

LETTER TO THE EDITOR

Gene therapy renews hope to lower the global rural sickle cell disease burden

RO Tachere¹, AO Umunna²

¹Canadian Mental Health Association, Kitchener, ON, Canada

²Department of Development Studies, University of South Africa, Pretoria, South Africa.

Submitted: 7 December 2016; **Accepted:** 19 April 2017; **Published:** 7 September 2017

Tachere RO, Umunna AO

Gene therapy renews hope to lower the global rural sickle cell disease burden

Rural and Remote Health 17: 4291. (Online) 2017

Available: <http://www.rrh.org.au>

There is an urgent need for health policymakers to pay attention to recent developments in gene therapy for sickle cell disease (SCD), a treatment approach directed principally at treating the cause rather than the symptoms of genetic diseases¹. Sickle cell anaemia (SCA), one of the variants of SCD, is an inherited disease in which mutated red blood cells are curved into sickle (crescent) shapes, resulting in poor oxygenation of cells. It occurs globally, with more than 230 000 infants born with the condition in Africa annually². Patients with SCA suffer from recurrent anaemia, infections, tissue damage, strokes, excruciating pain and fatal organ failures, with vaso-occlusive crises being the hallmark of its acute presentation. Sadly, 50–80% of infants born with the disease die before the age of 5 years in Africa². The financial impact is devastating, especially for rural households in Sub-Saharan Africa – where 60% of the population live – with very limited access to even routine health care^{3,4}.

Early diagnosis through newborn screening, prophylactic therapy, and comprehensive care programs including

hydroxyurea therapy as well as bone marrow therapy, are current treatment options, in well-resourced countries. Bone marrow transplant offers a promising prospect for cure⁵; however, this line of treatment is limited because it carries significant risks, including infections, graft rejection and up to a 10% chance of mortality⁶. Moreover, human leucocyte antigen matching and other associated costs (pre-, peri- and post-treatment) are often outside the reach of many urban, let alone rural, families affected or afflicted by the disease.

Currently, several innovative approaches are at different stages of trials. These include:

- gene addition, whereby a new haemoglobin gene is inserted into the cells' DNA using a viral vector with the old, faulty haemoglobin gene still being present (the latter goes silent as the new gene takes over)
- gene editing, which corrects sickle cell genes with tools such as nucleases and others including zinc



finger nuclease, transcription activator-like effector nuclease and clustered regularly interspaced short palindromic repeats¹

- disabling of the *BCL11A* gene, which causes the switch from foetal to adult haemoglobin, so that patients can continue to produce foetal haemoglobin instead of the mutated adult variant⁷.

Although some challenges remain, including how to minimise off-target or unwanted injurious effects and ensuring that the edited/new stem cells survive and generate healthy red blood cells after they are reinserted into the bone marrow, considerable improvements have been made⁸.

These new approaches can potentially alter the public health impacts, clinical effects and financial difficulties associated with SCD and similar haemoglobinopathies in rural parts of Africa, the Middle East and worldwide. It is hoped that through this publication and similar platforms, a wider dissemination of these ongoing research projects will improve the policy salience and institutional research support that will facilitate these approaches. This will increase the prospect of enduring relief for families, especially in rural areas, where financial, social and physical conditions are daily crippled by the debilitating effects of SCD.

Richardson O. Tachere, Flexible Assertive Community Treatment (FACT) Program, Canadian Mental Health Association, Ontario, Canada
Anthony O. Umunna, Department of Development Studies, University of South Africa, Pretoria, South Africa

References

- 1 Gammon K. Gene therapy: editorial control. *Nature* 2014; 515: S11-S13. <https://doi.org/10.1038/515S11a>
- 2 Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. *Bulletin of the World Health Organization* 2008; 86: 480-487. <https://doi.org/10.2471/BLT.06.036673>
- 3 Olatunya OS, Ogundare EO, Fadare JO, Oluwayemi IO, Agaja OT, Adeyefa BS, et al (Eds). The financial burden of sickle cell disease on households in Ekiti, Southwest Nigeria. *ClinicoEconomics & Outcomes Research* 2015; 7: 545-553. <https://doi.org/10.2147/CEOR.S86599>
- 4 Trading Economics. Rural population growth (annual %) in sub-Saharan Africa. Available: <http://www.tradingeconomics.com/sub-saharan-africa/rural-population-growth-annual-percent-wb-data.html> (Accessed 2 December 2016).
- 5 Mulumba LL, Wilson L. Sickle cell disease among children in Africa: an integrative literature review and global recommendations. *International Journal of Africa Nursing Sciences* 2015; 3: 56-64.
- 6 Apperley J. Bone marrow transplant for hemoglobinopathies: past, present and future. *Baillieres Clinical Haematology* 1993; 6: 299-325.
- 7 Hoban MD, Orkin SH, Bauer DE. Genetic treatment of a molecular disorder: gene therapy approaches to sickle cell disease. *Blood* 2016; 127(7): 839-848. <https://doi.org/10.1182/blood-2015-09-618587>
- 8 Ribiel J, Haccin-Bey-Abina S, Payen E, Alessandra Magnani A, Semeraro M, Magrin E, et al. Gene therapy in a patient with sickle cell disease. *New England Journal of Medicine* 2017; 376: 848-855. <https://doi.org/10.1056/NEJMoa1609677>