(51) International Patent Classification:
    A61K 45/06 (2006.01)      A61P 35/00 (2006.01)

(21) International Application Number:
    PCT/HU2007/000055

(22) International Filing Date:
    14 June 2007 (14.06.2007)

(25) Filing Language:
    English

(26) Publication Language:
    English

(30) Priority Data:
    P0600497 14 June 2006 (14.06.2006)   HU
    P0600508 19 June 2006 (19.06.2006)   HU

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(81) Designated States (unless otherwise indicated, for every
    kind of national protection available):
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    GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
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    MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
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    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, MT, NL, PL, PT, RO, SE,
    SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
    MR, NE, SN, TD, TG).

(88) Date of publication of the international search report:
    18 June 2009

(57) Abstract: ABCG2, a member of the ATP-Binding Cassette transporters has been identified as a protective pump against endogenous and exogenous toxic agents. ABCG2 was shown to be expressed at high levels in stem cells, and variably regulated during cell differentiation. It is demonstrated herein that functional ABCG2 is expressed in human monocyte-derived dendritic cells by the activation of a nuclear hormone receptor, PPARg. The present results uncovered a mechanism by which up-regulation of functional ABCG2 expression can be achieved via exogenous or endogenous activation of the lipid activated transcription factor, PPARg. Thus the invention relates to combined treatments by PPARg agonists and cytotoxic drugs transportable by ABCG2, various treatments in the field of neoplastic diseases as well as cell therapy, including autologous cell therapy, as well as kits and composition therefor. Method for protecting cells against cytotoxic drugs are also provided.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K45/06 A61P35/00

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)
A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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Further documents are listed in the continuation of Box C. See patent family annex.

Date of the actual completion of the international search
8 May 2008

Date of mailing of the international search report
02. 2009

Name and mailing address of the ISA
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Fax (+31-70) 340-3016

Authorized officer
Escolar Blasco, P

Form PCT/ISA/210 (Second sheet) (April 2005)
INTERNATIONAL SEARCH REPORT

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material
      🔊 a sequence listing
      ☐ table(s) related to the sequence listing

   b. format of material
      🔊 on paper
      🔊 in electronic form

   c. time of filing/furnishing
      🔊 contained in the international application as filed
      🔊 furnished together with the international application in electronic form
      ☐ furnished subsequently to this Authority for the purpose of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:
INTERNATIONAL SEARCH REPORT

Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 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:

1. [X] Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
   Claims 7-11, 21: Rule 39.1(iv) PCT - 'Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-6, 13
   Combination of a PPARg agonist and a chemotherapeutic or cytotoxic drug transportable by ABCG2

2. claims: 7-12
   Cell therapy based on an increase of the expression of PPARg in isolated cells before exposing them to a drug transportable by ABCG2

3. claims: 14-20
   Nucleotide sequence with ID No 1, 2, 3, 4, 5 or 6, the vectors comprising them and a repressor protein capable of binding to any of the sequences.

4. claims: 21-23
   Method and use for alleviating multidrug resistance due to overexpression of ABCG2 by administering a transcription repressor capable of binding to PPARg, a PPARg antagonist, or a siRNA against PPARg.
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<tr>
<td>P,X</td>
<td>MEIER YVONNE ET AL: &quot;ABCG2, encoding the human, breast cancer resistance protein (BCRP), is transactivated by the peroxisome proliferator-activated receptor-gamma (PPARgamma)&quot; HEPATOLOGY, WILLIAMS AND WILKINS, BALTIMORE, MD, US, vol. 44, no. 4, suppl 1, October 2006 (2006-10), page 595A, XP009095383 ISSN: 0270-9139 abstract -----</td>
<td>1-6</td>
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<td>WO 09/18234 A (UNIV TEXAS [US]) 6 April 2009 (2009-04-06) claims 4,6 -----</td>
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<td>A</td>
<td>GUTMANN H ET AL: &quot;Distribution of breast cancer resistance protein (BCRP/ABCG2) mRNA expression along the human GI tract&quot; BIOCHEMICAL PHARMACOLOGY, PEGAMON, OXFORD, GB, vol. 70, no. 5, 1 September 2005 (2005-09-01), pages 695-699, XP004996351 ISSN: 0006-2952 -----</td>
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<td>HUISMAN MAARTEN T ET AL: &quot;MRP2 (ABCC2) transports taxanes and confers paclitaxel resistance and both processes are stimulated by probenecid&quot; INTERNATIONAL JOURNAL OF CANCER, vol. 116, no. 5, September 2005 (2005-09), pages 824-829, XP002468076 ISSN: 0020-7136 -----</td>
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<td>WD 2004/101776 A (UNIV DEBRECEN [HU]; NAGY LASZLO [HU]; SZATMARI ISTVAN [HU]; RAJNAVOELG) 25 November 2004 (2004-11-25) page 4, paragraph 15 page 6, paragraph 50 page 10, paragraph 112-115</td>
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<td>X</td>
<td>SAITO HIKARU ET AL: &quot;A new strategy of high-speed screening and quantitative structure-activity relationship analysis to evaluate human ATP-binding cassette transporter ABCG2-drug interactions&quot; JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, vol. 317, no. 3, 17 February 2006 (2006-02-17), pages 1114-1124 URL, XP002468078 online ISSN: 0022-3565 page 1114, left-hand column, paragraph 1 - page 1115, left-hand column, paragraph 2 page 1122, right-hand column, paragraphs 2,3 page 1123, right-hand column, paragraph 4 -----</td>
<td>1-6</td>
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<td>A</td>
<td>DANG ZHI-CHAO ET AL: &quot;Peroxisome proliferator-activated receptor gamma (PPARgamma ) as a molecular target for the soy phytoestrogen genistein.&quot; THE JOURNAL OF BIOLOGICAL CHEMISTRY 10 JAN 2003, vol. 278, no. 2, 10 January 2003 (2003-01-10), pages 962-967, XP002468079 ISSN: 0021-9258 page 965, right-hand column, paragraph 2 page 966, right-hand column, paragraph 2 - page 967, left-hand column, paragraph 1 -----</td>
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