METHODS FOR DIAGNOSING AND TREATING CANCER

The present invention relates to compositions and methods for characterizing, diagnosing, and treating cancer. In particular the invention provides the means and methods for the diagnosis, characterization, prognosis and treatment of cancer and specifically targeting cancer stem cells. The present invention provides a soluble FZD receptor comprising an extracellular domain of a human FZD receptor that inhibits growth of tumor cells. The present invention still further provides a soluble receptor comprising a Fri domain of a human FZD receptor that binds a ligand of a human FZD receptor and said soluble receptor is capable of inhibiting tumor growth. The present invention still further provides a method of treating cancer comprising administering a soluble FZD receptor comprising for example, either an extracellular domain of a human FZD receptor or a Fri domain of a human FZD receptor, in an amount effective to inhibit tumor growth.
INTERNATIONAL SEARCH REPORT

INTERNATIONAL APPLICATION

PCT/US07/05443

A CLASSIFICATION OF SUBJECT MATTER

IPC C07K 1/00( 2006 01)

USPC 530/350

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)

US 530/350

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 practicable, search terms used)

Please See Continuation Sheet

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>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>US 200201 37129 A1 (Barnes et al) 26 September 2002 (26 09 2002), sec entire document, e.g., SEQ ID NO 2 and paragraphs [0034-0037], [0053] and [0105]</td>
<td>1-6, 29 and 40-41</td>
</tr>
<tr>
<td>L</td>
<td>US 20030229023 A1 (Oliner et al) 11 December 2003 (11 12 2003) see e.g., SEQ ID NO 60</td>
<td>6</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C See patent family annex

Date of the actual completion of the international search

21 August 2008 (21 08 2008)

Date of mailing of the international search report

30 OCT 2008

Name and mailing address of the ISA/US

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Form PCT/ISA/2 10 (second sheet) (April 2007)
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. **Claims Nos**
   - because they relate to subject matter not required to be searched by this Authority, namely

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)

This International Searching Authority found multiple inventions in this international application, as follows. Please See Continuation 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 additional fees, this Authority did not invite payment of any 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. **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 1-6, 29, 40 and 41.

**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.
BOX III OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13:

Group I, claims 1-6, 29 and 40-41, insofar as the claims are drawn to a polypeptide comprising a Fn domain of a human FZD4 receptor comprising an amino acid sequence shown in SEQ ID NO 8, or compositions thereof.

Group II, claims 7-10 and 38-39, insofar as the claims are drawn to an isolated nucleic acid sequence encoding a nucleic acid sequence encoding a Fn domain of human FZD4 comprising an amino acid sequence shown in SEQ ID NO 8.

Group III, claims 1, 11-15, 29 and 40-41, insofar as the claims are drawn to a polypeptide comprising a Fn domain of a human FZD5 receptor comprising an amino acid sequence shown in SEQ ID NO 9, or compositions thereof.

Group IV, claims 16-19 and 38-39, insofar as the claims are drawn to an isolated nucleic acid sequence encoding a nucleic acid sequence encoding a Fn domain of human FZD5 comprising an amino acid sequence shown in SEQ ID NO 9.

Group V, claims 11, 20-24, 29 and 40-41, insofar as the claims are drawn to a polypeptide comprising a Fn domain of a human FZD8 receptor comprising an amino acid sequence shown in SEQ ID NO 7, or compositions thereof.

Group VI, claims 25-28 and 38-39, insofar as the claims are drawn to an isolated nucleic acid sequence encoding a nucleic acid sequence encoding a Fn domain of human FZD8 comprising an amino acid sequence shown in SEQ ID NO 7.

Group VII, claims 30-37, insofar as the claims are drawn to a method of treating cancer in a subject in need thereof, the method comprising administering to the subject a soluble receptor comprising a Fn domain of a human FZD4 receptor in an amount effective to inhibit tumor cell growth.

Group VIII, claims 30-37, insofar as the claims are drawn to a method of treating cancer in a subject in need thereof, the method comprising administering to the subject a soluble receptor comprising a Fn domain of a human FZD5 receptor in an amount effective to inhibit tumor cell growth.

Group IX, claims 30-37, insofar as the claims are drawn to a method of treating cancer in a subject in need thereof, the method comprising administering to the subject a soluble receptor comprising a Fn domain of a human FZD8 receptor in an amount effective to inhibit tumor cell growth.

1 This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13 1, 13 2 and 13 3) for the reasons indicated below.

The inventions listed as Groups MX do not relate to a single general inventive concept under PCT Rule 13 1 because, under PCT Rule 13 2, they lack the same or corresponding special technical features for the following reasons:

In this case, the special technical feature presented in claim 1 is a polypeptide comprising an N-terminal extracellular Fn domain of a human FZD receptor. However, US 2003/0165500A1 (Rhee et al., 2003) teaches peptides comprising an N-terminal extracellular domain of PCT/ISA/2 10 (extra sheet) (April 2007)
Fn domain of a human FZD receptor, see entire document (e.g., Figure 6 and Example 1). Accordingly, the technical feature recited in claim 1, does not constitute a special technical feature as defined by PCT Rule 13 1, as it does not define a contribution over the prior art.

Therefore, the special technical feature of the invention of Group I is making a polypeptide comprising a Fn domain of a human FZD4 receptor comprising an amino acid sequence shown in SEQ ID NO 8.

The special technical feature of the invention of Group II is making an isolated nucleic acid sequence encoding a nucleic acid sequence encoding a Fn domain of human FZD4 comprising an amino acid sequence shown in SEQ ID NO 8.

The special technical feature of the invention of Group III is making a polypeptide comprising a Fn domain of a human FZD5 receptor comprising an amino acid sequence shown in SEQ ID NO 9.

The special technical feature of the invention of Group IV is making an isolated nucleic acid sequence encoding a nucleic acid sequence encoding a Fn domain of human FZD5 comprising an amino acid sequence shown in SEQ ID NO 9.

The special technical feature of the invention of Group V is making a polypeptide comprising a Fn domain of a human FZD8 receptor comprising an amino acid sequence shown in SEQ ID NO 7.

The special technical feature of the invention of Group VI is making an isolated nucleic acid sequence encoding a nucleic acid sequence encoding a Fn domain of human FZD8 comprising an amino acid sequence shown in SEQ ID NO 7.

The special technical feature of the invention of Group VII is treating cancer in a subject in need thereof, the method comprising administering to the subject a soluble receptor comprising a Fn domain of a human FZD4 receptor in an amount effective to inhibit tumor cell growth.

The special technical feature of the invention of Group VIII is treating cancer in a subject in need thereof, the method comprising administering to the subject a soluble receptor comprising a Fn domain of a human FZD5 receptor in an amount effective to inhibit tumor cell growth.

The special technical feature of the invention of Group IX is treating cancer in a subject in need thereof, the method comprising administering to the subject a soluble receptor comprising a Fn domain of a human FZD8 receptor in an amount effective to inhibit tumor cell growth.

Accordingly, the inventions of Groups I-IX do not share the same or corresponding special technical feature so as to form a single general inventive concept under PCT Rules 13 1 and 13 2.

Continuation of B FIELDS SEARCHED Item 3
WEST (PGPB, USPT, USOC, JPAB, EPAB, DWPI) and MEDLINE search terms-FZD4, human Fc, IgGl, kit and inventor search, sequence search of SEQ ID NO 4 and 8.