

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
4 August 2011 (04.08.2011)

(10) International Publication Number
WO 2011/094545 A2

PCT

(51) International Patent Classification:

C07D 401/06 (2006.01) **A61K 31/4439** (2006.01)
C07D 403/06 (2006.01) **A61K 31/4025** (2006.01)
C07D 207/323 (2006.01) **A61P 25/28** (2006.01)

(21) International Application Number:

PCT/US2011/022929

(22) International Filing Date:

28 January 2011 (28.01.2011)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/336,959 28 January 2010 (28.01.2010) US
61/373,404 13 August 2010 (13.08.2010) US

(71) Applicant (for all designated States except US): **PRESIDENT AND FELLOWS OF HARVARD COLLEGE** [US/US]; 17 Quincy Street, Cambridge, MA 02138 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **FINLEY, Daniel** [US/US]; 4 Agassiz Park, Jamaica Plain, MA 02130 (US). **KING, Randall, W.** [US/US]; 310 Tappin Street, #5, Brookline, MA 02146 (US). **LEE, Byung-Hoon** [KR/US]; 2 Peabody Terrace, Cambridge, MA 02138 (US). **LEE, Min, Jae** [KR/US]; 20 Burroughs #3, Jamaica Plain, MA 02130 (US). **GAHMAN, Timothy, C.** [US/US]; 1654 Orchard Wood Road, Encinitas, CA 92024 (US).

(74) Agents: **SMITH, DeAnn, F.** et al.; Patent Group, Foley Hoag LLP, 155 Seaport Boulevard, Boston, MA 02210-2600 (US).

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

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report (Rule 48.2(g))

(54) Title: COMPOSITIONS AND METHODS FOR ENHANCING PROTEASOME ACTIVITY

(57) Abstract: Proteinopathies result from the proteasome not acting efficiently enough to eliminate harmful proteins and prevent the formation of the pathogenic aggregates. As described herein, inhibition of proteasome-associated deubiquitinase Usp 14 results in increased proteasome efficiency. The present invention therefore provides novel compositions and methods for inhibition of Usp14, enhancement of proteasome activity and treatment of proteinopathies.



WO 2011/094545 A2