α-subunit pair, but differ on the other subunit.

Fetal hemoglobin carries a type of globin that can bind oxygen more effectively, allowing the fetus to pull oxygen from the mother’s blood during pregnancy.

After birth, fetal hemoglobin is substituted by adult hemoglobin, which is mutated in Sickle Cell Disease.





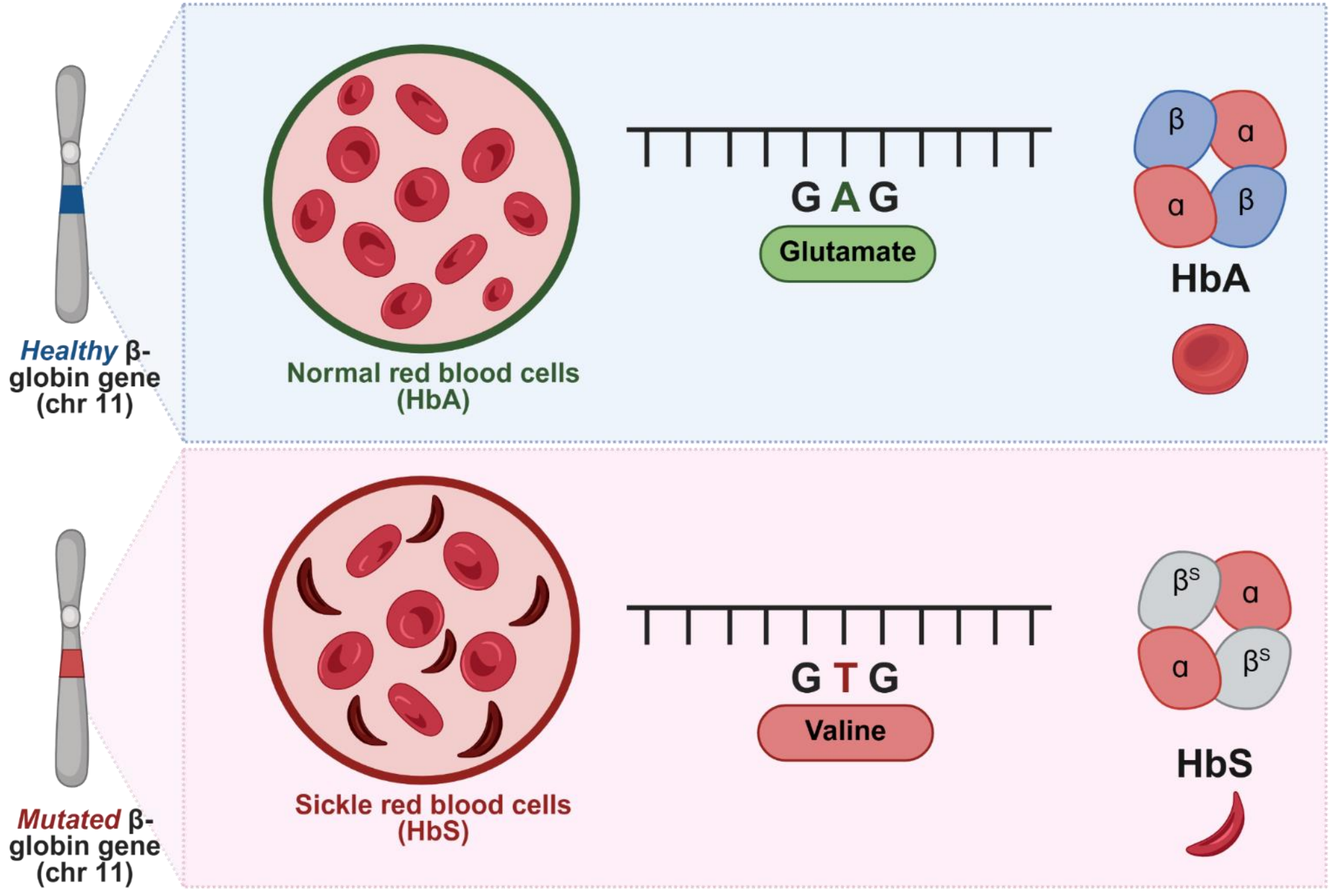
From Gene to Disease: The Mutation Behind Sickle Cell

Mutations in the gene encoding the β-chain of hemoglobin cause Sickle Cell Disease

Mutations are a change in a single letter of the cell's "instruction manual", the DNA.

Mutations can alter the meaning of these instructions. Mutations in the gene encoding the beta-globin chain cause the production of a mutant sickle beta-globin (beta S) that forms HbS instead of HbA. HbS is a different hemoglobin protein that gives red blood cells their sickled shape.

THE FAT CAT ATE THE RAT	Original meaning
THE HAT CAT ATE THE RAT	Wrong meaning

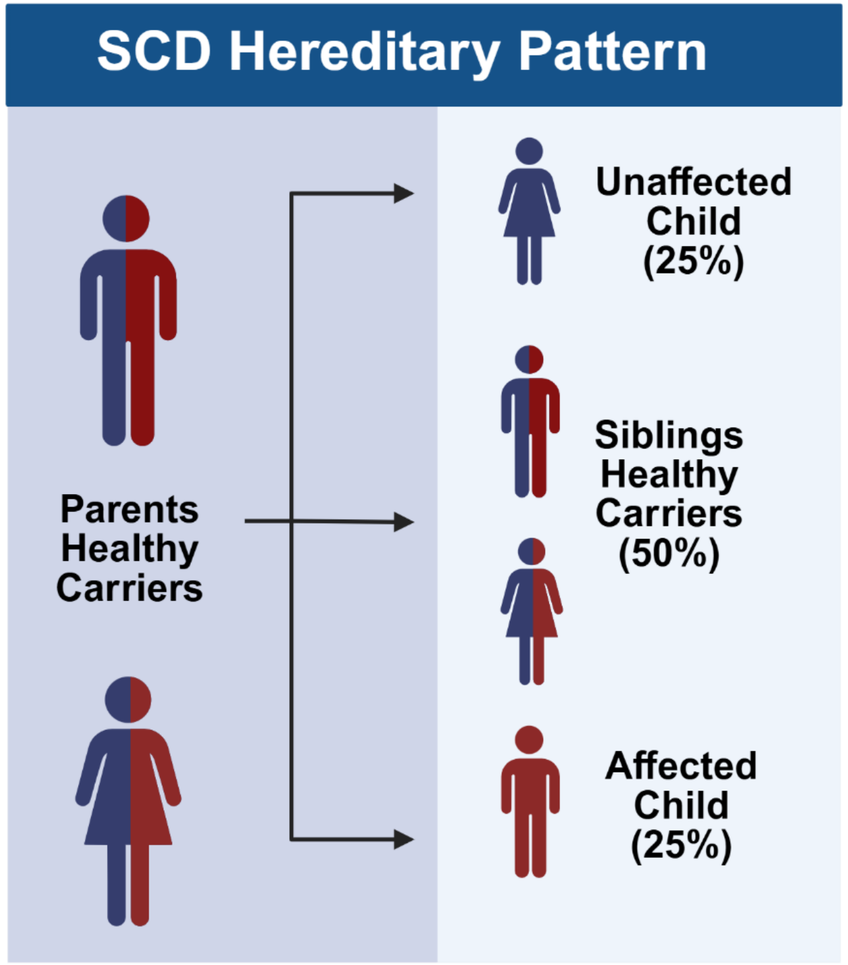


Inheritance of Sickle Cell Disease

SCD is an autosomal recessive condition

To trigger the disease both copies of the gene, also called alleles must be mutated

People whose only one of the allele is mutated may never know they have the mutation. Therefore, they are dubbed healthy carriers... However, if two healthy carriers have kids, one kid out of four (25%) may carry both mutated allele and show the symptoms.



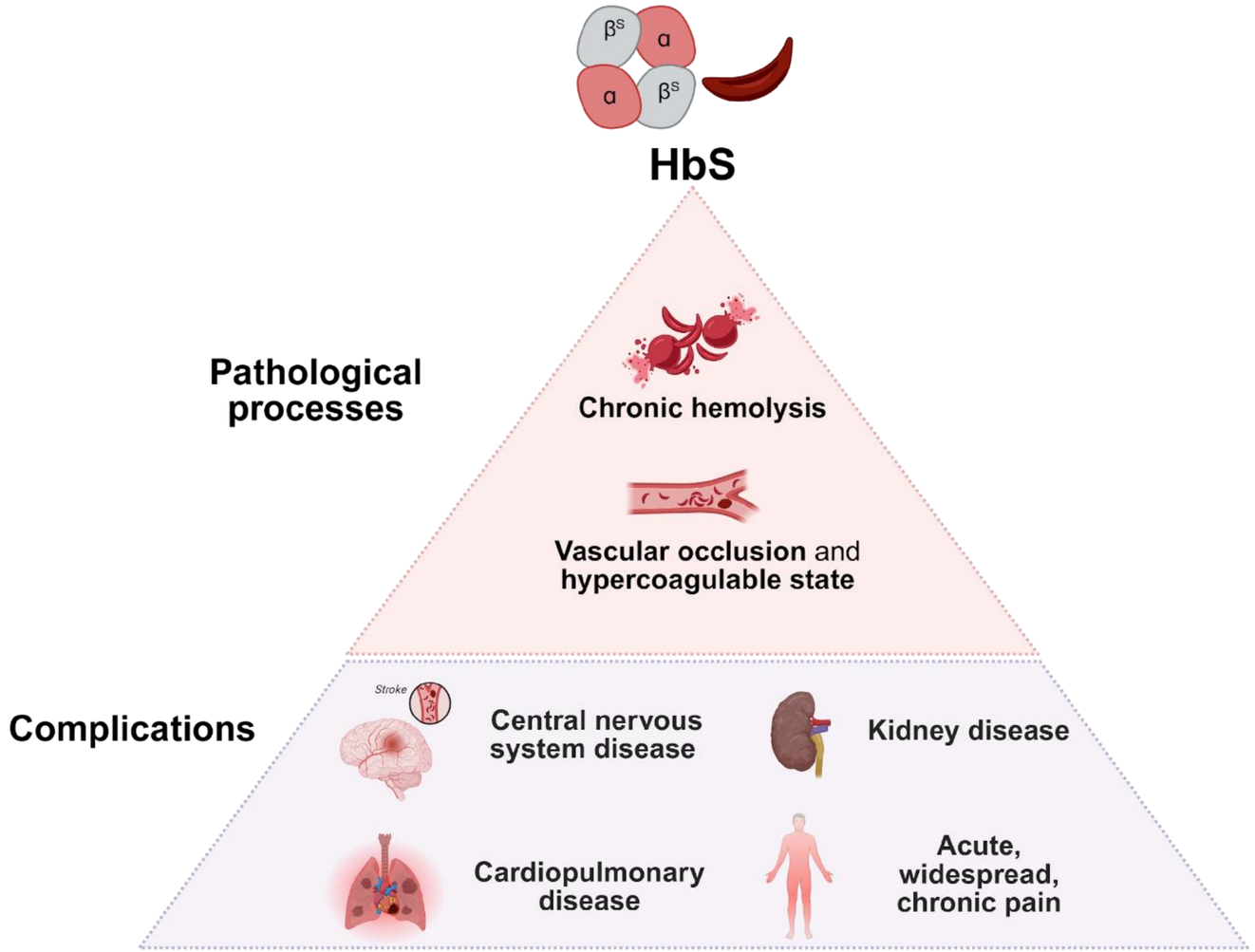
Symptomatology of Sickle Cell Disease

Mutations in hemoglobin cause Sickle Cell Disease

Sickle red blood cells tend to break inside small vases, causing several severe complications.

Cell breaking (hemolysis) causes iron release into the bloodstream, increasing iron levels to dangerous levels.

Vascular occlusion resulting from cell accumulation and breakage causes complications in different organs, as well as widespread, chronic pain.



03

CURRENT THERAPIES FOR SICKLE CELL DISEASE

Advantages and drawbacks of current therapeutic options for SCD.

Michaela Semeraro
APHP

Current Therapies for SCD –Hydroxyurea

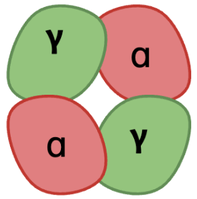
Hydroxyurea increases fetal hemoglobin (HbF) to replace the mutant HbS.

High HbF levels are beneficial for patients with SCD as HbF is a functional to generate healthier red blood cells

Increase fetal hemoglobin (HbF).

Reduce sickling and related complications.

Improve quality of life and survival.



HbF (Fetal Hemoglobin)

What

Oral drug that increases fetal hemoglobin (HbF)

When

For patients with frequent pain crises or severe complications

How

Daily oral tablets

Risks

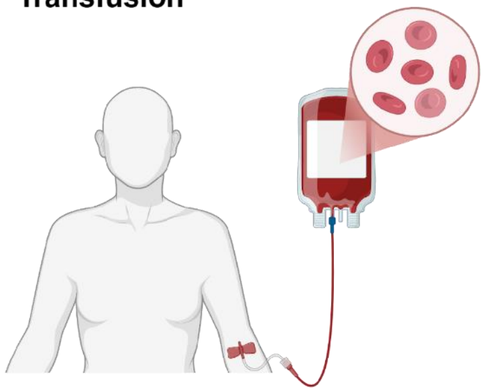
- Low blood counts
- More infections
- Upset stomach
- Skin or nail changes
- Possible fertility problems

Current Therapies for SCD – Red Blood Cell Transfusions

Red blood cell transfusions provide new, healthy cells

Replacing sickle-shaped red blood cells with healthy ones reduces the proportion of circulating sickle cells and improves oxygen carrying capacity.

Transfusions can be simple (adding healthy red cells) or exchange (replacing some sickle red blood cells with healthy ones) depending on the indication.



	Simple Transfusion	Exchange Transfusion
What	**Adds healthy red blood cells** without removing your own Used during anemia, surgery, or certain crises	**Removes sickle red blood cells** and replaces it with healthy ones Reduces the sickle cell load and avoids blood thickening
When	Stroke prevention Acute chest syndrome (ACS) Silent strokes	Before surgery During pregnancy Severe anemia or organ sequestration
How	**Occasionally** for surgery or acute illness **Regularly** (every 3–4 weeks) for long-term stroke prevention or severe disease	
Risks	Alloimmunization Iron overload Other: transfusion reactions, infections (rare), time and cost involved with frequent hospital visits	

Current Therapies for SCD – Hematopoietic Stem Cell (HSC) Transplantation

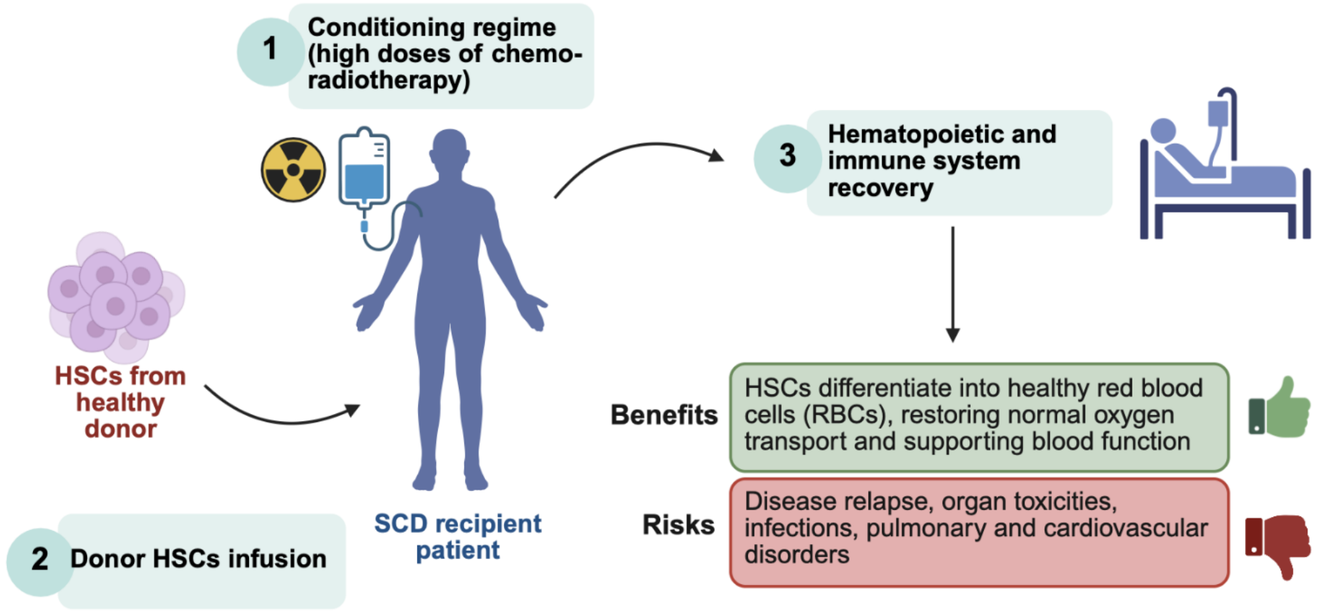
HSC transplantation provides a source to produce new red blood cells

Also known as bone marrow transplant, HSC transplantation was, for a long time, the only definitive cure for SCD.

Hematopoietic stem cells (HSCs) are the cells that make all of our blood cells. Replacing mutant HSCs with healthy ones from a donor can completely cure SCD.

However, the approach requires chemotherapy to completely remove the patient's HSCs, with associated risks on health and fertility.

Unfortunately, not all patients are eligible for HSC transplantation. Thankfully, approaches using half-matching donors have shown promise for expanding the therapy in the future.



From: https://link.springer.com/chapter/10.1007/978-3-031-55080-5_17

Further Learning

Bone Marrow Transplant: survival infertility and other complications

Youtube: https://www.youtube.com/watch?v=GxxnACWR0Wk&ab_channel=ERN-EuroBloodNet%27sEDU

Website: https://eurobloodnet.eu/education-2/patients/webinars/topic-on-focus-for-patient/topic-on-focus-on-scd/topic-on-focus-on-sickle-cell-disease-for-patients/9/bone-marrow-transplant-survival-infertility-and-other-complications

New therapies for Sickle Cell Disease

Youtube: https://www.youtube.com/watch?v=_ceAUg1oYwI&ab_channel=ERN-EuroBloodNet%27sEDU

Website: https://eurobloodnet.eu/education-2/patients/webinars/topic-on-focus-for-patient/topic-on-focus-on-scd/topic-on-focus-on-sickle-cell-disease-for-patients/1/new-therapies-for-sickle-cell-disease

Spotlight on Bone Marrow Transplant

Youtube: https://www.youtube.com/watch?v=r9KwJ5u4rRM&ab_channel=ERN-EuroBloodNet%27sEDU

Website: https://eurobloodnet.eu/news/313/available-videos-on-the-experience-of-the-scd-patients-educational-session-at-ascat-2022

04

GENETIC THERAPIES FOR SICKLE CELL DISEASE

Gene therapy approaches to treat SCD. Advantages and limitations of new therapeutic approaches.

Annarita Miccio
Imagine Institute

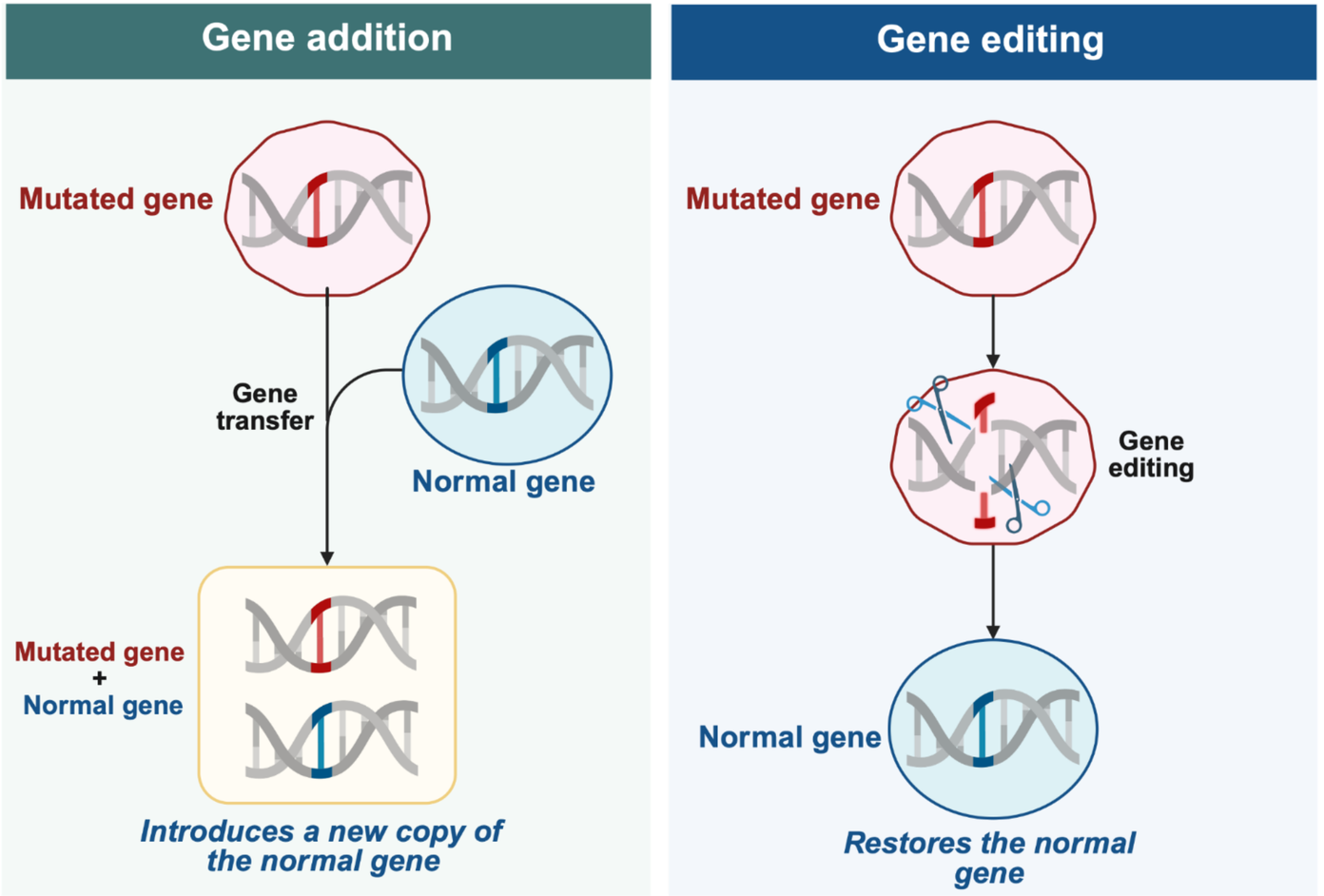
Gene therapy – Curing Disease at the Genetic Level

Gene therapy treats genetic diseases at the root

Addressing the genetic cause of disease promises a complete therapeutic solution. Scientists can follow two approaches.

Gene addition introduces a new, correct copy of the gene, giving the cell a new set of instructions to use.

Gene editing seeks to repair the mutated gene, fixing the “typo” to correct the incorrect instructions.



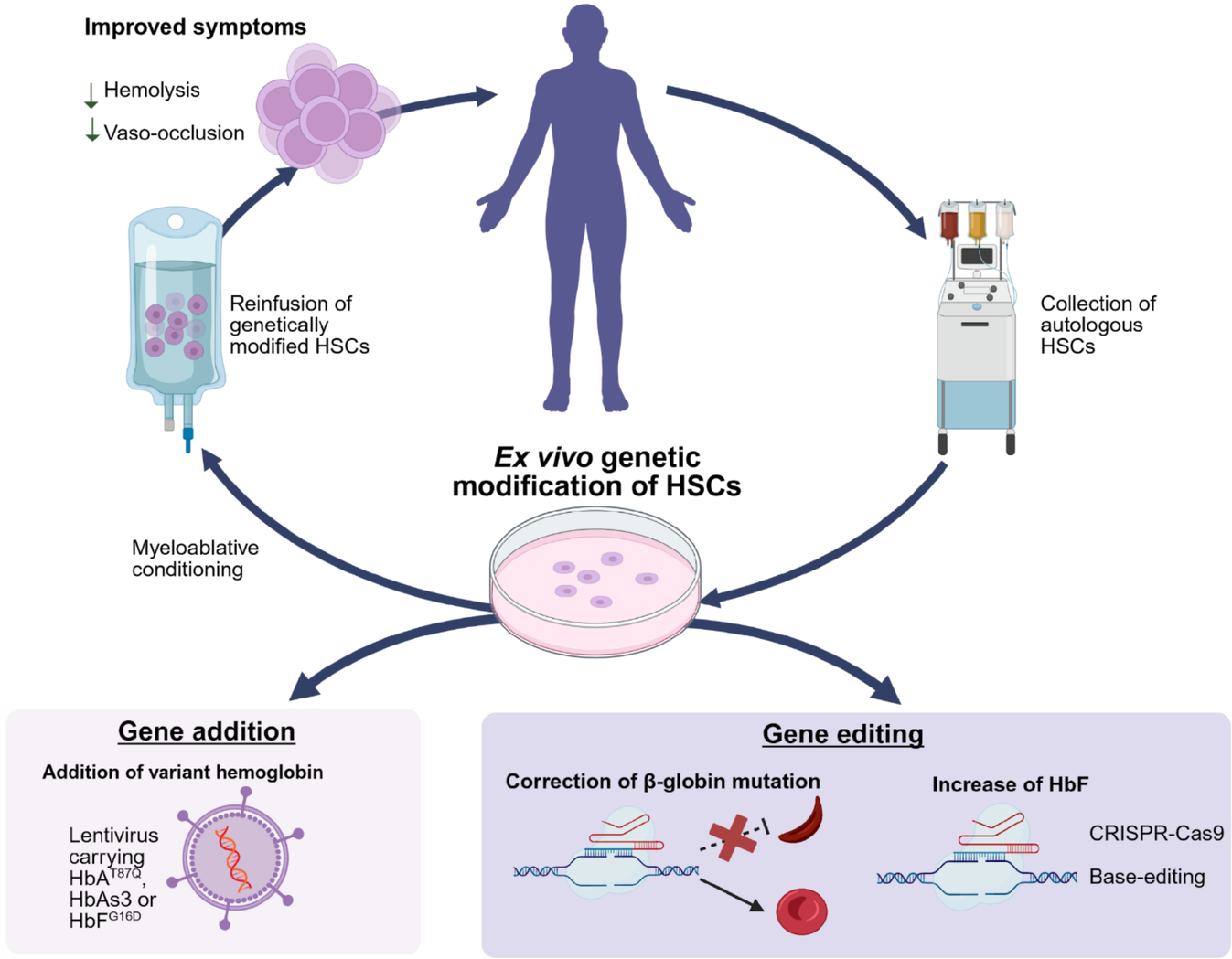
Gene Therapy for Sickle Cell Disease

Ex vivo gene therapy modifies HSCs outside the body

Scientists can modify HSCs extracted from the patient and correct them. Corrected HSCs can produce different types of hemoglobin depending on the therapeutic strategy.

Ex vivo gene therapy requires collecting and culturing the HSCs, as well as using chemotherapy to remove all remaining mutant HSCs before reinfusion.

Despite the potential risks associated, the approach has managed to dramatically improve symptoms like haemolysis and vaso-occlusion in SCD patients.



From: https://onlinelibrary.wiley.com/doi/10.1111/vox.13612

Gene Addition for SCD – Where Are We?

The first gene therapy for SCD was approved in 2023

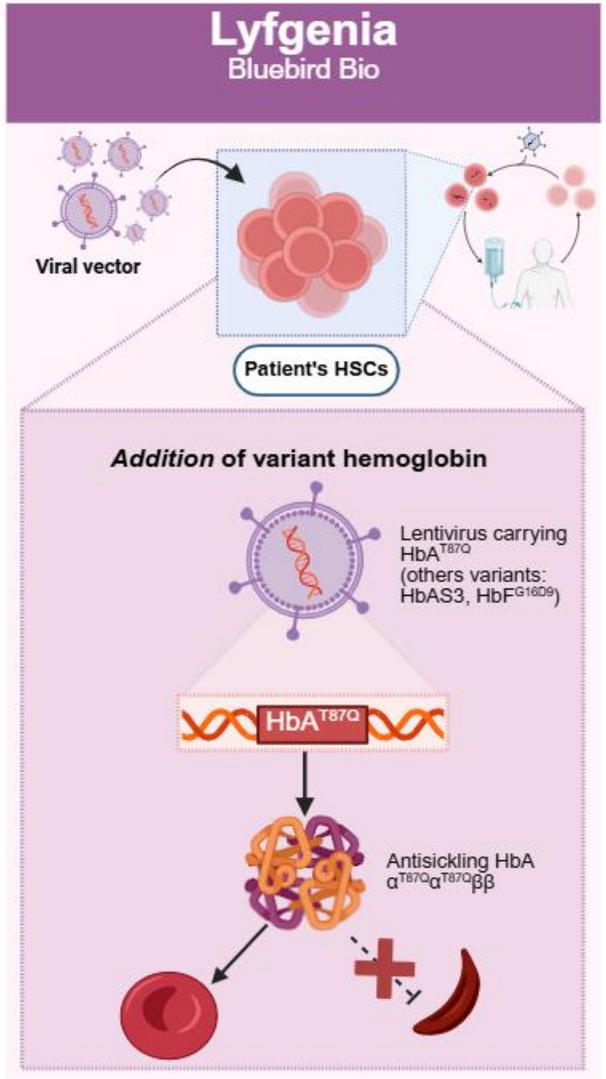
Lyfgenia (lovo-cel) uses a viral vector to provide the patient's HSCs with a correct copy of the HbA gene.

Lyfgenia has achieved functional cure in many patients worldwide. Most treated patients stopped suffering from vaso-occlusive crisis and requiring blood transfusions, with benefits lasting several years.

To learn more about this topic, scan the QR code!

Session 2: Basics of Gene Therapy with Lentiviral Vectors

Scan the QR code to register to the next session!



FDA approved (2023)

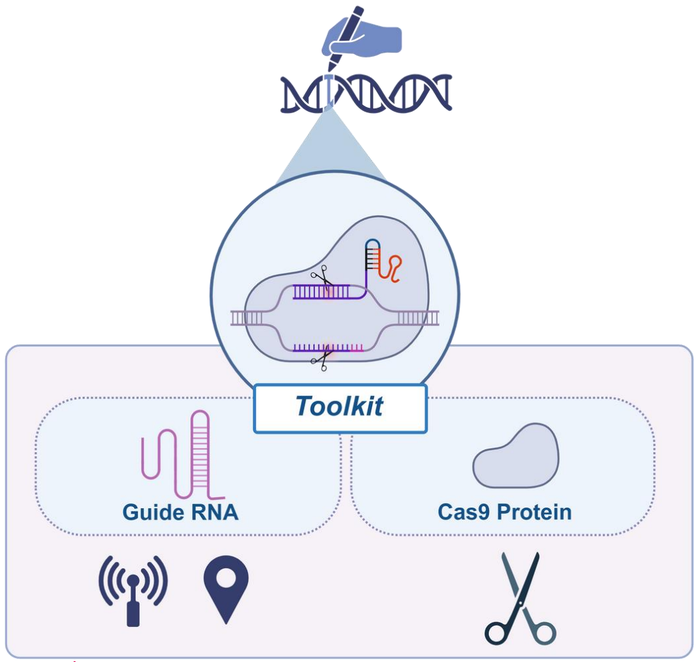
~88% VOC-free at 6–18 months

Gene Editing – What is It and How Does It Work?

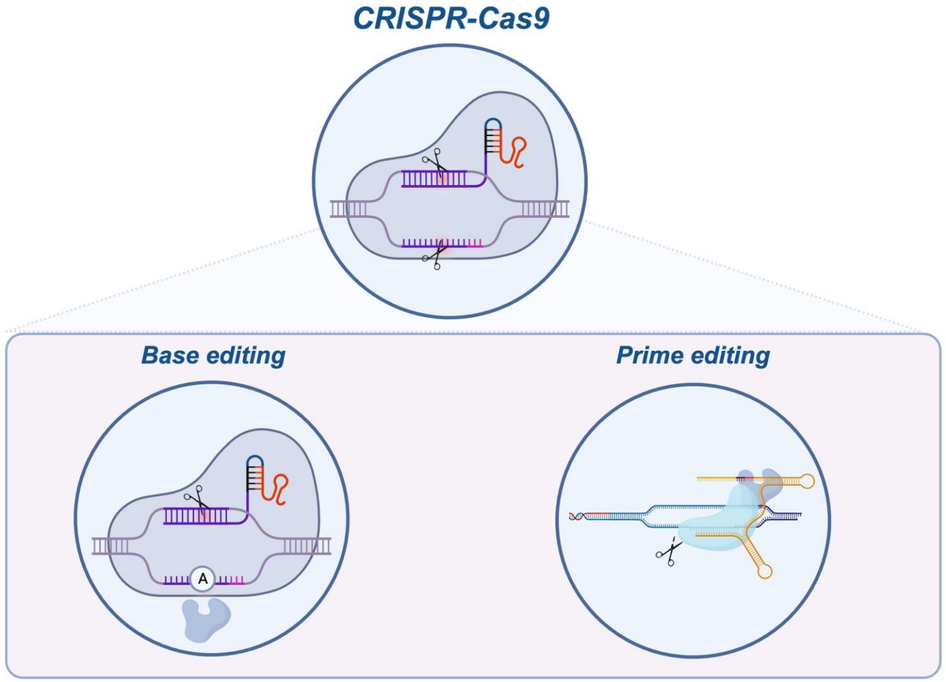
Gene Editing tool kit is broad

It includes tools like CRISPR (double scissors) and Base Editing/Prime Editing which allows for fine modifications (single scissors)

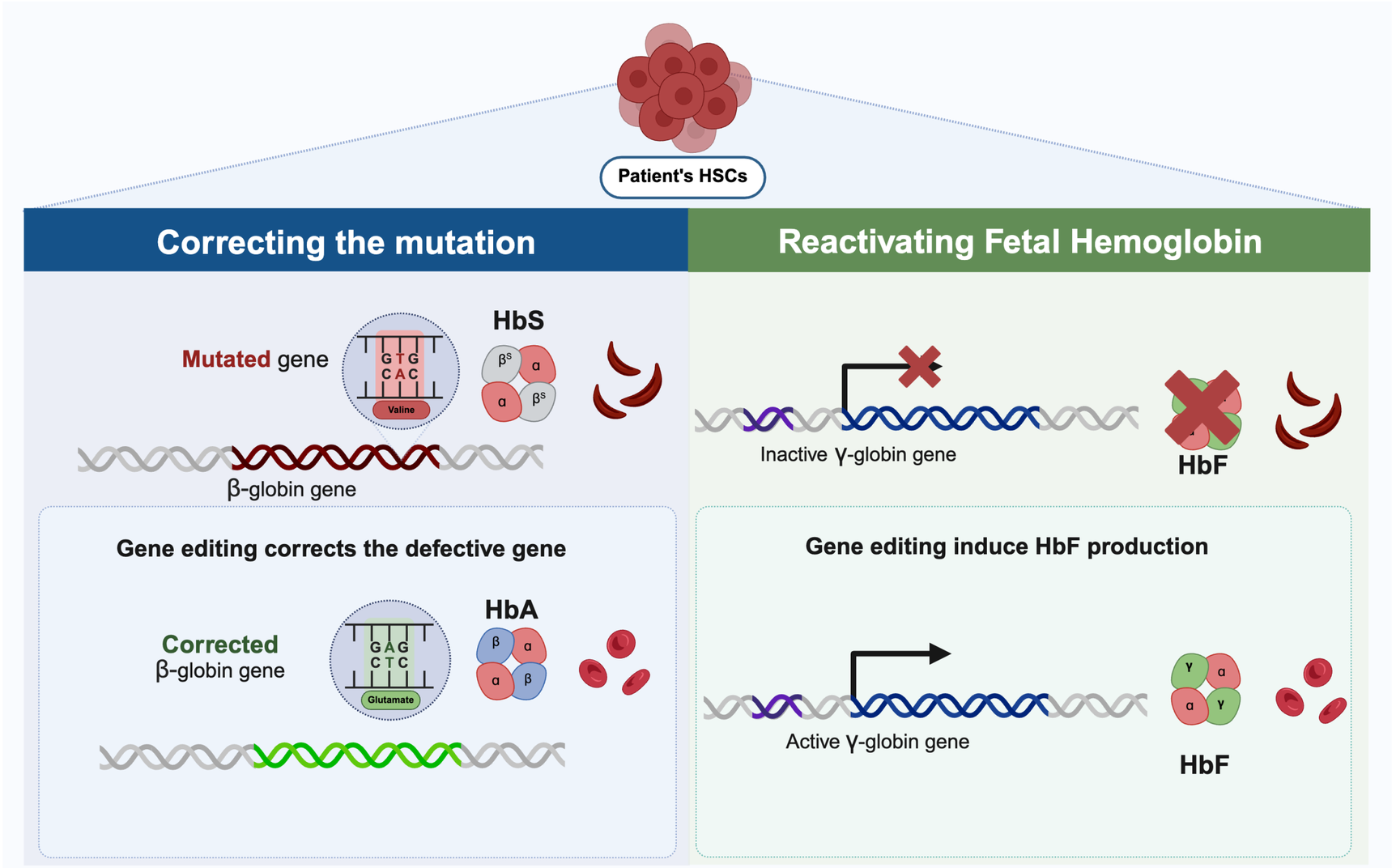
CRISPR-Cas9



Base editing/Prime Editing



Gene Editing Approaches to Treat Sickle Cell Disease

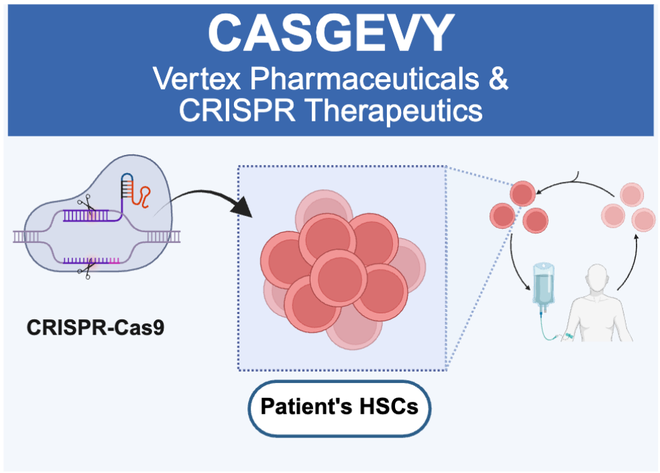


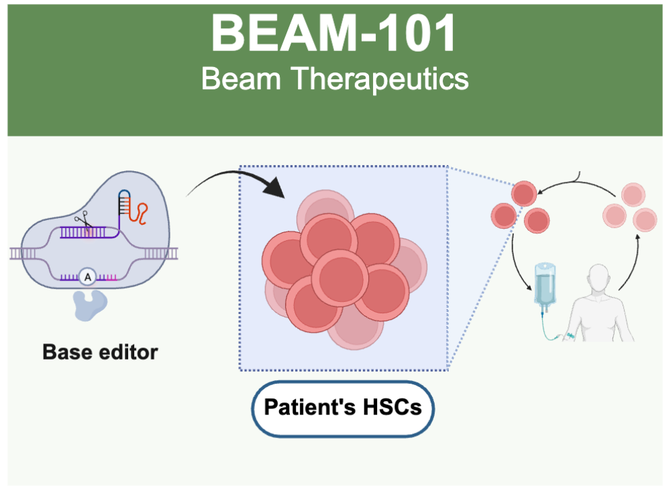
Gene Editing for Sickle Cell Disease – Where Are We At?

The first gene editing for SCD was approved in 2023

CASGEVY uses CRISPR-Cas9 to activate fetal hemoglobin (HbF) to replace the mutant HbS.

An alternative approach developed by Beam Therapeutics* uses base editing to activate fetal hemoglobin. This approach is still undergoing clinical trials.





FDA/EMA approved (2023)

93% VOC-free at 12 months

Phase I/II clinical trial

- Sustained high Hb
- No VOCs in early trial

*Currently being tested in USA only

To learn more about these topics, stay tuned for:

Session 3: Genome Editing: CRISPR/Cas9 and SCD – how it works and its uses

Session 4: Genome Editing: CRISPR/Cas9 Advanced Tools and SCD – using new methods

Scan the QR codes to register to the next sessions!

webinar

Gene Editing for Sickle Cell Disease – Success Stories

CASGEVY has already changed many lives.

Jimi Olaghere and Victoria Gray were among the first patients treated with CASGEVY in a clinical trial. CASGEVY was approved for clinical use in the UK, Europe and US in 2023.

Victoria Gray was the first person to ever receive a gene editing therapy in 2019. Since then, she hasn't had a single pain crisis, no longer needs transfusions, and has been able to stop taking opioid pain medications.

Jimi Olaghere was also treated in 2019, and his symptoms disappeared within months. In 2024, he climbed Mount Kilimanjaro to bring awareness to SCD, the CASGEVY therapy and its accessibility issues.

Scan the QR codes to access their incredible stories!

Jimi's interview

Victoria's interview

webinar

05

INTRODUCTION TO FUTURE WEBINARS

We will introduce the topics of the next webinars in this 7-part series.

Annarita Miccio
Imagine Institute

Future Webinars

Session 2: Basics of Gene Therapy with Lentiviral Vectors
Annarita Miccio and Giuliana Ferrari
November 2025

Session 3: Genome Editing: CRISPR/Cas9 and SCD – how it works and its uses
Claudio Mussolino, Mario Amendola, and Annarita Miccio
February 2026

Session 4: Genome Editing: CRISPR/Cas9 Advanced Tools and SCD – using new methods
Marcello Maresca Annarita Miccio
April 2026

Session 5: Safety of CRISPR/Cas9
Ayal Hendel and Toni Cathomen
May 2026

Session 6: Future Developments and CRISPR/Cas9 for SCD
Annarita Miccio
July 2026

Session 7: Regulatory path to the clinic
Annarita Miccio
September 2026

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