From: Stephen S. Key & USPTO Public Search Associates.

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.

patentkey@msn.com
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.

Confidential, Independent, Neutral Searching, Analysis & Reporting. This e-mail message and any attachments are intended only for the use of those to whom it is addressed and may contain information that is confidential and prohibited from further disclosure under law. If you have received this e-mail message in error, its review, use, retention, and/or distribution is strictly prohibited. If you are not the intended recipient, please contact the sender by reply e-mail message and destroy all copies of the original message and any attachments.
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. 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:

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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:

(copied only 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.
Guilford
CT
N/A
N/A

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 Kirschmeier; 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:
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.

**See application file for complete search history**

**REF-CITED:**

**U.S. PATENT DOCUMENTS**

**PAT-NO ISSUE-DATE PATENTEE-NAME US-CL**

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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.

Claim: 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): 

- X₁, X₂ and X₃, 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;

References:
- Levitzki, Current Opinion In Cell Biology vol. 8, pp. 239-244, 1996.
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. 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. 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. The method of claim 1 wherein said FPT inhibitor, and said antineoplastic agent and/or radiation are administered concurrently.

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

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

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

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; \( Y_{sub.1} = ##\text{STR229}## \)

where \( R_{sub.1} \) is a hydrogen atom or a lower alkyl, \(--\text{CONH}_{sub.2}--\) or \(--\text{COR}_{sub.2}--\) group, where \( R_{sub.2} \) is a lower alkyl group, or

\( Y_{sub.1} = ##\text{STR230}## \)

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

\( R_{sub.6} \) is a \(--\text{NR}_{sub.7}(\text{CH}_{sub.2})_{n}--\text{R}_{sub.4} \) group, where \( n \) is 2 or 3; \( R_{sub.4} \) is a \##\text{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

\( R_{sub.6} = ##\text{STR232}## \)

where \( R_{sub.4} \) is defined the same as above; and

\( Y_{sub.2} \) is a \( X_{sub.6}--\text{cycloalkyl} \) group, where \( X_{sub.6} \) is a \( \text{CH}_{sub.2}, \text{O} \) or \( \text{NH} \) group;

with the proviso that the FPT inhibitor is not the following compound: \##\text{STR233}##

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

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

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

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

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

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

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

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

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

24. The method of claim 18 wherein the proliferative disease is pancreatic cancer.
**ASSIGNEE INFORMATION:**

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**APPL-NO:** 08677970
**DATE FILED:** July 10, 1996

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

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**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; 20 435/70.1; 20 435/71.1; 20 435/71.2; 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:**

**U.S. PATENT DOCUMENTS**

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Herrmann et al.
N/A
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June 2000
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N/A

FOREIGN PATENT DOCUMENTS
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5  WO 95/17511
June 1995
WO

5  WO 96 26275
August 1996
WO

OTHER PUBLICATIONS Philipp et al. PNAS 93:3132-37 4/96.*


10  Ellis, R.W., see Chapter 29 of "Vaccines" PLotkin et al. (ed.), published by WB Saunders Company (Philadelphia), see p. 571, 2nd full paragraph, 1988.*


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.

Claims:

What we claim is:

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.

2. The isolated nucleic acid fragment as claimed in claim 1 which is amplifiable 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).

3. The nucleic acid fragment of claim 2 from a Mycobacterium strain of Mycobacterium tuberculosis.

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

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

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

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

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.

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.

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.
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 333/02 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 N/A
2 3629438 December 1971 Schmeling et al. N/A N/A N/A
2 3686216 August 1972 Relyea et al. N/A N/A N/A
2 4436748 March 1984 Ong et al. N/A N/A N/A
2 4737519 April 1988 Yamashita et al. N/A N/A N/A
2 5093351 March 1992 Batt N/A N/A N/A
N/A
N/A
N/A

2 5496851
March 1996
Grinnell
N/A
N/A
N/A

10 5863936
January 1999
Gaeta et al.
514/443
N/A
N/A

10 5977098
November 1999
Palkowitz
514/212
N/A
N/A

10 6040309
March 2000
Duck et al.
514/253
N/A
N/A

2 6271642
April 2001
Kunisch et al.
N/A
N/A
N/A

2 6251936
June 2001
Wrobel et al.
N/A
N/A
N/A

2 6294537
September 2001
Bichon et al.
N/A
N/A
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2 6310061
October 2001
Ito et al.
N/A
N/A
N/A

10 6329421
December 2001
Prasit et al.
514/443
N/A
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10 6433005
August 2002
McLaren et al.
FOREIGN PATENT DOCUMENTS
FOREIGN-PAT-NO PUBN-DATE COUNTRY US-CL
5_1585930 February 1970 DE
5_0 659 418 June 1995 EP
5_57-122080 July 1982 JP
5_2-288856 November 1990 JP
5_4-364163 December 1992 JP
5_9-310078 December 1997 JP
5_10-298180 November 1998 JP
5_591474 May 1978 RU
5_95/27710 October 1995 WO
5_96/24356 August 1996 WO
5_98/55454 October 1998 WO

OTHER PUBLICATIONS

What is claimed is:

1. An inhibitor of interleukin-6 and/or interleukin-12 production comprising, as an active ingredient, a fused thiophene derivative of the formula (I) wherein [character pullout] is a single or double bond, Y is hydrogen, and when [character pullout] is a double bond, Y is hydrogen, and when [character pullout] is a single bond, Y is hydrogen.

2. A compound of general formula (I) wherein Y is hydrogen.

3. A compound of general formula (I) wherein Y is hydrogen.

4. A compound of general formula (I) wherein Y is hydrogen.
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 alkyl or --COR.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 alkyl, 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) benzyl, (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.

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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.

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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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