



US009505839B2

(12) **United States Patent**  
**Lonberg et al.**

(10) **Patent No.:** **US 9,505,839 B2**  
(45) **Date of Patent:** **Nov. 29, 2016**

(54) **OPTIMIZATION OF ANTIBODIES THAT BIND LYMPHOCYTE ACTIVATION GENE-3 (LAG-3), AND USES THEREOF**

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(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 438 days.

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(21) Appl. No.: **14/093,867**

(22) Filed: **Dec. 2, 2013**

(65) **Prior Publication Data**

US 2014/0093511 A1 Apr. 3, 2014

**Related U.S. Application Data**

(63) Continuation of application No. PCT/US2013/048999, filed on Jul. 2, 2013.

(60) Provisional application No. 61/667,058, filed on Jul. 2, 2012.

(51) **Int. Cl.**

**A61K 39/395** (2006.01)  
**C07K 16/28** (2006.01)  
**C07K 16/30** (2006.01)  
**C07K 16/18** (2006.01)  
**A61K 45/06** (2006.01)  
**A61K 47/48** (2006.01)  
**A61K 39/00** (2006.01)

(52) **U.S. Cl.**

CPC ..... **C07K 16/28** (2013.01); **A61K 39/3955** (2013.01); **A61K 45/06** (2013.01); **A61K 47/48561** (2013.01); **C07K 16/18** (2013.01); **C07K 16/2803** (2013.01); **C07K 16/2818** (2013.01); **C07K 16/2827** (2013.01); **A61K 39/39558** (2013.01); **A61K 2039/507** (2013.01); **C07K 16/3061** (2013.01); **C07K 2317/21** (2013.01); **C07K 2317/565** (2013.01); **C07K 2317/76** (2013.01); **C07K 2317/92** (2013.01); **C07K 2317/94** (2013.01)

(58) **Field of Classification Search**

None  
See application file for complete search history.

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(57) **ABSTRACT**

The present invention provides isolated monoclonal antibodies that specifically bind LAG-3, and have optimized functional properties compared to previously described anti-LAG-3 antibodies, such as antibody 25F7 (US 2011/0150892 A1). These properties include reduced deamidation sites, while still retaining high affinity binding to human LAG-3, and physical (i.e., thermal and chemical) stability. Nucleic acid molecules encoding the antibodies of the invention, expression vectors, host cells and methods for expressing the antibodies of the invention are also provided, as well as immunoconjugates, bispecific molecules and pharmaceutical compositions comprising the antibodies. The present invention also provides methods for detecting LAG-3, as well as methods for treating stimulating immune responses using an anti-LAG-3 antibody of the invention. Combination therapy, in which the antibodies are co-administered with at least one additional immunostimulatory antibody, is also provided.

**16 Claims, 15 Drawing Sheets**