Sickle cell disease: understanding pathophysiology, clinical features and advances in gene therapy approaches

Frontiers in Pharmacology • Review • *Open Access* • 2025 •
DOI: 10.3389/fphar.2025.1630994

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Abstract

Sickle cell disease (SCD) is an inherited blood disorder marked by the production of abnormal hemoglobin, leading to the distortion—or sickling—of red blood cells. The SCD arises from a single-point mutation that substitutes glutamic acid with valine at the sixth codon of the β-globin chain in hemoglobin. This substitution promotes deoxyhemoglobin aggregation, elevating red blood cell stiffness, and triggering vaso-occlusive and hemolytic repercussions. To explore therapeutic advances in tackling this disease, this review analyzed articles published from January 2015 to January 2025 using the three databases using relevant keywords focusing on SCD and advancement in therapy. It was found that allogeneic hematopoietic stem cell (HSC) transplantation can alleviate symptoms but is limited by a shortage of well-matched donors and immunological challenges. In contrast, autologous gene-modified HSC transplantation via gene therapy offers comparable

therapeutic benefits without associated immunological complications. Clinical trials utilizing lentiviral vector-mediated gene insertion have demonstrated promising therapeutic outcomes by preventing hemoglobin aggregation. Emerging gene editing approaches such as CRISPR/Cas9 are expanding treatment options, marking the transition of SCD gene therapy from theoretical concept to clinical application.

Author keywords

anemia; CRISPR; gene editing; gene therapy; hematopoietic stem cell transplantation; hemoglobinopathies

Indexed keywords

EMTREE drug terms

deoxyhemoglobin; glutamic acid; hemoglobin; hemoglobin beta chain; hemoglobin variant; lentivirus vector

EMTREE medical terms

allogeneic hematopoietic stem cell transplantation; anemia; clinical feature; clustered regularly interspaced short palindromic repeat; codon; drug therapy; erythrocyte; gene; gene editing; gene insertion; gene therapy; hematopoietic stem cell transplantation; hemoglobinopathy; hemolysis; human; pathophysiology; point mutation; review; sickle cell anemia; therapy

Chemicals and CAS Registry Numbers

Unique identifiers assigned by the Chemical Abstracts Service (CAS) to ensure accurate identification and tracking of chemicals across scientific literature.

glutamic acid	11070-68-1, 138-15-8, 56-86-0, 6899-05-4
hemoglobin	9008-02-0

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