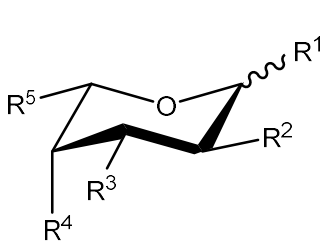
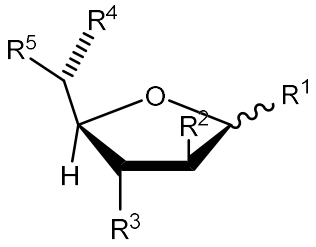
SUMMARY

[0005] In one example**,** methods for producing T cells having reduced surface fucosylation are provided. In some examples, the methods include culturing T cells in the presence of a fucose analog in a cell culture medium; wherein the fucose analog has formula (**I**) or (**II**):



(**I**)



(**II**)

or a pharmaceutically acceptable salt or solvate form thereof, wherein each of formula (**I**) or (**II**) can be the alpha or beta anomer or the corresponding aldose form;

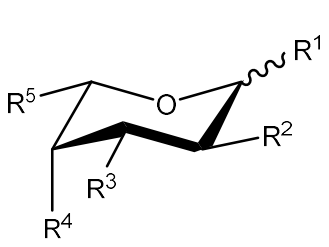
R^2 is halogen; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is –CH_3, or

each of R^1, R^2, R^3, and R^4 is independently -OH or a hydrolyzable ester group; and R^5 is -C≡CH; and

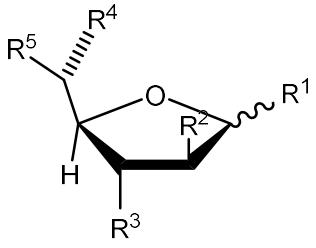
wherein the T cells having reduced surface fucosylation relative to T cells cultured in the absence of the fucose analog.

[0005a] In one aspect, the present disclosure refers to use of a mixture comprising T cells with reduced surface fucosylation in the manufacture of a medicament for providing an adoptive cell therapy to a subject having cancer, wherein said T cells with reduced surface fucosylation are produced by

culturing T cells in the presence of a fucose analog in a cell culture medium; wherein said fucose analog is selected from the group consisting of formulae (**I**) or (**II**):



(I)



(II)

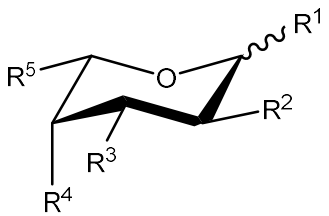
or a pharmaceutically acceptable salt or solvate form thereof, wherein each of formula (**I**) or (**II**) can be the alpha or beta anomer or the corresponding aldose form;

R^2 is halogen; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is $–CH_3$, or

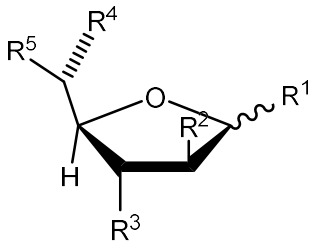
each of R^1, R^2, R^3, and R^4 is independently -OH or a hydrolyzable ester group; and R^5 is -C≡CH; and

wherein said T cells have at least about 80% reduced surface fucosylation relative to T cells cultured in the absence of said fucose analog.

[0006] In another example, methods for producing T cells having reduced surface fucosylation are provided. In some examples, the methods include providing a fucose analog to an animal and obtaining T cells having reduced surface fucosylation from the animal; wherein the fucose analog has formula (**I**) or (**II**):



(**I**)



(**II**)

or a pharmaceutically acceptable salt or solvate form thereof, wherein each of formula (**I**) or (**II**) can be the alpha or beta anomer or the corresponding aldose form;

R^2 is halogen; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is – CH_3, or

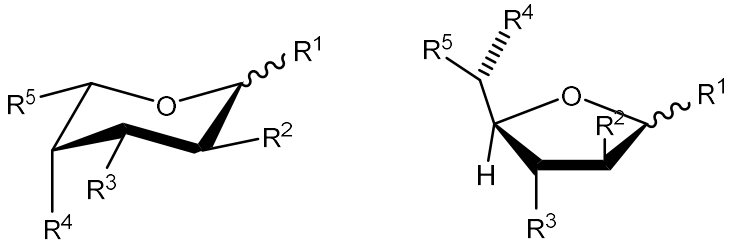
each of R^1, R^2, R^3, and R^4 is independently -OH or a hydrolyzable ester group; and R^5 is -C≡CH; and

wherein the T cells obtained from the animal have reduced surface fucosylation relative to T cells present in or obtained from a control animal that was not provided with said fucose analog.

[0006a] In one aspect, the present disclosure refers to use of a mixture comprising T cells with reduced surface fucosylation in the manufacture of a medicament for providing an adoptive cell therapy to a subject having cancer, wherein said T cells with reduced surface fucosylation are produced by

enriching T cells obtained from an animal to which a fucose analog has been provided, wherein the T cells obtained from the animal have reduced surface fucosylation, wherein

said fucose analog is selected from the group consisting of formulae (**I**) or (**II**):



(**I**) (**II**)

or a pharmaceutically acceptable salt or solvate form thereof, wherein each of formula (**I**) or (**II**) can be the alpha or beta anomer or the corresponding aldose form;

R^2 is halogen; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is – CH_3, or

each of R^1, R^2, R^3, and R^4 is independently -OH or a hydrolyzable ester group; and R^5 is -C≡CH; and

wherein said T cells obtained from the animal have at least about 80% reduced surface fucosylation relative to T cells present in or obtained from a control animal that was not provided with said fucose analog.

[0007] In still another example, methods for providing an adoptive cell therapy to a subject are provided. In some examples, the methods include administering a mixture having T cells with reduced surface fucosylation to the subject in need of the cell therapy.

[0008] In still another example, methods for treating a cancer are provided. In some examples, the methods include administering a mixture having T cells with reduced surface fucosylation to the subject in need of the cancer treatment.

[0009] In still another example, methods for treating a cancer are provided. In some examples, the method include administering a mixture having T cells with reduced surface fucosylation to the subject in need of the cancer treatment, wherein the T cells with reduced surface fucosylation are produced according to any methods for producing such T cells.

[0010] These and other examples of the disclosures provided herein can be more fully understood by reference to the following detailed description, non-limiting examples, and the appended figures.

BRIEF DESCRIPTION OF THE DRAWINGS

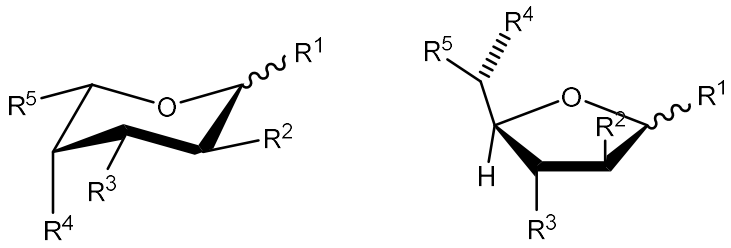
[0011] FIG. 1 shows a graph demonstrating *in vivo* effects of the adoptive transfer of splenocytes from KLH-A20 Id Fab vaccinated donor mice that were either treated or not with 2FF on the growth of IV implanted A20 mouse lymphoma cells in naïve BALB/c mice.

[0012] FIG. 2 shows a graph demonstrating *in vivo* effects of 2FF on the growth of SQ implanted A20 mouse lymphoma cells in naïve BALB/c mice that were used to generate isolated Cd3+ T cells.

WHAT IS CLAIMED IS:

1. Use of a mixture comprising T cells with reduced surface fucosylation in the manufacture of a medicament for providing an adoptive cell therapy to a subject having cancer, wherein said T cells with reduced surface fucosylation are produced by

culturing T cells in the presence of a fucose analog in a cell culture medium; wherein said fucose analog is selected from the group consisting of formulae (**I**) or (**II**):



(**I**) (**II**)

or a pharmaceutically acceptable salt or solvate form thereof, wherein each of formula (**I**) or (**II**) can be the alpha or beta anomer or the corresponding aldose form;

R^2 is halogen; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is $–CH_3$, or

each of R^1, R^2, R^3, and R^4 is independently -OH or a hydrolyzable ester group; and R^5 is -C≡CH; and

wherein said T cells have at least about 80% reduced surface fucosylation relative to T cells cultured in the absence of said fucose analog.

2. The use of claim **1**, further comprising a step of isolating the T cells having reduced surface fucosylation.

3. The use of claim **1** or **2,** wherein R^2 is halogen; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is $–CH_3$; wherein optionally

R^2 is -F; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is $–CH_3$; wherein optionally

each of R^1, R^3 and R^4 is independently selected from the group consisting of -OH and $–OC(O)C_1$-C_{10} alkyl; wherein optionally

each of R^1, R^3 and R^4 is independently selected from the group consisting of -OH and $–OC(O)CH_3$; and wherein optionally

each of R^1, R^2, R^3, and R^4 is independently -OH or a hydrolyzable ester group; and R^5 is -C≡CH.

4. The use of claim **1**, wherein the fucose analog is 2-deoxy-2-fluoro-L-fucose or alkynyl fucose peracetate.

5. The use of any one of claims **1-4**, wherein said T cells having reduced surface fucosylation are T cells comprising at least 80% reduction of surface fucosylation relative to T cells cultured in the absence of said fucose analog; wherein

the culture medium comprises CD3 and CD28 antibodies; wherein optionally

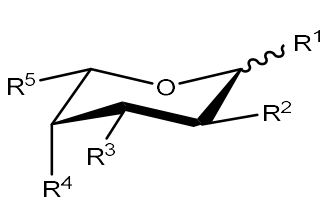
the culture medium further comprises interleukin 2 (IL2); wherein optionally

said T cells comprise human peripheral T cells.

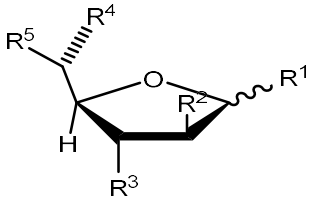
6. Use of a mixture comprising T cells with reduced surface fucosylation in the manufacture of a medicament for providing an adoptive cell therapy to a subject having cancer, wherein said T cells with reduced surface fucosylation are produced by

enriching T cells obtained from an animal to which a fucose analog has been provided, wherein the T cells obtained from the animal have reduced surface fucosylation, wherein

said fucose analog is selected from the group consisting of formulae (**I**) or (**II**):



(**I**)



(**II**)

or a pharmaceutically acceptable salt or solvate form thereof, wherein each of formula (**I**) or (**II**) can be the alpha or beta anomer or the corresponding aldose form;

R^2 is halogen; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is $–CH_3$, or

each of R^1, R^2, R^3, and R^4 is independently -OH or a hydrolyzable ester group; and R^5 is -C≡CH; and

wherein said T cells obtained from the animal have at least about 80% reduced surface fucosylation relative to T cells present in or obtained from a control animal that was not provided with said fucose analog.

7. The use of claim **6**, wherein R^2 is halogen; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is $–CH_3$; wherein optionally

R^2 is -F; each of R^1, R^3, and R^4 is independently –OH or a hydrolyzable ester group; and R^5 is $–CH_3$; wherein optionally

each of R^1, R^3 and R^4 is independently selected from the group consisting of -OH and $–OC(O)C_1$-C_{10} alkyl; wherein optionally

each of R^1, R^3 and R^4 is independently selected from the group consisting of -OH and $–OC(O)CH_3$; and wherein optionally

each of R^1, R^2, R^3, and R^4 is independently -OH or a hydrolyzable ester group; and R^5 is -C≡CH.

8. The use of claim **6**, wherein the fucose analog is 2-deoxy-2-fluoro-L-fucose or alkynyl fucose peracetate.

9. The use of any one of claims **6-8**, wherein said T cells having reduced surface fucosylation are T cells comprising at least 80% reduction of surface fucosylation relative to T cells cultured in the absence of said fucose analog; wherein the T cells are obtained from a spleen of the animal.

10. The use of any one of claims **1-9**, wherein said T cells are human T cells.

11. The use of any one of claims 1-10, wherein said T cells with reduced surface fucosylation originated from said subject.

12. The use of any one of claims 1-10, wherein said T cells with reduced surface fucosylation originated from an animal different from said subject.

13. The use of any one of claims **1-12**, wherein said mixture is substantially free of red blood cells.

14. The use of any one of claims **1-13**, wherein the mixture is to be administered locally.

15. The use of any one of claims **1-13**, wherein the mixture is to be administered systemically.