[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 invention listed below is owned by an agency of the U.S. Government and is available for licensing to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT: Amy F. Petrik, Ph.D., 240-627-3721; amy.petrik@nih.gov. Licensing information and copies of the U.S. patent application listed below may be obtained by communicating with the indicated licensing contact at the Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, 5601 Fishers Lane, Rockville, MD, 20852; tel. 301-496-2644. A signed Confidential Disclosure Agreement will be required to receive copies of unpublished patent applications.

SUPPLEMENTARY INFORMATION: Technology description follows:

Recombinant Prefusion Measles and Mumps F and F-HN (H) Glycoproteins for Vaccine Development.

Description of Technology:

The Measles virus (MeV) and Mumps virus (MuV) are highly contagious paramyxoviruses that can be transmitted by respiratory droplets from or on direct contact with an infected person. The resulting diseases can lead to serious complications or death among children. The existing vaccines for MeV and MuV are live attenuated virus vaccines which are administered in two subcutaneous doses at 1 year of age and as early as one month later. Two doses of a combination measles, mumps and rubella vaccine are 97% effective against measles and 88% against mumps. A single dose of a combination measles, mumps, and rubella vaccine is 93% effective against measles and 78% effective against mumps.

Despite the effectiveness of the current licensed vaccines against MeV and MuV, incidences of both have increased in recent years. Contributing factors include reduced vaccination rates (especially in the U.S) due to vaccine hesitancy and circulation of divergent strains against which the licensed MMR vaccine offers limited protection.

In the case of MuV, recent studies have shown that immunity wanes significantly after the second MMR vaccination which normally occurs in childhood. In response to recent recurring MuV disease outbreaks in the U.S and Europe, the Advisory Committee on Immunization Practices is advising a third MMR vaccination to boost protection. However, existing immunity neutralizes a third MMR vaccination limiting its

effectiveness. Genotype G MuV is the main cause of recent outbreaks in the US and Europe, and a genotype-matched vaccine has been suggested as a solution for the recurring outbreaks.

Researchers at the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID) used structure-guided design to create immunogen constructs aimed at stabilizing the measles and mumps F glycoproteins in their prefusion conformations. This was achieved by following the discovery that the pre-fusion stabilized F glycoproteins from other members of the paramyxoviridae family induced high titer neutralizing responses.

The researchers developed recombinant immunogens based on: (a) the measles F glycoprotein trimer stabilized in its prefusion conformation (preF-MeV); (b) genotype G mumps F glycoprotein trimers stabilized in its prefusion conformation (preF-MuV); (c) a chimera in which a genotype G mumps F glycoprotein trimer stabilized in its prefusion conformation is fused with mumps HN protein (preF-HN); and (d) a chimera in which a genotype G mumps F glycoprotein trimer stabilized in its prefusion conformation is fused with measles H protein (preF-MuV/MeV H).

The prefusion stabilization of both the mumps and measles F glycoproteins relies on amino acid substitutions to allow the formation of intra-protomer disulfide bonds.
Researchers found that the preF and preF-HN immunogens are stable for over a month at 37°C and hypothesize that lyophilized product would be stable at room temperature for months.

When mice are immunized in a prime-boost-boost regimen with the MuV immunogen constructs, the group receiving the preF-HN immunogens elicited similar

antibody titers against genotype G MuV and Jeryl Lynn strain of MuV (genotype A) indicating that the preF-HN immunogens offer broad protection against divergent strains of MuV. Interestingly, mice immunized in a prime-boost regimen with the pre-F MuV/MeV H chimeric immunogen elicited antibody titers to both MuV and MeV that are above the determined protective thresholds.

This technology is available for licensing for commercial development in accordance with 35 U.S.C. § 209 and 37 CFR Part 404.

Potential Commercial Applications:

- The products can be used as measles or mumps vaccines.

Competitive Advantages:

- Currently, there is no licensed recombinant measles or mumps vaccine for use as boosters as a third vaccination.
- The preF-HN immunogens offer broad protection against divergent strains of mumps.
- The stabilized prefusion F molecules may be deliverable as mRNA vaccines, increasing yields of expressed antigen and presentation of the optimal conformation of target proteins.
- PreF and preF-HN immunogens are stable for over a month at 37°C, the lyophilized product may be stable at room temperature for months.
- Recombinant vaccine production is scalable, cost-effective vaccine production can be achieved.

Development Stage: Preclinical Research.

Inventors: Barney Graham, PhD (NIAID); Guillaume Stewart-Jones, PhD (NIAID).

Intellectual Property: HHS Reference Number E-153-2019 includes U.S. Provisional Patent Application Number 62/946,902 filed 12/11/2019.

Licensing Contact: To license this technology, please contact Amy F. Petrik, Ph.D., 240-627-3721; amy.petrik@nih.gov.

Dated: April 12, 2020.

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Wade W. Green,

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[FR Doc. 2020-08561 Filed: 4/22/2020 8:45 am; Publication Date: 4/23/2020]