



US006344192B1

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

(10) **Patent No.:** **US 6,344,192 B1**
(45) **Date of Patent:** **Feb. 5, 2002**

(54) **USE OF INTERLEUKIN-15**

OTHER PUBLICATIONS

(75) Inventors: **Johan Adriaan Marc Grooten**,
Lovendegem; **Hans Peter Raf Dooms**,
Ypres; **Walter Charles Fiers**,
Destelbergen, all of (BE)

(73) Assignee: **Vlaams Interuniversitair Instituut**
voor Biotechnologie, Zwijnaarde (BE)

(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/380,049**

(22) PCT Filed: **Feb. 23, 1998**

(86) PCT No.: **PCT/EP98/01127**

§ 371 Date: **Aug. 23, 1999**

§ 102(e) Date: **Aug. 23, 1999**

(87) PCT Pub. No.: **WO98/36768**

PCT Pub. Date: **Aug. 27, 1998**

(30) **Foreign Application Priority Data**

Feb. 21, 1997 (EP) 9720051

(51) **Int. Cl.⁷** **A61K 45/00**

(52) **U.S. Cl.** **424/85.2**; 424/85.1; 435/69.5;
435/69.52; 435/386; 530/351; 930/140;
930/141

(58) **Field of Search** 424/85.2, 85.1;
435/69.52, 69.5, 386; 530/351; 930/140,
141

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,574,138 A * 11/1996 Grabstein et al. 530/351
5,698,194 A * 12/1997 Hadden 424/85.1
5,747,024 A * 5/1998 Grabstein et al. 424/85.2

FOREIGN PATENT DOCUMENTS

WO PCT/US95/05585 5/1995
WO PCT/US96/16870 10/1996

Janeway C. Immunobiology, 2nd Ed. 1996, 1:16–1:18, 7:17
and 7:19, Garland Publishing Inc. New York.*

Moore G.J. Designing peptide mimetics, Trends in Protein
Science. vol. 15 (1994) pp. 124–129.*

Juan Flo et al., Oral administration of a bacterial immuno-
modulator enhances the immune response to cholera toxin,
Vaccine, vol. 14, No. 12, 1996, pp. 1167–1173.

Imtiaz A. Khan et al., IL–15 Augments CD8+ T Cell–Me-
diated Immunity Against *Toxoplasma gondii* Infection in
Mice, *The American Association of Immunologists*, 1996,
pp. 2103–2108.

Hirokazu Kanegane et al., Activation of Naive and Memory
T Cells by Interleukin–15, *Blood*, vol. 88, No. 1, Jul. 1,
1996, pp. 230–235.

* cited by examiner

Primary Examiner—Jeffrey Stucker

Assistant Examiner—Ulrike Winkler

(74) *Attorney, Agent, or Firm*—Knobbe, Martens, Olson &
Bear, LLP

(57) **ABSTRACT**

The invention relates to the use of IL-15 or active variants
thereof and/or IL-15 activity enhancing compounds for the
manufacture of a pharmaceutical composition for manipu-
lating memory cells of the immune system, such as manipu-
lating viability ad/or responsiveness of said memory cells.
The IL-15 activity enhancing compound is for example
lipopolysaccharide (LPS). The invention further relates to
the use of IL-15 inhibiting or eliminating compounds for the
manufacture of a pharmaceutical composition for manipu-
lating memory cells of the immune system. Such inhibiting
or eliminating compounds are for example anti-IL-15
antibodies, anti-IL-15R α antibodies, fragments of these
antibodies, e.g. the Fab or F(ab)₂ fragment, soluble
IL-15R α , fusion proteins consisting of soluble IL-15R α , and
Fc fragment, compounds, e.g. peptides, binding and/or
inhibiting functional IL-15 receptor, IL-15 antisense oligo-
nucleotides.

7 Claims, 11 Drawing Sheets