Dated: April 28, 1999.

Jane M. Harrison,

Director, Division of Policy Review and Coordination.

[FR Doc. 99–11251 Filed 5–4–99; 8:45 am]

BILLING CODE 4160–15–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Invention; Availability for Licensing; ''Receptor-Mediated Delivery of Third-Party Proteins and Peptides to the Cytosol of Mammalian Cells''

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by or controlled by an agency of the U.S. Government and is available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally funded research and development.

ADDRESSES: Licensing information and copies of U.S. patents and patent applications referenced below may be obtained by contacting J. R. Dixon, Ph.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804 (telephone 301/496–7056 ext 206; fax 301/402–0220; E-Mail: jd212g@NIH.GOV). A signed Confidential Disclosure Agreement is required to receive a copy of any patent application.

SUPPLEMENTARY INFORMATION: Invention Title: ''Recombinant Chimeric Proteins Deliverable Across Cellular Membranes into Cytosol of Target Cells''.

Inventors; Drs. Ira H. Pastan (NCI), Trevor Prior (NCI), Waldemar Y. Debinski (NCI), Clay Siegall (NCI).

DHHS Ref. No. E–020–91/0 [= USP SN: 5,328,984 (= 07/663,455)—Filed March 4, 1991].

The following patent applications and patents are also available, to the extent necessary to practice the technology disclosed in the U.S.P. SN: 5,328,984, for licensing from the National Institutes of Health's Office of Technology Transfer:

1. 08/683,621, entitled: ''Hybrid Molecules Having Translocation Region and Cell-Binding Region'', inventor: John R. Murphy, Filed: July 17, 1996. [E–998–98/7]

2. 5,668,255 [= 08/102,387], entitled: ''Hybrid Molecules Having Translocation Region and Cell-Binding Region'', inventor: John R. Murphy, Filed: August 4, 1993. [E–998–98/6]

3. 07/722,484, entitled: ''Hybrid Molecules Having Translocation Region and Cell-Binding Region'', inventor: John R. Murphy, Filed: June 26, 1991. [E–998–98/5]

4. 07/538,276, entitled: ''Hybrid Molecules Having Translocation Region and Cell-Binding Region'', inventor: John R. Murphy, Filed: June 14, 1990. [E–998–98/4]

5. 07/456,095, entitled: ''Hybrid Molecules Having Translocation Region and Cell-Binding Region'', inventor: John R. Murphy, Filed: December 22, 1998. [E–998–98/3]

6. 06/742,554, entitled: ''Hybrid Protein and Fused Gene Encoding Same'', inventor: John R. Murphy, Filed June 7, 1985. [E–998–98/2]

7. 06/726,808, entitled: ''Hybrid Protein and Fused Gene Encoding Same'', inventor: John R. Murphy, Filed: April 25, 1985. [E–998–98/1]

8. 06/618,199, entitled: ''Hybrid Protein and Fused Gene Encoding Same'', inventor: John R. Murphy, Filed: June 7, 1984. [E–998–98/0].

Background

Protein toxins have several distinctive properties that allow them to facilitate the delivery of third-party proteins to the cell cytosol. First, they are modular in nature and possess separate domains that function independently to perform distinct functions. By domain swapping, toxins can be converted into delivery agents. Toxins enter cells by receptor-mediated endocytosis, avoid degradation, and translocate to the cell cytosol where they are cytotoxic. By disabling the toxin's cytotoxicity domain, it is possible to replicate this delivery pathway without causing damage to the cell. Further, by altering toxin-expressing vectors to include cDNAs encoding non-toxin related proteins and peptides, it is possible to mediate delivery of third-party proteins from the cell exterior to the cytosol. Thus, functionally active proteins can be joined to the toxin translocation module and the resulting chimeric protein developed into a delivery vehicle. Further the toxins' binding domain can be replaced with receptor-binding ligands of choice. By combining domains of different origins, various therapeutic proteins can be generated. Toxin-mediated delivery to the cytosol can be used for: enzyme replacement (to complement a genetic defect), peptide delivery for the generation of cytotoxic lymphocytes, delivery of anti-viral peptides, agonist of antagonist peptides of signaling pathways, etc.

Invention

This invention provides a method of making a hybrid foreign protein that can be delivered into the cytosol of the target cells across the cellular membranes. Further, the present invention provides a suitable vector containing a nucleotide sequence that encodes a hybrid protein.

The advantages of the invention are achieved by (1) providing a recombinant molecule possessing at least a recognition element, a translocation function, and one or more recombinant sites for inserting foreign proteins or polypeptides, and (2) making a recombinant chimeric protein translocatable across cellular membranes into the cytosol of target cells, said chimeric protein having at least one segment which is a functionally active foreign protein desired to be introduced *de novo* into cytosol of target cells, a recognition element that directs the hybrid protein to the target cells, and an additional segment having at least a translocation function which internalizes the protein and delivers the foreign protein into the cytosol of the target cells. In the case of *Pseudomonas* Exotoxin (''PE''), the recombinant sites could be located in either or both of domains Ib or III, but not in domain II. These chimeric proteins can be used for cytotoxic, diagnostic, or therapeutic purposes, such as for compensating the deficiency or defect of an enzyme or a protein which may be causative of a disease or an abnormality. The above mentioned invention is available, including any available foreign intellectual property rights, for licensing on an exclusive or non-exclusive basis.

Dated: April 28, 1999.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 99–11204 Filed 5–4–99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Fogarty International Center; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of meetings of the Fogarty International Center Advisory Board.

The meetings will be open to the public as indicated below, with attendance limited to space available.