**[Billing Code 4140-01-P]**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institutes of Health**

# Government-Owned Inventions; Availability for Licensing

**AGENCY:** National Institutes of Health, HHS.

**ACTION:** Notice.

**SUMMARY:** The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. to achieve expeditious commercialization of results of federally-funded research and development.

**FOR FURTHER INFORMATION CONTACT:** Licensing information may be obtained by emailing the indicated licensing contact at the National Heart, Lung, and Blood, Office of Technology Transfer and Development Office of Technology Transfer, 31 Center Drive Room 4A29, MSC2479, Bethesda, MD 20892-2479; telephone: 301-402-5579. A signed Confidential Disclosure Agreement may be required to receive any unpublished information.

**SUPPLEMENTARY INFORMATION:** Technology description follows.

## Lentiviral Protein Delivery System For RNA-guided Genome Editing

Available for licensing and commercial development is an HIV-1-based lentiviral vector system for gene correction strategies involving a homologous recombination with a variation of the CRISPR/Cas9 system. Other such lentivirus-based vectors encode a guide RNA, which contains a specific sequence that recognizes a target gene, and a Cas9 endonuclease, which cuts at the specific site. Such systems are being explored as potential therapies for certain hereditary diseases (e.g., sickle-cell disease). However, such systems present some problems due to constitutive expression of Cas9 endonuclease in lentiviral vector-transduced cells and the large size of the Cas9 gene. The variation of this invention delivers the Cas9 endonuclease directly, instead of the gene encoding the protein. This system comprises (a) a lentivirus vector particle comprising a lentiviral genome which encodes at least one guide RNA sequence that is complementary to a first DNA sequence in a host cell genome, (b) a Cas9 protein, and optionally (c) a donor nucleic acid molecule comprising a second DNA sequence. In addition, the invention provides a host cell comprising the foregoing system, as well as a method of altering a DNA sequence in a host cell comprising contacting a host cell with the foregoing system. Alternatively, the invention also provides a fusion protein comprising a Cas9 protein and a cyclophilin A (CypA) protein, wherein the fusion protein binds to the lentivirus vector particle, as well as a lentiviral vector particle comprising such a fusion protein. Gene correction using the disclosed lentiviral vector systems are being tested with respect to the beta-globin gene and the BCL11A gene (to treat sickle-cell disease) and will be used for induced pluripotent stem cell (iPS) generation.

**Potential Commercial Applications:**

- sickle cell disease
- gene therapy

**Development Stage:**

- Early stage

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**Relevant Publications:** Demirci et al., Cytotherapy. 2018 Jul;20(7):899-910. doi: 10.1016/j.jcyt.2018.04.003. Epub 2018 May 30.

**Intellectual Property:** HHS Reference No. E-165-2015; U.S Provisional Patent Application 62/236,223 filed October 2, 2015; International Patent Application PCT/US2016/054759 filed September 30, 2016, U.S. Continuation-in-Part Application 15/942,673 filed April 2, 2018 and European Patent Application 16782163.6 having an international filing date of September 30, 2016.

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