

WHAT IS CLAIMED IS:

1. A method of identifying cancer stem cell markers in a human primary tumor comprising:

(a) in vivo passaging the primary tumor in an immunodeficient non-human mammal, wherein each passage is effected for 1-3 months or until the tumor reaches a size of 1-3 cm diameter, and wherein cells of the primary tumor and passaged cells of the primary tumor are not subjected to immunoisolation; and

(b) comparing a level of at least one antigen in a first population of passaged tumor cells of the primary tumor with a second population of tumor cells of the primary tumor, wherein said second population of tumor cells are:

(i) non-passaged cells of the human primary tumor; or

(ii) in vivo passaged cells of the human primary tumor, wherein said second population of tumor cells has been in vivo passaged for at least one less number of passages than said first population of passaged tumor cells,

and wherein said comparing is effected at a ratio of frequency of cancer stem cells in said first population of tumor cells to frequency of cancer stem cell in said second population of tumor cells greater than 5:1, wherein an increase in the amount of said antigen in said first population of tumor cells as compared to the amount of said antigen in said second population of tumor cells is indicative of a cancer stem cell marker in the human primary tumor.

2. A method of identifying cancer stem cell markers in a human primary tumor comprising:

(a) in vivo passaging the primary tumor in an immunodeficient non-human mammal, wherein each passage is effected for 1-3 months or until the tumor reaches a size of 1-3 cm diameter, and wherein cells of the primary tumor and passaged cells of the primary tumor are not subjected to immunoisolation; and

(b) comparing a level of at least one antigen in a first population of passaged tumor cells of the primary tumor with a second population of tumor cells of the primary tumor, wherein the number of passages of said first population of passaged cells is

selected such that a ratio of cancer stem cells to non cancer stem cells in said first population of passaged cells is greater than 1:1000 and wherein said second population of tumor cells are:

- (i) non-passaged cells of the human primary tumor; or
 - (ii) in vivo passaged cells of the human primary tumor, wherein said second population of tumor cells has been in vivo passaged for at least one less number of passages than said first population of passaged tumor cells,
- wherein an increase in the amount of said antigen in said first population of tumor cells as compared to the amount of said antigen in said second population of tumor cells is indicative of a cancer stem cell marker in the human primary tumor.

3. A method of identifying cancer stem cell markers in a human primary tumor comprising:

(a) in vivo passaging the primary tumor in an immunodeficient non-human mammal, wherein each passage is effected for 1-3 months or until the tumor reaches a size of 1-3 cm diameter, and wherein cells of the primary tumor and passaged cells of the primary tumor are not subjected to immunoisolation; and

(b) comparing a level of at least one antigen in a first population of passaged tumor cells of the primary tumor with a second population of tumor cells of the primary tumor, wherein said first population of passaged cells are passaged in vivo for at least 10 passages and wherein said second population of tumor cells are:

- (i) non-passaged cells of the human primary tumor; or
 - (ii) in vivo passaged cells of the human primary tumor, wherein said second population of tumor cells has been in vivo passaged for at least one less number of passages than said first population of passaged tumor cells,
- wherein an increase in the amount of said antigen in said first population of tumor cells as compared to the amount of said antigen in said second population of tumor cells is indicative of a cancer stem cell marker in the human primary tumor.

4. The method of any one of claims 1-3, wherein the number of passages of said first population of passaged cells is selected such that there is an apparent tumor

aggressiveness phenotype selected from the group consisting of a level of a cancer cell marker, a gene expression profile, a time for xenograft to take, a number of cells required for generation of xenograft, an ability to migrate, an ability to invade non-cancerous tissue and a level of proliferation, which is not significantly increased for at least two consecutive passages.

5. The method of any one of claims 1-3, wherein the number of passages of said first population is selected such that the frequency of initiating a later generation xenograft using 5000 cells of said first population of passaged cells is increased by at least 5 fold as compared to non-passaged cells of the human primary tumor.

6. The method of any one of claims 1-5, wherein said antigen is a polypeptide.

7. The method of claim 6, wherein said increase in the amount of said polypeptide is an increase in a level of expression of said polypeptide per cell.

8. The method of claim 6, wherein said increase in the amount of said polypeptide is an increase in an amount of cells expressing said polypeptide.

9. The method of claim 6, wherein said increase in the amount of said polypeptide is an increase in a level of expression of said polypeptide per cell and an increase in an amount of cells expressing said polypeptide.

10. The method of any one of claims 1-9, wherein said primary tumor is a pediatric tumor.

11. The method of any one of claims 1-9, wherein said primary tumor is selected from the group consisting of atypical teratoid/rhabdoid tumor (ATRT), Ewings's sarcoma, Angiomyolipoma, Pleuropulmonary Blastoma and Wilms' tumor.

12. The method of any one of claims 1-11, wherein said first population of passaged tumor cells are passaged for 10-30 passages.

13. The method of any one of claims 1-12, wherein said second population of tumor cells are sequentially passaged in vivo for no more than 5 passages.

14. The method of any one of claims 1-12, wherein said first population of passaged tumor cells are passaged in vivo for 10-20 passages.

15. The method of any one of claims 1-14, wherein said passaging is effected in mice.

16. The method of any one of claims 1-15, wherein said passaging is effected by implanting into an animal non-dissociated cells of a tissue sample of a xenograft of the primary tumor.

17. The method of any one of claims 1-15, wherein said passaging is effected by implanting into an animal a single cell suspension of a xenograft of the primary tumor.

18. The method of any one of claims 1-5, wherein said level of said at least one antigen is determined on the mRNA level.

19. The method of any one of claims 1-5, wherein said level of said antigen is determined on the protein level.

20. A method of selecting an agent for the treatment of cancer in a subject:

- (a) identifying at least one cancer stem cell marker in a primary tumor of the subject according to the method of any one of claims 1-19; and
- (b) selecting an agent which down regulates expression and/or inhibits an activity of said cancer stem cell marker, thereby selecting an agent for the treatment of cancer.

21. A method of monitoring a cancer treatment in a subject comprising:
- (a) identifying at least one cancer stem cell marker in a primary tumor of the subject according to the method of any one of claims 1-19;
 - (b) analyzing an amount of said cancer stem cell marker in the tumor of the subject following the cancer treatment, wherein a decrease in the amount of said cancer stem cell marker in the tumor as compared to the amount of said cancer stem cell marker prior to the treatment is indicative of an efficacious cancer treatment.
22. A method of diagnosing cancer in a subject comprising identifying at least one cancer stem cell marker in a biological sample of the subject according to the method of any one of claims 1-19, wherein the presence of the cancer stem cell marker is indicative of the cancer.
23. The method of claim 22, wherein when said cancer stem cell marker is selected from the group consisting of semaphorin3C (SEMA3C), lysyl oxidase (LOX), glycoprotein M6A (GPM6A), hepatocyte growth factor (HGF/SF) and aldehyde dehydrogenase1 (ALDH1), the cancer is ATRT.