From:
Sent: Tuesday, March 09, 2010 8:40 AM
To: patent_quality_comments
Subject: public comment

Please see attached document for details.

for any Prior Art & Searching
for all Technology Art Units

Best Regards,

Stephen S. Key
& USPTO Public Search Associates.
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703-201-0098

On-Site USPTO Public Search Facility Madison East Alexandria 8am-8pm Monday-Friday.
Examiner Exclusive Databases: US, USPUB, USCOR, IPC, IPCR, EPO, JPO, Derwent , etc.
Pertinent Prior Art for Prosecution & Litigation in All Technological Fields and Art Units.

PATENT_QUALITY_COMMENTS@USPTO.GOV

By Stephen Key

I would like to suggest a computerized method for use in creating quantifiable metrics to be used for developing a system which would offer a measurement indicia reflecting the quality of an issued U.S. patent (past, present & future). These metrics, if adopted, could then be used to place a measurement indicia from 100-1000 points on all issued U.S. patents. The computerized quantifiable metrics would be based on points allotted for various elements of the front page and claims of a U.S. patent (as shown at end of document).

There are many metric systems in societies, but this quantifiable metrics system would be analogous to that used by the present American credit score system, a continual, quarterly, ever changing metric . To this point, it is noted that,

*" The **credit score system** in the United States is a number representing the creditworthiness of a person or the likelihood that person will pay his or her debts. It has shown to be very predictive of risk, made credit more widely available to consumers and lowered the cost of providing credit.[1][2] A credit score is primarily based on a statistical analysis of a person's credit report information, typically from the three major American credit bureaus: Equifax, Experian, and TransUnion . "*

In terms of U.S. patents, the selected elements of information on **the front page and the claims** of the patent would each be quantified with a certain number of points, for example:

Front Page Elements & Points:

Inventors : 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, 0, 0, 0…

First inventor 10 pts, second 9 pts… zeroing out in order to recognize everyone but not be abused as a metric

Continuations or Divisions: -50, -40, -30, -20, -10, 0, 0, 0...

First (minus 50 pts) , second (minus 40 pts)… zeroing out in order to not wipe out long continuations . Also the parent patent is recognized by no minus it is only the children that are negated knowing we have many, many children in the system.

International Classifications: **10, 5, 4, 3, 2, 1, 0, 0, 0...**

First 10 pts, second 5pts, third 4pts etc….zeroing out in order to not inflate multi ipc's. Also it is international recognition of our international system.

U.S. Classifications (each): **20, 10, 5, 4, 3, 2, 1, 0, 0, 0...**

First 20pts, second 10 pts, third 5pts, …zeroing out in order to not inflate multi classifications. Also it is a historical recognition of the quality of work done, past, present and future.

Field of Search: **20, 20, 20... for each class** **20, 20, 20... for each subclass**

20 points for every class and 20 points for every subclass in recognition of where the real quality of a patent can be found on the front page. Well examined Design patents will still have large fields of search. Really old patents will be disadvantaged but most technologies are multi classified.

Cited References (each): **10, 10, 10... for cited by examiner**

2, 2, 2... for cited by applicant

5, 5, 5... for cited foreign patents

2, 2, 2... for cited other publications

A heavily weighted system favoring the examiners found art, acknowledging the international significance of art, and still permitting large numbers of cited references and npl without inflating this art unit trend in comparison to other art units.

Examiner (each): **20 per primary** **10 assistant**

Recognition of everyone's important work in the quality of the system.

……end of front page elements points……..

Claims points: **100, 80, 60, 40, 20, 0, 0, 0... per independent**

10, 9, 8, 7, 6, 5, 4, 3, 2, 1, 0, 0, 0... per dependent

5, 4, 3, 2, 1, 0, 0, 0... per dependent on dependent

3, 2, 1, 0, 0, 0... per dependent on dependent on dependent

You have to start somewhere and these are most likely the most contentious debatable points system. This is designed to not over inflate over claimed patents, but not lower too much the simple art forms with a few independent claims.

The above points scoring system applied to a random sample shows:

Patent No.	Front Page Pts	Claims Pts	Total Points
6,000,000	83	399	482
6,111,111	164	119	283
6,222,222	227	310	537
6,333,333	212	284	496
6,444,444	696	218	914
6,555,555	275	280	555
6,666,666	290	406	696
6,777,777	182	159	341
6,888,888	532	385	917
6,999,999	310	327	637

These quantifiable metrics do not claim to reflect the arguable monetary dollar value of a patent (as determined by IP organizations such as Ocean Tomo) but rather attempt to reveal recognizable trends in the quality a U.S. patent. For example, possibly those with points under 300 may be under examined. For example, those with points over 800 may be over claimed. For example, those art units with all low points may be simple yet relatively high quality. For example, those art units with all high points may not be high quality but score high because their complexity. Application of a metric to 7,770,000 U.S patents is a huge task so I streamlined how the front page & claims elements are worked out. Following is my first system, those with more expertise & more experience could develop a much better system.

Examples of calculations of Points System:

(copying only front page and claims from the text databases)

US-PAT-NO: 6333333
DOCUMENT-IDENTIFIER: US 6333333 B1
See image for Certificate of Correction
TITLE: Methods for treating proliferative diseases
DATE-ISSUED: December 25, 2001
INVENTOR-INFORMATION:
NAME CITY STATE ZIP CODE COUNTRY

10 Bishop; Walter R.
Pompton Plains
NJ

9 Catino; Joseph J.
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CT
N/A
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8 Doll; Ronald J.
Maplewood
NJ
N/A
N/A

7 Ganguly; Ashit
Upper Montclair
NJ
N/A
N/A

6 Girijavallabhan; Viyyoor M.
Parsippany
NJ
N/A
N/A

5 Kirschimeier; Paul
Basking Ridge
NJ
N/A
N/A

4 Liu; Ming
Fanwood
NJ
N/A
N/A

3 Nielsen; Loretta L.
Millington
NJ
N/A
N/A

2 Cutler; David L.
Morristown
NJ
N/A
N/A
ASSIGNEE INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY TYPE CODE
Schering Corporation
Kenilworth
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N/A
N/A
02
APPL-NO: 09503513
DATE FILED: February 14, 2000

PARENT-CASE:

This application is a continuation of 09/217,335 filed Dec. 21, 1998; now U.S. Pat. No. 6,096,757 which claims benefit to Provisional Application No. 60/068,423 Filed Dec. 22, 1997 which claims benefit to Provisional Application No. 60/098,339 Filed Aug. 28, 1998 which claims benefit to Provisional Application No. 60/106,096 Filed Oct. 29, 1998.

10 INT-CL-ISSUED: [07] A61K031/44

INT-CL-CURRENT:
TYPE IPC DATE
CIPS A61 K 31/475 20060101
CIPS A61 K 31/505 20060101
CIPS A61 K 31/675 20060101
CIPS A61 K 31/445 20060101
CIPS A61 K 31/53 20060101

US-CL-ISSUED: 514/290 , 514/274

20 + 10 US-CL-CURRENT: 514/290, 514/274

20 + 20 FIELD-OF-CLASSIFICATION-SEARCH: 514/290; 514/274
See application file for complete search history

REF-CITED:
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PAT-NO ISSUE-DATE PATENTEE-NAME US-CL
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August 1994
Graham et al.
514/357
N/A
N/A

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May 1995
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N/A
N/A

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August 1997
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February 1998
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September 1998
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February 1999
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514/290
N/A
N/A

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FOREIGN-PAT-NO PUBN-DATE COUNTRY US-CL
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August 1998
EP

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July 1992
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April 1995
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July 1997
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October 1997
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December 1997
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August 1998
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October 1998
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5 WO98/54966
December 1998
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2 Moasser, et al. Proc. Natl. Acad. Sci. USA, vol. 95, pp. 1369-1374, Feb. 1998.

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2 Nagasu, et al., Cancer Research 55, 5310-5314, Nov. 1995.

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2 SHI, et al., "Enhanced efficacy of the farnesyl protein transferase inhibitor SCH66336 in combination with paclitaxel", Proceedings of the American Association For Cancer Research Annual Meeting, 1999 (Abstract No. 3457).

2 Schlitzer, "Hemmstoffe der Farnesyltransferase: Ein neuer Ansatz zur Entwicklung potentieller Krebstherapeutika," Pharmazie in Unserer Zeit, vol. 27, No. 6, Nov. 1998 pp. 278-288.

2 Omer et al.: "CA1A2X-competitive inhibitors of farnesyltransferase as anti-cancer agents," Trends in Pharmacological Sciences, vol. 18, No. 11, Nov. 1, 1997, pp. 437-445.

2 Miller, et al., Increased radioresistance of Ejras-transformed human osteosarcoma cells and its modulation by lovastatin, an inhibitor of p21ras isoprenylation, (Abstract from Int. J. Cancer, 53 (2): 302-7 (Jan. 21, 1993).

2 Hausheer et al., "Ab initio quantum mechanica I and x-ray crystallographic studies of gemcitabine and 2'-deoxycytosine", Comput. Chem., 20(4), 459-467, 1996.

ART-UNIT: 164
20 PRIMARY-EXAMINER: Reamer; James H.
ATTY-AGENT-FIRM: Kutzenco; Allan N. Gould; James M. Albanese; Margaret M.

ABSTRACT:

Methods are provided for treating proliferative diseases, especially cancers, comprising administering (1) a farnesyl protein transferase inhibitor in conjunction with (2) an antineoplastic agent and/or radiation therapy.

24 Claims, 38 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 38

CLAIMS:

What is claimed is:

100 1. A method of treating a proliferative disease in a patient in need of such treatment, said treatment comprising administering, concurrently or sequentially, an effective amount of (1) a FPT inhibitor and (2) an antineoplastic agent and/or radiation therapy; wherein the FPT inhibitor comprises a compound having the formula (I) or (III): ##STR220##

where,

X.sub.1, X.sub.2 and X.sub.3, independently of one another, are each a hydrogen, chlorine or bromine atom;

the dotted line between Z and the 7-membered carbocyclic ring represents a single or double bond;

Z is a nitrogen atom or a CH radical when the bond between Z and the 7-membered carbocyclic ring is a single bond;

Z is a C radical when the bond between Z and the 7-membered carbocyclic ring is a double bond;

Y.sub.1 = ##STR221##

where R.sub.1 is a hydrogen atom or a lower alkyl, --CONH.sub.2 or --COR.sub.2 group, where R.sub.2 is a lower alkyl group, or

Y.sub.1 = ##STR222##

or one of its isomers in the 1, 2 or 3 position;

R.sub.6 is a --NR.sub.7 (CH.sub.2).sub.n --R.sub.4 group, where n is 2 or 3; R.sub.4 is a ##STR223##

group attached at the 1, 2, 4 or 5 position, where R.sub.5 is a hydrogen atom or a lower alkyl group; and R.sub.7 is a hydrogen atom or an alkyl group substituted with a phenyl group, or

R.sub.6 is ##STR224##

where R.sub.4 is defined the same as above; and

Y.sub.2 is a X.sub.6 -cycloalkyl group, where X.sub.6 is a CH.sub.2, O or NH group;

with the proviso that the FPT inhibitor is not the following compound: ##STR225##

10 2. The method of claim 1 wherein the FPT inhibitor is a compound having the formula (I): ##STR226##

where,

X.sub.1, X.sub.2, X.sub.3, Z, Y.sub.1 and the dotted line are defined the same as above.

9 3. The method of claim 1 wherein the FPT inhibitor is a compound having the formula (III): ##STR227##

where,

X.sub.1, X.sub.2, X.sub.3, Y.sub.2 and R.sub.6 are defined the same as above.

8 4. The method of claim 1 wherein said FPT inhibitor, and said antineoplastic agent and/or radiation are administered concurrently.

7 5. The method of claim 1 wherein said FPT inhibitor, and said antineoplastic agent and/or radiation are administered simultaneously.

6 6. The method of claim 1 wherein said FPT inhibitor, and said antineoplastic agent and/or radiation are administered sequentially.

5 7. The method of claim 1 wherein said antineoplastic agent and/or radiation therapy is administered first.

4 8. The method of claim 1 wherein said FPT inhibitor is administered first.

3 9. The method of claim 1 wherein said proliferative disease is: lung cancer, pancreatic cancer, colon cancer, myeloid leukemia, melanoma, thyroid follicular cancer, bladder carcinoma, glioma, myelodysplastic syndrome, breast cancer or prostate cancer.

2 10. The method of claim 1 wherein said antineoplastic agent is selected from: Uracil mustard, Chlormethine, Cyclophosphamide, Ifosfamide, Melphalan, Chlorambucil, Pipobroman, Triethylenemelamine, Triethylenethiophosphoramine, Busulfan, Carmustine, Lomustine, Streptozocin, Dacarbazine, Temozol-omide, Methotrexate, 5-Fluorouracil, Floxuridine, Cytarabine, 6-Mercaptopurine, 6-Thioguanine, Fludarabine phosphate, Pentostatine, Gemcitabine, Vinblastine, Vincristine, Vindesine, Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Paclitaxel, Mithramycin, Deoxycoformycin, Mitomycin-C, L-Asparaginase, Interferons, Etoposide, Teniposide 17-Ethinylestradiol, Diethylstilbestrol, Testosterone, Prednisone, Fluoxymesterone, Dromostanolone propionate, Testolactone, Megestrolacetate, Tamoxifen, Methylprednisolone, Methyltestosterone, Prednisolone, Triamcinolone, Chlorotrianisene, Hydroxyprogesterone, Aminoglutethimide, Estramustine, Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, Goserelin, Cisplatin, Carboplatin, Hydroxyurea, Amsacrine, Procarbazine, Mitotane, Mitoxantrone, Levamisole, Navelbene, CPT-11, Anastrazole, Letrazole, Capecitabine, Reloxafine, Droloxafine, or Hexamethylmelamine.

1 11. The method of claim 1 wherein said antineoplastic agent is 5-Fluorouracil.

0 12. The method of claim 1 wherein said antineoplastic agent is temozolomide.

0 13. The method of claim 1 wherein said radiation is .gamma.-radiation.

80 14. A method of treating a proliferative disease in a patient in need of such treatment, said treatment comprising administering, concurrently or sequentially, an effective amount of (1) a FPT inhibitor and (2) gemcitabine; wherein the FPT inhibitor is a compound having the formula (I)

or (III): ##STR228##

where,

X.sub.1, X.sub.2 and X.sub.3, independently of one another, are each a hydrogen, chlorine or bromine atom;

the dotted line between Z and the 7-membered carbocyclic ring represents a single or double bond;

Z is a nitrogen atom or a CH radical when the bond between Z and the 7-membered carbocyclic ring is a single bond;

Z is a C radical when the bond between Z and the 7-membered carbocyclic ring is a double bond; Y.sub.1 = ##STR229##

where R.sub.1 is a hydrogen atom or a lower alky, --CONH.sub.2 or --COR.sub.2 group, where R.sub.2 is a lower alkyl group, or

Y.sub.1 = ##STR230##

or one of its isomers in the 1, 2 or 3 position;

R.sub.6 is a --NR.sub.7 (CH.sub.2).sub.n --R.sub.4 group, where n is 2 or 3; R.sub.4 is a ##STR231##

group attached at the 1, 2, 4 or 5 position, where R.sub.5 is a hydrogen atom or a lower alkyl group; and R.sub.7 is a hydrogen atom or an alkyl group substituted with a phenyl group, or

R.sub.6 is ##STR232##

where R.sub.4 is defined the same as above; and

Y.sub.2 is a X.sub.6 -cycloalkyl group, where X.sub.6 is a CH.sub.2, O or NH group;

with the proviso that the FPT inhibitor is not the following compound: ##STR233##

10 15. The method of claim 14 wherein the proliferative disease is an epithelial cancer.

9 16. The method of claim 14 wherein the proliferative disease is: prostate cancer, lung cancer, or pancreatic cancer.

8 17. The method of claim 14 wherein the proliferative disease is pancreatic cancer.

0 18. The method of claim 1, wherein the antineoplastic agent is a microtubule affecting agent.

5 19. The method of claim 18 wherein the microtubule affecting agent is paclitaxel or a paclitaxel derivative.

4 20. The method of claim 18 wherein the microtubule affecting agent is Taxotere.

3 21. The method of claim 18 wherein the proliferative disease is: prostate cancer, lung cancer, pancreatic cancer, colon cancer, or bladder carcinoma.

2 22. The method of claim 18 wherein the proliferative disease is prostate cancer.

1 23. The method of claim 18 wherein the proliferative disease is lung cancer.

0 24. The method of claim 18 wherein the proliferative disease is pancreatic cancer.

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US-PAT-NO: 6444444
DOCUMENT-IDENTIFIER: US 6444444 B1
TITLE: Genes encoding mycobacterial proteins associated with cell binding and cell entry and uses thereof

DATE-ISSUED: September 3, 2002

INVENTOR-INFORMATION:
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N/A
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APPL-NO: 08677970
DATE FILED: July 10, 1996

INT-CL-ISSUED: [07] C12P021/06 , C12N015/09 , C12N015/00 , C07H021/04

INT-CL-CURRENT:
TYPE IPC DATE
10 CIPS C07 K 14/35 20060101
5 CIPS C07 K 14/195 20060101
4 CIPN A61 K 48/00 20060101
3 CIPN A61 K 39/00 20060101

US-CL-CURRENT: **20** 435/69.3 , **10** 435/70.1 , **5** 435/71.1 , **4** 435/71.2 , **3** 435/252.3 , **2** 435/254.11 , **1** 435/320.1 , **0** 435/325 , **0** 514/44 , **0** 536/23.7 , **0** 935/9 , **0** 935/11 , **0** 935/12 , **0** 935/22 , **0** 935/52 , **0** 935/66

FIELD-OF-CLASSIFICATION-SEARCH **20** 435/69.3; **20** 435/320.1 ; ; **20** 435/70.1 ; ; **20** 435/71.1 ; ; **20** 435/71.2 ; ; **20** 435/325 ; ; **20** 435/252.3 ; ; **20** 435/254.11 ; ; **20** 530/350 ; ; **20** 536/23.7 ; ; **20** 514/44 ; ; **20** 935/9 ; ; **20** 935/11 ; ; **20** 935/12 ; ; **20** 935/22 ; ; **20** 935/52 ; ; **20** 935/66
See application file for complete search history

REF-CITED:
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PAT-NO ISSUE-DATE PATENTEE-NAME US-CL
10 5580859
December 1996
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December 1999
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June 2000
Riley
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N/A
N/A

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FOREIGN-PAT-NO PUBN-DATE COUNTRY US-CL
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June 1995
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August 1996
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ART-UNIT: 1645
20 PRIMARY-EXAMINER: Duffy; Patricia A.
ATTY-AGENT-FIRM: Sim & McBurney

ABSTRACT:

A gene from a strain of Mycobacterium encoding a protein of molecular weight between about 45 to about 60 kDa and associated with cell binding and cell entry was cloned. The genes and encoded protein have utility in immunogenic preparations or diagnostic applications.

10 Claims, 57 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 55

CLAIMS:

What we claim is:

100 1. An isolated nucleic acid fragment comprising a nucleic acid sequence that has at least 85% homology as compared to the full length of SEQ ID NO: 2 and encodes a mycobacterial protein associated with cell binding and cell entry having a molecular weight of about 45 to about 60 kDa.

10 2. The isolated nucleic acid fragment as claimed in claim 1 which is amplificable by polymerase chain reaction (PCR) by a pair of primers consisting of the sequences of primers 4879 (SEQ ID NO:12) and 4882 (SEQ ID NO: 15); or 4879 (SEQ ID NO: 12) and 4865 (SEQ ID NO: 11); or 4879 (SEQ ID NO: 12) and 4812 (SEQ ID NO: 10).

10 3. The nucleic acid fragment of claim 9 from a Mycobacterium strain of Mycobacerium tuberculosis.

5 4. The nucleic acid fragment of claim 2 from a Mycobacterium strain of Mycobacterium bovis.

4 5. A vector for transformation of a host comprising the nucleic acid fragment of claim 2.

3 6. The vector of claim 5 further comprising DNA sequences for expression of said protein in said host.

2 7. An isolated host cell transformed to contain an expression vector as claimed in claim 6.

80 8. A method of producing a substantially pure recombinant mycobacterial protein associated with cell binding and cell entry and having a molecular weight between about 45 kDa and 60 kDa, which comprises: transforming a host with a vector as claimed in claim 6; growing the transformed host to express the protein, and isolating and purifying the protein free from other proteinaceous and cellular material.

10 9. An immunogenic composition, comprising at least one nucleic acid fragment as claimed in claim 2 as an active component thereof, and a pharmaceutically acceptable carrier.

60 10. A method of generating an immune response in a host, which comprises administering to the host an immunoeffective amount of the immunogenic composition of claim 9.

……..

US-PAT-NO: 6555555
DOCUMENT-IDENTIFIER: US 6555555 B1
TITLE: Fused thiophone derivatives and drugs containing the same as the active ingredient

DATE-ISSUED: April 29, 2003

INVENTOR-INFORMATION:
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10 Konishi; Mikio
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JP

9 Katsube; Nobuo
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N/A
N/A
JP

8 Konno; Mitoshi
Osaka
N/A
N/A
JP

7 Kishimoto; Tadamitsu
Osaka
N/A
N/A
JP

ASSIGNEE INFORMATION:
NAME CITY STATE ZIP CODE COUNTRY TYPE CODE
Ono Pharmaceutical Co., Ltd.
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N/A
N/A
JP
03

APPL-NO: 10127409
DATE FILED: April 23, 2002

PARENT-CASE:

(- 50) This application is a Divisional of U.S. application Ser. No. 09/647,430, filed Oct. 2, 2000, U.S. Pat. No. 6,420,391; which in turn is a 371 of PCT/JP99/01648, filed Mar. 31, 1999. The disclosure of each of which is incorporated herein by reference.

FOREIGN-APPL-PRIORITY-DATA:
COUNTRY APPL-NO APPL-DATE
JP
10-104210
April 1, 1998

JP
11-46887
January 19, 1999

INT-CL-ISSUED: [07] **10** A61K031/445 , **5** A61K031/40 , **4** A61K031/38

INT-CL-CURRENT:
TYPE IPC DATE
CIPS C07 D 413/04 20060101
CIPS C07 D 495/00 20060101
CIPS C07 D 495/04 20060101
CIPS C07 D 413/12 20060101
CIPS C07 D 521/00 20060101
CIPS C07 D 409/12 20060101
CIPS C07 D 409/04 20060101
CIPS C07 D 409/00 20060101
CIPS C07 D 409/14 20060101
CIPS C07 D 417/00 20060101
CIPS C07 D 413/00 20060101
CIPS C07 D 417/12 20060101
CIPS C07 D 333/62 20060101
CIPS C07 D 333/00 20060101

US-CL-ISSUED: 514/324 , 514/422 , 514/443

US-CL-CURRENT: **20** 514/324, **10** 514/422 , **5** 514/443

FIELD-OF-CLASSIFICATION-SEARCH: **20** 514/324; **20** 514/422 ; **20** 514/443
See application file for complete search history

REF-CITED:
U.S. PATENT DOCUMENTS
PAT-NO ISSUE-DATE PATENTEE-NAME US-CL
2 2930800
March 1960
Kloetzel et al.
N/A
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2 3629438
December 1971
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N/A
N/A

2 3686216
August 1972
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N/A
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March 1984
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ART-UNIT: 1626
20 RIMARY-EXAMINER: Lambkin; Deborah C.
ATTY-AGENT-FIRM: Sughrue Mion, PLLC
ABSTRACT:
The present invention relates to a fused thiophene derivative of the formula (I) (wherein all the symbols are defined as described in the specification) and an inhibitor of producing interleukin-6 and/or interleukin-12 comprising the said derivative as an active ingredient.
A fused thiophene derivative of the formula (I) is useful as an agent for the prevention and/or treatment of various inflammatory diseases, sepsis, multiple myeloma, plasma cell leukemia, osteoporosis, cachexia, psoriasis, nephritis, renal cell carcinoma, Kaposi's sarcoma, rheumatoid arthritis, gammopathy, Castleman's disease, atrial myxoma, diabetes mellitus, autoimmune diseases, hepatitis, multiple sclerosis, colitis, graft versus host immune diseases, infectious diseases. ##STR1##
4 Claims, 0 Drawing figures
Exemplary Claim Number: 1

CLAIMS:

What is claimed is:

100 1. An inhibitor of interleukin-6 and/or interleukin-12 production comprising, as an active ingredient, a fused thiophene derivative of the formula (I) ##STR2283## wherein [character pullout] is a single or double bond, Y is (i) ##STR2284## or (ii) hydrogen (with the proviso that when [character pullout] is a double bond, Y is hydrogen, and when [character pullout] is a single bond, Y is ##STR2285## m and n are each independently 0 or an integer of 1-2, p is 0 or an integer of 1-4, q is 0 or an integer of 1-5, Z is single bond, C1-8 alkylene, C2-8 alkenylene or C2-8 alkynylene, ##STR2286## is (i) benzene ring or (ii) 6-membered monocyclic hetero aryl containing 1-2 nitrogen atom(s), ##STR2287## is (i) C3-15 mono-, bi- or tricyclic carbo ring or (ii) 4-18 membered mono-, bi- or tricyclic hetero ring containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or one sulfur atom, each R.sup.1 of (R.sup.1)p is independently, (i) C1-8 alkyl, (ii) C2-8 alkenyl, (iii) C2-8 alkynyl, (iv) nitro, (v) cyano, (vi) halogen, (vii) Cyc.sup.1, (viii) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with halogen or Cyc.sup.1 or (ix) --A.sup.1 --A.sup.2 --A.sup.3, A.sup.1 is (i) single bond, (ii) C1-8 alkylene, (iii) C2-8 alkenylene or (iv) C2-8 alkynylene, A.sup.2 is (i) --O--, (ii) --NR.sup.3 --, (iii) --C(O)--, (iv) --CH(OH)--, (v) --C(O)NR.sup.4 --, (vi) --NR.sup.5 C(O)--, (vii) --C(O)O--, (viii) --OC(O)--, (ix) --SO.sub.2 NR.sup.6 --, (x) --NR.sup.7 SO.sub.2 --, (xi) --C(O)NR.sup.9 O--, (xii) --OC(O)NR.sup.10 --, (xiii) --NR.sup.11 C(O)NR.sup.12 --, (xiv) --NR.sup.13 C(O)O-- or (xv) --OC(O)O-- wherein R.sup.3, R.sup.4, R.sup.5, R.sup.6, R.sup.7, R.sup.9, R.sup.10, R.sup.11, R.sup.12 and R.sup.13 are each independently, hydrogen, C1-8 alkyl, phenyl or C1-8 alkyl substituted with Cyc.sup.1, cyano, --OR.sup.14, wherein R.sup.14 is hydrogen or C1-8 alkyl, with the proviso that the linkage of the right side of each group represented by A.sup.2 binds to A.sup.3, A.sup.3 is (i) hydrogen, (ii) C1-8 alkyl, (iii) C2-8 alkenyl, (iv) C2-8 alkynyl, (v) Cyc.sup.1 or (vi) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-3 groups selected from the following (a)-(i): (a) halogen, (b) cyano, (c) --P(O)(R.sup.15).sub.2, (d) --Si(R.sup.16).sub.3, (e) Cyc.sup.1, (f) --C(O)R.sup.17, (g) --OR.sup.18, (h) --NR.sup.19 R.sup.20, (i) --SR.sup.21 ; each R.sup.15 is independently, hydroxy or C1-8 alkoxy, each R.sup.16 is independently C1-8 alkyl, R.sup.17 is (i) hydrogen, (ii) C1-8 alkyl, (iii) hydroxy, (iv) C1-8 alkoxy, (v) Cyc.sup.1 or (vi) --NR.sup.22 R.sup.23, (wherein R.sup.22 is hydrogen, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl, and wherein R.sup.23 is hydrogen, C1-8 alkyl, Cyc.sup.1 or C1-8 alkyl substituted with Cyc.sup.1 or NR.sup.24 R.sup.25, wherein R.sup.24 and R.sup.25 are each independently hydrogen, C1-8 alky, phenyl, C1-8 alkyl substituted with phenyl, R.sup.18 is (i) hydrogen, (ii) C1-8 alkyl, (iii) C2-8 alkenyl, (iv) Cyc.sup.1 or (v) C1-8 alkyl substituted with (a) Cyc.sup.1, (b) Si(R.sup.26).sub.3 wherein each R.sup.26 is independently C1-8 alkyl, or (c) --OR.sup.27, wherein R.sup.27 is hydrogen, C1-8 alkyl or C2-5 acyl, R.sup.19 is (i) hydrogen, (ii) C1-8 alkyl, (iii) phenyl or (iv) C1-8 alkyl substituted with phenyl, R.sup.20 is (i) hydrogen, (ii) C1-8 alkyl or (iii) --C(O)R.sup.28, wherein R.sup.28 is C1-8 alkyl, C1-8 alkoxy, Cyc.sup.1 or NR.sup.29 R.sup.30, wherein R.sup.29 and R.sup.30 are each independently, hydrogen or C1-8 alkyl, (iv) Cyc.sup.1 or (v) C1-8 alkyl substituted with Cyc.sup.1 or cyano, R.sup.21 is (i) hydrogen, (ii) C1-8 alkyl or (iii) Cyc.sup.1, Cyc.sup.1 is (i) C3-15 mono-, bi- or tricyclic carbo ring or (ii) 4-18 membered mono-, bi- or tricyclic hetero ring containing 1-4 nitrogen atom(s), 1-2 oxygen atom(s) and/or one sulfur atom, wherein the said carbocyclic ring or heterocyclic ring may be substituted with one or more of (i) C1-8 alkyl, (ii) C2-8 alkenyl, (iii) C2-8 alkynyl, (iv) oxo, (v) cyano, (vi) nitro, (vii) trihalomethyl, (viii) trihalomethoxy, (ix) halogen, (x) diphenylmethyl, (xi) triphenylmethyl, (xii) Cyc.sup.2, (xiii) --OR.sup.31, (xiv) --SR.sup.32, (xv) --NR.sup.33 R.sup.34, (xvi) --SO.sub.2 NR.sup.35 R.sup.36, (xvii) --C(O)R.sup.37 or (xviii) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc.sup.2, hydroxy, halogen or --C(O)--Cyc.sup.2, R.sup.31 and R.sup.32 are each independently, hydrogen, C1-8 alkyl or Cyc.sup.2, R.sup.33 is hydrogen or C1-8 alkyl, R.sup.34 is hydrogen, C1-8 alkyl or --C(O)--Cyc.sup.2, R.sup.35 is hydrogen or C1-8 alkyl, R.sup.36 is hydrogen, C1-8 alkyl or Cyc.sup.2, R.sup.37 is hydrogen, C1-8 alkyl, --OR.sup.38, --NR.sup.39 R.sup.40, Cyc.sup.2, or C1-8 alkyl substituted with Cyc.sup.2 or --C(O)--Cyc.sup.2, R.sub.38, R.sup.39 and R.sup.40 are each independently, hydrogen, C1-8 alkyl, or C1-8 alkyl substituted with Cyc.sup.2, CyC.sup.2 is (i) C3-15 mono-, bi- or tricyclic carbo ring or (ii) 4-18 membered mono-, bi- or tricyclic hetero ring containing 1-4 nitrogen atom(s), 1-2 oxygen atom(s) and/or one sulfur atom, wherein the said carbocyclic ring or heterocyclic ring may be substituted with one or more of (i) C1-8 alkyl, (ii) C2-8 alkenyl, (iii) C2-8 alkynyl, (iv) oxo, (v) cyano, (vi) nitro, (vii) trihalomethyl, (viii) trihalomethoxy, (ix) halogen, (x) --OR.sup.41, (xi) --SR.sup.42, (xii) --NR.sup.43 R.sup.44, (xiii) --SO.sub.2 NR.sup.45 R.sup.46, (xiv) --C(O)R.sup.47, (xv) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with hydroxy or halogen or (xvi) phenyl, R.sup.41, R.sup.42, R.sup.43, R.sup.44, R.sup.45 and R.sup.46 are each independently, hydrogen or C1-8 alkyl, R.sup.47 is hydrogen, C1-8 alkyl or C1-8 alkoxy each R.sup.2 of (R.sup.2)q is independently, (i) C1-8 alkyl, (ii) C2-8 alkenyl, (iii) C2-8 alkynyl, (iv) --OR.sup.48, (v) --NR.sup.49 R.sup.50, (vi) --C(O)R.sup.51, (vii) nitro, (viii) cyano, (ix) halogen or (x) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with --OR.sup.48, --NR.sup.49 R.sup.50, --C(O)R.sup.51, halogen or Cyc.sup.3,

R.sup.48 is (i) hydrogen, (ii) C1-8 alkyl, (iii) C2-8 alkenyl, (iv) C2-8 alkynyl, (v) Cyc.sup.3 or (vi) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with halogen, --OR.sup.52, --NR.sup.53 R.sup.54, --C(O)R.sup.55 or Cyc.sup.3, R.sup.49 and R.sup.50 are each independently, hydrogen, C1-8 alkyl or --COR.sup.59, R.sup.51 is hydrogen, C1-8 alkyl, hydroxy, C1-8 alkoxy or --NR.sup.60 R.sup.61, R.sup.52 is hydrogen, C1-8 alkyl, Cyc.sup.3, or C1-8 alkyl substituted with Cyc.sup.3, R.sup.53 and R.sup.54 are each independently, hydrogen, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl or --C(O)R.sup.56, wherein R.sup.56 is C1-8 alkyl, C1-8 alkoxy, Cyc.sup.3, or C1-8 alkyl substituted with Cyc.sup.3, R.sup.55 is hydroxy, C1-8 alkoxy, or --NR.sup.57 R.sup.58, wherein R.sup.57 and R.sup.58 are each independently, hydrogen, C1-8 alkyl, or C1-8 alkyl substituted with Cyc.sup.3, R.sup.59 is C1-8 alkyl or C1-8 alkoxy, R.sup.60 and R.sup.61 are each independently, hydrogen or C1-8 alkyl, Cyc.sup.3 is (i) C3-15 mono-, bi- or tricyclic carbo ring or (ii) 4-18 membered mono-, bi- or tricyclic hetero ring containing 1-4 nitrogen atom(s), 1-2 oxygen atom(s) and/or one sulfur atom, wherein the said carbocyclic ring or heterocyclic ring may be substituted with one or more of (i) C1-8 alkyl, (ii) C1-8 alkoxy, (iii) nitro, (iv) halogen, (v) cyano, (vi) hydroxy, (vii) benzyloxy, (viii) --NR.sup.62 R.sup.63, (ix) --COOR.sup.64, (x) trihalomethyl, (xi) trihalomethoxy, (xii) phenyl, (xiii) phenoxy, (xiv) phenylthio, (xv) C1-8 alkyl or C1-8 alkoxy substituted with phenyl, phenoxy, phenylthio, hydroxy, --NR.sup.62 R.sup.63 or --COOR.sup.64, R.sup.62 and R.sup.63 are each independently, hydrogen or C1-8 alkyl, R.sup.64 is hydrogen or C1-8 alkyl, with the proviso that when A.sup.2 is (vi) --NR.sup.5 C(O)--, (x) --NR.sup.7 SO.sub.2 --, (xiv) --NR.sup.13 C(O)O-- or (xv) --OC(O)O--, then A.sup.3 is not hydrogen, an N-oxide derivative thereof or a non-toxic salt thereof.

80 2. An agent for the prevention and/or treatment of various inflammatory diseases, sepsis, multiple myeloma, plasma cell leukemia, osteoporosis, cachexia, psoriasis, nephritis, renal cell carcinoma, Kaposi's sarcoma, rheumatoid arthritis, gammopathy, Castleman's disease, atrial myxoma, diabetes mellitus, autoimmune diseases, hepatitis, multiple sclerosis, colitis, graft versus host immune diseases, infectious diseases, wherein said agent contains a fused thiophene derivative of the formula (I), as set forth in claim 1, an N-oxide derivative thereof or a non-toxic salt thereof as an active ingredient.

60 3. An inhibitor of interleukin-6 and/or interleukin-12 production according to claim 1, comprising a compound which is (1) 3-(thiophen-2-yl)thio-2,3-dihydro-1,1-dioxidebenzo[b]thiophene, (2) 6-nitro-3-(thiophen-2-yl)thio-2,3-dihydro-1,1-dioxidebenzo[b]thiophene, (3) 3-(thiophen-2-yl)sulfonyl-2,3-dihydro-1,1-dioxidebenzo[b]thiophene, (4) 4,5-dimethyl-1,1-dioxidebenzo[b]thiophene, (5) 4,6-dimethyl-1,1-dioxidebenzo[b]thiophene, (6) 4,7-dimethyl-1,1-dioxidebenzo[b]thiophene, (7) 5,6-dimethyl-1,1-dioxidebenzo[b]thiophene, (8) 5,7-dimethyl-1 1-dioxidebenzo[b]thiophene, (9) 6,7-dimethyl-1,1-dioxidebenzo[b]thiophene, (10) 4-carboxymethyl-1,1-dioxidebenzo[b]thiophene, (11) 6-(2,2-bis(ethoxycarbonyl)ethenyl)amino-1,1-dioxidebenzo[b]thiophene, (12) 4-methylaminocarbonyloxy-1,1-dioxidebenzo[b]thiophene, (13) 5-(2-(N-(5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamino) ethyl)-1,1-dioxidebenzo[b]thiophene, (14) 5-(2-hydroxyethyl)-1,1-dioxidebenzo[b]thiopherie, (15) 5-bromo-7-methyl-1,1-dioxidebenzo[b]thiophene, (16) 7-bromo-5-methyl-1,1-dioxidebenzo[b]thiophene, (17) 5-bromo-6-methyl-1,1-dioxidebennzo[b]thiophene, (18) 5-bromo-4-methyl-1,1-dioxidebenzo[b]thiophene, (19) 6-bromo-5-methyl-1,1-dioxidebenzo[b]thiophene, (20) 4-bromo-5-methyl-1,1-dioxidebenzo[b]thiophene, (21) 6-amino-1,1-dioxidebenzo[b]thiophene, (22) 6-acetylamino-1,1-dioxidebenzo[b]thiophene, (23) 6-(4-diethylaminophenyl)-1,1-dioxidebenzo[b]thiophene, (24) 1,1-dioxidethieno[2,3-b]pyridine,

40 4. A method for preparation of a compound of the formula (XI) ##STR2288##

said method comprising cyanization of a compound of formula (XII) ##STR2289##

to obtain a compound of the formula (XIII) ##STR2290##

dehydration of the compound of the formula (XIII) to obtain a compound of formula (XIV) ##STR2291##

and hydrolysis of the compound of the formula (XIV).

This is a humble first attempt at a system of quantifiable metrics that is very likely to need further input and evaluation by many experts. Hopefully it sets forth a basic example in a points system which may be used to assist the USPTO measure patent quality.

Best Regards,
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