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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 May 2010 (14.05.2010)

PCT

(10) International Publication Number
WO 2010/053584 A3

(51) International Patent Classification:
C07K 14/705 (2006.01)

(21) International Application Number:
PCT/US2009/006050

(22) International Filing Date:
10 November 2009 (10.11.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/198,823 10 November 2008 (10.11.2008) US
61/278,317 5 October 2009 (05.10.2009) US

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(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, 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, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
2 September 2010

(54) Title: COMPOSITIONS AND METHODS FOR MODULATING CELL-CELL FUSION VIA INTERMEDIATE-CONDUCTANCE CALCIUM-ACTIVATED POTASSIUM CHANNELS

(57) Abstract: Compositions and methods are provided for modulating cell-cell fusion by using agents that modulate expression, activity, or function of intermediate- conductance calcium-activated potassium (SK4) channel. In some embodiments, the compositions and methods of the invention provide for inhibition of multi-nucleated osteoclastogenesis and cell-cell fusion, especially cell fusion involving macrophages. In such embodiments, the compositions can comprise inhibitory nucleic acids, monoclonal antibodies or small molecule inhibitors of the SK4 channels and find use in preventing and/or treating various diseases or disorders including bone loss, autoimmune and inflammatory diseases or disorders, implant and transplant rejection, and cancer metastasis. In other embodiments, the compositions and methods of the invention provide for activation of cell-cell fusion. Also provided are methods to screen for SK4 channel modulators (inhibitors or activators) that modulate cell-cell fusion, particularly macrophage cell fusion.

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