



US007449188B2

(12) **United States Patent**  
**De Filette et al.**(10) **Patent No.:** **US 7,449,188 B2**  
(45) **Date of Patent:** **Nov. 11, 2008**(54) **RECOMBINANT OLIGOMETRIC PROTEIN  
COMPLEXES WITH ENHANCED  
IMMUNOGENIC POTENTIAL**WO WO 99/62953 \* 12/1999  
WO WO 00/32227 6/2000  
WO WO 0069907 A1 \* 11/2000  
WO WO 01/02440 1/2001  
WO WO 01/49886 7/2001  
WO WO 01/49886 A2 7/2001  
WO WO 01/59886 A3 7/2001(75) Inventors: **Marina De Filette**, Brussels (BE); **Tom  
Maria Deroo**, Ghent (BE); **Walter  
Fiers**, Destelbergen (BE); **Marleen  
Maras**, Sint-Martens-Lierde (BE); **Willy  
Alfons Min Jou**, Destelbergen (BE)(73) Assignee: **Vlaams Interuniversitair Instituut  
Voor Biotechnologie**, Zwijnaarde (BE)

## OTHER PUBLICATIONS

(\*) Notice: Subject to any disclaimer, the term of this  
patent is extended or adjusted under 35  
U.S.C. 154(b) by 75 days.Chang, C. et al., Phenotype mixing between different hepadnavirus  
nucleocapsid proteins reveals C protein dimerization to be cis prefer-  
ential. *J. Virol.* Aug. 1994;68(8):5225-31.\*(21) Appl. No.: **10/466,655**Fields Virology, 3<sup>rd</sup> Ed. edited by Fields, B.N. et al.  
Lippincott—Raven Publishers, Philadelphia, 1996,  
"Orthomyxoviridae: The Viruses and their Replication" pp. 1355 and  
1362-1365.\*(22) PCT Filed: **Jan. 18, 2002**Weissenhorn, W. et al. Assembly of a rod-shaped chimera of a  
trimeric GCN4 zipper and the HIV-1 gp41 ectodomain expressed in  
*Escherichia coli*. *Proc Natl Acad Sci U S A.* Jun. 10,  
1997;94(12):6065-9.\*(86) PCT No.: **PCT/EP02/00628**§ 371 (c)(1),  
(2), (4) Date: **Jul. 18, 2003**Cooper et al., "Mapping of Conformational B Cell Epitopes within  
Alpha-Helical Coiled Coil Proteins," *Molecular Immunology*, vol.  
34, No. 6 (433-440)(1997).\*(87) PCT Pub. No.: **WO02/074795**PCT Pub. Date: **Sep. 26, 2002**Harbury et al., "A Switch Between Two-, Three-, and Four-Stranded  
Coiled Coils in GCN4 Leucine Zipper Mutants," *Science*, vol. 262,  
pp. 1401-1407 (1993).\*(65) **Prior Publication Data**

US 2004/0116664 A1 Jun. 17, 2004

Landschulz et al., "The Leucine Zipper: A Hypothetical Structure  
Common to a New Class of DNA Binding Proteins," *Science*, vol.  
240 pp. 1759-1763 (1988).\*(30) **Foreign Application Priority Data**

Jan. 18, 2001 (EP) ..... 01200193

Bucher, D.J., et al., "A<sub>2</sub> (N2) Neuraminidase of the X-7 Influenza  
Virus Recombinant: Determination of Molecular Size and Subunit  
Composition of the Active Unit," *J Virol*, 10:60-66 (1972).(51) **Int. Cl.****A61K 39/145** (2006.01)  
**A61K 39/385** (2006.01)  
**C07K 19/00** (2006.01)  
**C07K 14/11** (2006.01)  
**C12N 15/62** (2006.01)  
**C12N 15/44** (2006.01)  
**C12N 15/63** (2006.01)  
**C12N 1/21** (2006.01)  
**C12N 5/10** (2006.01)Burton, D.R., "A Vaccine for HIV Type 1: The Antibody Perspective,"  
*Proc. Natl. Acad. Sci. USA*, 94:10018-10023 (1997).(52) **U.S. Cl.** ..... **424/192.1**; 424/196.11;  
424/209.1; 424/210.1; 530/350; 536/23.4;  
536/23.72; 435/320.1; 435/325; 435/252.3Chang, Z., et al., "*Mycobacterium Tuberculosis* 16-kDa Antigen  
(Hsp16.3) Functions as an Oligomeric Structure in Vitro to Suppress  
Thermal Aggregation," *J Biol Chem*, 271:7218-7223 (1996).(58) **Field of Classification Search** ..... 424/210.1,  
424/206.1, 192.1, 196.11, 204.1, 1.49, 135.1,  
424/159.1; 530/350, 387.3; 435/69.1, 69.7,  
435/5; 536/23.4Bowie, J.U., et al., "A Method to Identify Protein Sequences that Fold  
into a Known Three-Dimensional Structure," *Science*, 253:164-170  
(1991).

See application file for complete search history.

Deroo, T., et al., "Recombinant Neuraminidase Vaccine Protects  
Against Lethal Influenza," *Vaccine*, 14:561-569 (1996).(56) **References Cited**

## U.S. PATENT DOCUMENTS

5,463,024 A 10/1995 Kingsman et al. .... 530/350  
5,721,340 A \* 2/1998 Halazonetis ..... 530/350  
7,229,624 B2 \* 6/2007 Renner et al. .... 424/196.11Kodihalli, S., et al., "Selection of a Single Amino Acid Substitution in  
the Hemagglutinin Molecule by Chicken Eggs Can Render Influenza  
A Virus (H3) Candidate Vaccine Ineffective," *J Virol*, 69:4888-4897  
(1995).

(Continued)

*Primary Examiner*—Mary E Mosher(74) *Attorney, Agent, or Firm*—Husch Blackwell Sanders  
Welsh and Katz(57) **ABSTRACT**The present invention relates to a chimeric protein compris-  
ing an antigen and an oligomerisation domain. The present  
invention relates further to recombinant oligomeric protein  
complexes comprising said chimeric protein and the use  
thereof for the manufacture of a vaccine.

## FOREIGN PATENT DOCUMENTS

WO WO 94/10308 5/1994

**11 Claims, 14 Drawing Sheets**