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Letter to Editor

Gene Based Therapies for Sickle Cell Disease: A Transformative Approach

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Dear Editor,

Sickle cell disease (SCD) is a hereditary blood disorder characterized by the production of abnormal hemoglobin, leading to distorted, sickle-shaped red blood cells leading to vaso-occlusive crises that obstruct blood flow and cause organ damage[1]. SCD poses a significant health challenge in context of Nepal, particularly among the indigenous Tharu population who are residing in terai region of the country. Screening tests done in Dang district revealed that 9.3% of the Tharu population in the region carries the sickle cell trait[2]. Despite this, access to healthcare services remains limited. The Nepali government has initiated health camps and provides ID cards for free medication. Traditional treatments have focused on symptom control and prevention of complications, but recent advancements in gene-editing technologies, particularly CRISPR-Cas9 have opened up potentially curative avenues. Clustered regularly interspaced short palindromic repeats-CRISPR associated protein-9 (CRISPR-Cas9) enables precise genome editing by targeting specific DNA sequences. In SCD, hematopoietic stem cells (HSCs) are extracted from patients and genetically modified using CRISPR to disrupt the BCL11A gene, which represses fetal hemoglobin (HbF) expression. By inactivating BCL11A, this strategy reactivates HbF production, compensating for the defective adult hemoglobin (hemoglobin S). The modified HSCs are then infused back into the patient, aiming to increase HbF levels and reduce the sickling of red blood cells, thereby alleviating SCD symptoms[3].

In December 2023, the FDA approved Casgevy (exagamglogene autotemcel), the first CRISPR-based therapy for SCD patients aged 12 and above experiencing recurrent vaso-occlusive crises. Clinical trials showed that Casgevy substantially reduced painful episodes[4]. A study by Frangoul et al. also demonstrated success in β-thalassemia using a similar CRISPR technique[5].

CRISPR-based therapy for sickle cell disease faces challenges such as off-target effects such as it can inadvertently modify unintended genomic sites which leads to potential side effects and complex ex vivo procedures. Long-term efficacy and safety data are ongoing, while researchers explore in vivo methods to improve accessibility and emphasize the need for large-scale trials[3].

Overall, CRISPR-Cas9 therapies signify a major milestone in treating monogenic disorders like SCD. The approval of Casgevy exemplifies the shift from symptom management to potential cures. As research evolves, CRISPR may redefine treatment paradigms for various genetic conditions. In regions like Nepal, continued investment and partnerships are crucial for delivering cutting-edge therapies[6].

In conclusion, the availability of such technologies is progressive in developing countries like Nepal and requires focused funding, legislative backing, strong commitments at national levels including policy support, investment in research infrastructure, training of skilled personnel, and equitable access strategies. CRISPR-based treatments have the potential to be revolutionary in management of SCD.

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