(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 November 2006 (02.11.2006)

PCT

(10) International Publication Number
WO 2006/116156 A3

(51) International Patent Classification:
A61K 47/48 (2006.01) *A61P 37/06* (2006.01)
C12N 15/62 (2006.01) *C07K 14/435* (2006.01)
A61K 38/16 (2006.01)

(21) International Application Number:
PCT/US2006/015199

(22) International Filing Date: 18 April 2006 (18.04.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/674,342 22 April 2005 (22.04.2005) US
Not furnished 17 April 2006 (17.04.2006) US

(71) Applicant: **AMGEN INC.** [US/US]; Patent Operations M/S 28-2-C, One Amgen Center Drive, Thousand Oaks, CA 91320-1799 (US).

(72) Inventors: **SULLIVAN, John K.**; 1085 Rotella Street, Newbury Park, California 91320 (US). **MCGIVERN, Joseph G.**; 6208 Normandy Terrace, Oak Park, California 91377 (US). **MIRANDA, Leslie P.**; 3586 Mapleknoll Place, Thousand Oaks, California 91362 (US). **NGUYEN, Hung Q.**; 881 Saint Charles Drive, #10, Thousand Oaks, California 91360 (US). **WALKER, Kenneth W.**; 175 Mesa Avenue, Newbury Park, California 91320 (US). **HU, Shaw-Fen Sylvia**; 986 Lynnmere Drive, Thousand Oaks, California 91360 (US). **GEGG JR., Colin V.**; 487 Delwood Court, Newbury Park, California 91320 (US). **MCDONOUGH, Stefan I.**; 12 Concord Avenue, #3, Cambridge, Massachusetts 02138 (US).

(74) Agent: **STEINBERG, Nisan A.**; Patent Operations M/S 28-2-C, One Amgen Center Drive, Thousand Oaks, CA 91320-1799 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
4 October 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: TOXIN PEPTIDES WITH EXTENDED BLOOD HALFLIFE

(57) Abstract: Disclosed is a composition of matter of the formula (I) $(X^1)_a$-$(F^1)_d$-$(X^2)_b$-$(F^2)_e$-$(X^3)_c$ and multimers thereof, in which F1 and F2 are half-life extending moieties, and d and e are each independently 0 or 1, provided that at least one of d and e is 1; X^1, X^2, and X^3 are each independently -$(L)_f$-P-$(L)_g$-, and f and g are each independently 0 or 1; P is a toxin peptide of no more than about 80 amino acid residues in length, comprising at least two intrapeptide disulfide bonds; L is an optional linker; and a, b, and c are each independently 0 or 1, provided that at least one of a, b and c is 1. Linkage to the half-life extending moiety or moieties increases the in vivo half-life of the toxin peptide, which otherwise would be quickly degraded. A pharmaceutical composition comprises the composition and a pharmaceutically acceptable carrier. Also disclosed are a DNA encoding the inventive composition of matter, an expression vector comprising the DNA, and a host cell comprising the expression vector. Methods of treating an autoimmune disorder, such as, but not limited to, multiple sclerosis, type 1 diabetes, obesity, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, transplant rejection, graft-versus-host disease, and lupus and of preventing or mitigating a relapse of a symptom of multiple sclerosis are also disclosed.

WO 2006/116156 A3