unexpectedly" that human LAG3 or derivatives thereof when inoculated into patients with highly malignant tumors induced a potent immunity which is monocyte dependent. The induced immunity manifests itself by a significant increase in blood monocyte counts. Despite the use of hLAG3 as a vaccine adjuvant to boost T-cell counts in known cancer patients, no one has yet been motivated to peremptorily screen for a LAG3 deficiency marker and, if found, ameliorate the consequent risk by treating prospective patients with recombinant human LAG3 by periodic administration of at different time points. The present inventor does this by pre-screening patients at risk for cardiovascular disease, other chronic inflammatory diseases, cardiovascular and/or non-cardiovascular morbidity and mortality using specific 2-point expression profiles (combinations of mutations and/or non-genetic causes , e.g., SCARB1 rs10846744 mutation and/or LAG-3 rs870849 or other genetic or non-genetic causes and a mutation), followed by a tailored therapeutic regimen using recombinant human lymphocyte activation gene-3 as a companion therapeutic.

SUMMARY OF THE INVENTION

It is, therefore, an object of the present innovation to provide a novel strategy for assessing patients at risk for cardiovascular disease, other chronic inflammatory diseases, cardiovascular and/or non-cardiovascular morbidity and mortality based on lymphocyte activation gene 3 (LAG3) protein deficiency, and for mediating said risk with a tailored therapeutic regimen including use of recombinant human lymphocyte activation gene-3 as a companion therapeutic.

In one aspect, the present invention provides for the use of a combination of hLAG3--Ig as an adjuvant with at least one chemotherapeutic agent in the manufacture of a medicament for treating chronic inflammatory and cardiovascular disease in a human adult

subject, wherein the use comprises that a qualitative pre-screen of said subject to detect a LAG3 deficiency marker indicative of a potential deficiency of LAG3 protein is to be carried out; that a quantitative test on said subject to confirm said LAG3 protein deficiency is to be carried out; and that the medicament is to be administered to the subject in form of a therapeutic regimen.

In one example, the method comprises a first step of qualitatively pre-screening a subject for one or more risk factors for developing cardiovascular disease, a second step of quantitatively detecting a LAG3 protein deficiency in a sample from the subject, and a third

I claim:

1. Use of a combination of hLAG3--Ig as an adjuvant with at least one chemotherapeutic agent in the manufacture of a medicament for treating chronic inflammatory and cardiovascular disease in a human adult subject, wherein the use comprises

that a qualitative pre-screen of said subject to detect a LAG3 deficiency marker indicative of a potential deficiency of LAG3 protein is to be carried out;

that a quantitative test on said subject to confirm said LAG3 protein deficiency is to be carried out; and

that the medicament is to be administered to the subject in form of a therapeutic regimen.

2. The use of claim 1, wherein said qualitative pre-screen of said subject comprises pre-screening a medical record for a LAG3 deficiency marker.

3. The use of claim 1, wherein said qualitative pre-screen of said subject comprises pre-screening a family history for a LAG- deficiency marker.

4. The use of claim 1, wherein said quantitative test comprises that a quantitative test is to be administered on a blood sample from said subject to confirm said LAG3 protein deficiency.

5. The use of claim 4, wherein said quantitative test on said blood sample is an assay.

6. The use of claim 4, wherein said quantitative test on said blood sample is a genetic test.

7. The use of claim 1, wherein said quantitative test comprises both a genetic test and an assay of a plasma sample from said subject for presence of low level expression of LAG3.

8. The use of claim 6, wherein said quantitative genetic test is configured to detect a polymorphism in the coding sequence of the *SCARB1* or *LAG3* genes.

9. The use of claim 8, wherein said polymorphism is a SCARB1 rs10846744 or LAG3 rs870849 mutation.

10. The use of claim 8, wherein said quantitative test on said blood sample includes amplifying at least a portion of a SCARB1 or LAG3 gene prior to identifying the allelic variant.

11. The use of claim 5, wherein said assay is configured to measure low LAG3 below 3400 pg/ml.

12. The use of claim 11, wherein said assay is an ELISA assay.

13. The use of claim 1, wherein the therapeutic regimen comprises that recombinant human LAG3 is to be administered periodically.

14. The use of claim 1, wherein the therapeutic regimen comprises that a recombinant LAG3 mimetic is to be administered periodically.

15. The use of claim 13, wherein the chemotherapeutic agent is probucol.

16. The use of claim 15, wherein probucol is to be administered periodically within a range of from three to four months.

17. The use of claim 15, wherein probucol is to be administered periodically for a remainder of said subject's lifetime.

18. The use of claim 13, wherein that the recombinant human LAG3 is to be administered periodically comprises that Human LAG3 protein is to be administered.

19. The use of claim 1, wherein said adjuvant comprises any one or more agents selected from the group consisting of an anti-inflammatory agent, an agent that improves

HDL-C function, size, and/or composition in the subject, an agent that decreases dysfunctional HDL-C in the subject, a PCSK9 inhibitors, and a LAG3 mimetic.

20. The use of claim 1, further comprising that the said subject is monitored during said periodic administration to determine effect on LDL oxidation and plasma-HDL cholesterol and plasma/serum cytokines.

21. The use of claim 18, wherein said monitoring comprises monthly safety labs with comprehensive profiles and EKGs.