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- (81) Designated States: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

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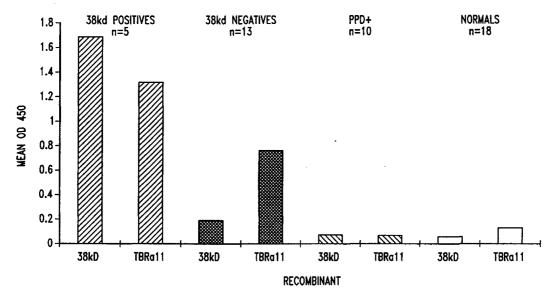
With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:

6 August 1998 (06.08.98)

(54) Title: COMPOUNDS AND METHODS FOR DIAGNOSIS OF TUBERCULOSIS



(57) Abstract

Compounds and methods for diagnosing tuberculosis are disclosed. The compounds provided include polypeptides that contain at least one antigenic portion of one or more M. tuberculosis proteins, and DNA sequences encoding such polypeptides. Diagnostic kits containing such polypeptides or DNA sequences and a suitable detection reagent may be used for the detection of M. tuberculosis infection in patients and biological samples. Antibodies directed against such polypeptides are also provided.

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Interna. .al Application No PCT/US 97/18214

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 C12N15/31 C071 C12N15/62 C07K14/35 C07K16/12 C12Q1/68 IPC 6 G01N33/53 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) C12N C07K C12O G01N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. EP 0 419 355 A (INNOGENETICS NV) 27 March 1,3,5-9, 13-18, 21-23, 26,27, 30-32, 35-41, 44,45, 48,49 see abstract see page 24, line 45 - page 26, line 19 see page 56 - page 72; claims WO 95 01441 A (STATENS SERUMSINSTITUT 50,51,54 Α ;ANDERSEN PETER (DK); ANDERSEN AASE BENGAAR) 12 January 1995 see abstract see page 20, line 13 - page 25, line 16 see page 73; claim 30 -/--Further documents are listed in the continuation of box C. X Patent family members are listed in annex. Χ Ospecial categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or document is combined with one or more other such doc ments, such combination being obvious to a person skilled other means in the art. *P* document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 2 3, 06, 98 5 March 1998 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 Macchia, G

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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ROMAIN ET AL: "PREPARATION OF TUBERCULIN ANTIGEN L" ANNALES DE L'INSTITUT PASTEUR / MICROBIOLOGIE, vol. 136B, 1985, pages 235-248, XP002026409	
P,X	WO 97 09429 A (CORIXA CORP) 13 March 1997 see abstract	1,3,5-9, 12-18, 21-23, 26,27, 30-32, 35-41, 44,45, 48-51
	see page 173-181; claims	
Ρ,Χ	WO 97 09428 A (CORIXA CORP) 13 March 1997 see abstract see page 158 - page 163; claims	1,3,5-8

national application No.

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Box I Observations where certain clair	ms were found unsearchable (Continuation of item 1 of first sheet)			
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:				
Claims Nos.: because they relate to subject matter n	ot required to be searched by this Authority, namely:			
	rnational Application that do not comply with the prescribed requirements to such nal Search can be carried out, specifically:			
3. Claims Nos.: because they are dependent claims an	d are not drafted in accordance with the second and third sentences of Rule 6.4(a).			
Box II Observations where unity of inv	ention is lacking (Continuation of item 2 of first sheet)			
This International Searching Authority found mu	Itiple inventions in this international application, as follows:			
see continuation-sheet				
As all required additional search fees we searchable claims.	vere timely paid by the applicant, this International Search Report covers all			
As all searchable claims could be sear of any additional fee.	ched without effort justifying an additional fee, this Authority did not invite payment			
As only some of the required additional covers only those claims for which fees	I search fees were timely paid by the applicant, this International Search Report swere paid, specifically claims Nos.:			
restricted to the invention first mention	re timely paid by the applicant. Consequently, this International Search Report is ed in the claims; it is covered by claims Nos.: ,27,30-32,35-41,44,45,48-51,53,54 all partially eet)			
Remark on Protest	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.			

1. Claims: 1, 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

A polypeptide comprising an antigenic portion of a soluble M. tuberculosis antigen or a variant, having an N-terminal aminoacid sequence as in Seq.ID:115 and/or encoded by a DNA molecule as in Seq.ID:96, complements of said sequence or sequences hybridizing to it. A DNA molecule comprising a sequence encoding said polypeptide. An expression vector comprising said DNA molecule, a host cell transformed with said expression vector. A method for detecting M. tuberculosis infection in a biological sample by detection of antibodies binding to said polypeptide or by detection of said polypeptide. A method for detecting M. tuberculosis infection in a biological sample by detection of said DNA sequence. Diagnostic kits thereof. An antibody binding to said polypeptide. A fusion protein comprising said polypeptide. Diagnostic kit comprising said fusion protein.

2. Claims: 1, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:116.

3. Claims: 1, 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:(1)17 and 25.

4. Claims: 1, 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:118 and 24.

5. Claims: 1, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:119.

6. Claims: 1, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:120.

7. Claims: 1, 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:121 and 52.

8. Claims: 1, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:122.

9. Claims: 1, 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:123 and 94.

10. Claims: 1, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:131.

11. Claims: 2, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:124.

12. Claims: 2, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:132.

13. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID:1.

14. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:2.

15. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:4 and 17.

16. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:5.

17. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:6.

18. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:7.

19. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:8.

20. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID:9.

21. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:10 and 13.

22. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID:14.

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23. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:15.

24. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:16.

25. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:18.

26. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:19.

27. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:20.

28. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:21.

29. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:22.

30. Claims: 3, 5-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:23.

31. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:26.

32. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID:27.

33. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:28.

34. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:29.

35. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:30.

36. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:31.

37. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:32.

38. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:33.

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39. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:34.

40. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:35.

41. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:36.

42. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:37.

43. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:38.

44. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:39.

45. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:40.

46. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:41.

47. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:42.

48. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:43, 44 and 178.

49. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:45.

50. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID: 46.

51. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:47.

52. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:48.

53. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:49.

54. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:50.

55. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:51.

56. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:133.

57. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:134.

58. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:158.

59. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:159.

60. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:160.

61. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:161.

62. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:162.

63. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID:163.

64. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:164 and 165.

65. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID:166 and 167.

66. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:168 and 169.

67. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:170 and 171.

68. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID:172 and 173.

69. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID: 174 and 175.

70. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq. ID: 176 and 177.

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71. Claims: 4-9, 12-18, 21-23, 26, 27, 30-32, 35-41, 44, 45, 48-51, 53, 54 all partially.

Same as invention 1 but for Seq.ID:196.

72. Claims: 10, 12-16, 28, 30, 31, 33, 35-39, 52, 54 all partially.

A method for detecting M. tuberculosis infection in a biological sample by detection of antibodies binding to a polypeptide having an N-terminal sequence as in Seq.ID:129, or by detection of a protein or polypeptide that binds to an agent binding to a polypeptide having an N-terminal sequence as in Seq.ID:129. Diagnostic kits thereof. A fusion protein comprising said polypeptide. Diagnostic kit comprising said fusion protein.

73. Claims: 10, 12-16, 28, 30, 31, 33, 35-39, 52, 54 all partially.

Same as invention 72 but for Seq.ID:130.

74. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

A method for detecting M. tuberculosis infection in a biological sample by detection of antibodies binding to a polypeptide encoded by a DNA sequence consisting of Seq.ID:3, complements or hybridizing sequences. A method for detecting M. tuberculosis infection in a biological sample by detection of said DNA sequence. A method for detecting M. tuberculosis infection in a biological sample by detection of a protein or polypeptide that binds to an agent binding to a polypeptide encoded by Seq.ID:3, complements or hybridizing sequences. Diagnostic kits thereof.

75. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:11.

76. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:12.

77. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:135.

78. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:136.

79. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:151.

80. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:152.

81. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:153.

82. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:154 and 155.

83. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:184.

84. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq. ID:185.

85. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:186.

86. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:187.

87. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:188.

88. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seq.ID:194 and 195.

89. Claims: 11-16, 19-21, 24-26, 29-31, 34-39, 42, 43, 46, 47 all partially.

Same as invention 74 but for Seg.ID:198.

Intermation on patent family members

Interna al Application No
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