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(72) Inventors; and

(75) Inventors/Applicants (for US only): **BELOUSKI, Edward, John** [US/US]; 4541 La Tuna Court, Camarillo, CA 93012 (US). **ELLISON, Murielle, Marie** [US/US]; 645 Camino Manzanas, Thousand Oaks, CA 91360 (US). **HAMBURGER, Agnes, Eva** [US/US]; 172 Donegal Avenue, Newbury Park, CA 91320 (US). **HECHT, Randy, Ira** [US/US]; 2569 Piccadilly, Thousand Oaks, CA 91362 (US). **LI, Yue-Sheng** [US/US]; 3025 Shadow Hill Circle, Thousand Oaks, CA 91360 (US). **MICHAELS, Mark, Leo** [US/US]; 5007 Texhoma Avenue, Encino, CA 91316 (US). **SUN, Jeonghoon** [KR/US]; 4340 Camino De La Rosa, Thousand Oaks, CA 91320 (US). **XU, Jing** [CN/US]; 1677 Glider Court, Thousand Oaks, CA 91320 (US).(21) International Application Number:
PCT/US2009/046113(74) Agent: **LAMERDIN, John, A.**; Amgen Inc., One Amgen Center Drive, Patent Operations, M/S 28-2-C, Thousand Oaks, CA 91320-1799 (US).(22) International Filing Date:
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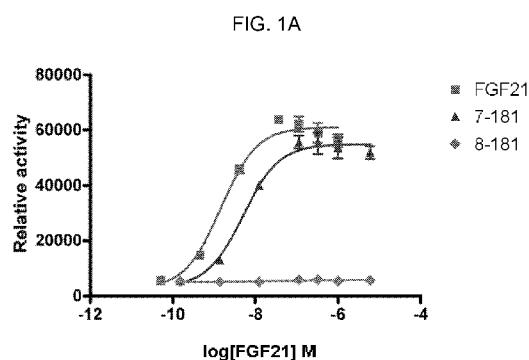
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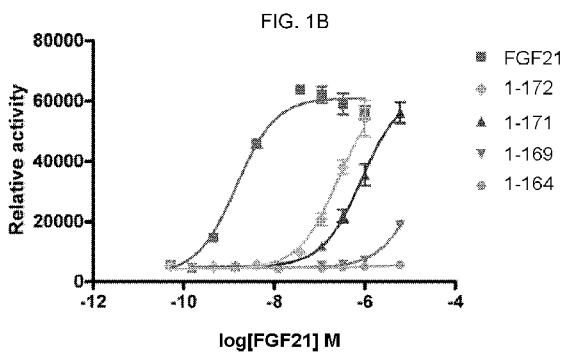
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(71) Applicant (for all designated States except US): **AMGEN INC.** [US/US]; One Amgen Center Drive, Thousand Oaks, CA 91320-1799 (US).*[Continued on next page]*

(54) Title: FGF21 MUTANTS AND USES THEREOF



(57) Abstract: The invention provides nucleic acid molecules encoding FGF21 mutant polypeptides, FGF21 mutant polypeptides, pharmaceutical compositions comprising FGF21 mutant polypeptides, and methods for treating metabolic disorders using such nucleic acids, polypeptides, or pharmaceutical compositions.





(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, 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.

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51. (New) A polypeptide comprising the amino acid sequence of SEQ ID NO:4, further comprising the mutations L98R and P171G.

52. (New) A fusion polypeptide comprising the polypeptide of claim 51 linked to a heterologous sequence.

53. (New) The fusion polypeptide of claim 52, wherein the heterologous sequence is a Fc sequence.

54. (New) The fusion polypeptide of claim 53, wherein the Fc sequence comprises the amino acid sequence of SEQ ID NO:13.

55. (New) The fusion polypeptide of claim 54, wherein the polypeptide is joined to the heterologous sequence by a linker.

56. (New) The fusion polypeptide of claim 55 wherein the linker is GGGGGSGGGSGGGGS (SEQ ID NO:23).

57. (New) The fusion polypeptide of claim 55 wherein the linker is GGGGSGGGGSGGGGS (SEQ ID NO:31).

58. (New) The fusion polypeptide 56, wherein the fusion polypeptide is encoded by the nucleic acid sequence of SEQ ID NO:37.

59. (New) A multimer comprising two or more copies of the fusion polypeptide of claim 58.

60. (New) A pharmaceutical composition comprising the fusion polypeptide of claim 58 and a pharmaceutically acceptable formulation agent.