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 human lymphocyte activation gene-3 (hLAG3)--Ig as an adjuvant with at least one agent in the manufacture of a medicament for combination therapy of chronic inflammatory and cardiovascular disease in a human adult

subject, wherein a qualitative pre-screen of said subject to detect a lymphocyte activation gene-3 (LAG3) deficiency marker indicative of a potential deficiency of LAG3 protein is to be carried out; a quantitative test on said subject to confirm said LAG3 protein deficiency is to be carried out if said qualitative pre-screen indicates an increased risk of a deficiency in LAG3 expression; a LAG3 expression profile is to be compiled from combined results of said qualitative prescreen and said quantitative testing and the medicament is to be administered to the subject when said LAG3 expression

profile indicates that the subject has a deficiency in LAG3 expression in form of a therapeutic regimen of soluble LAG3 in combination with one or more agents from a group including an anti-inflammatory agent, an anti-atherosclerotic agent, a statin, an anti-hyperlipidemic agent, a dysfunctional HDL-C lowering agent, a PCSK9 inhibitors, and a LAG3 mimetic.

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 human lymphocyte activation gene-3 (hLAG3)--Ig as an adjuvant with at least one agent in the manufacture of a medicament for combination therapy of chronic inflammatory and cardiovascular disease in a human adult subject, wherein

a qualitative pre-screen of said subject to detect a lymphocyte activation gene-3 (LAG3) deficiency marker indicative of a potential deficiency of LAG3 protein is to be carried out;

a quantitative test on said subject to confirm said LAG3 protein deficiency is to be carried out if said qualitative pre-screen indicates an increased risk of a deficiency in LAG3 expression;

a LAG3 expression profile is to be compiled from combined results of said qualitative prescreen and said quantitative testing; and

the medicament is to be administered to the subject when said LAG3 expression profile indicates that the subject has a deficiency in LAG3 expression in form of a therapeutic regimen of soluble LAG3 in combination with one or more agents from a group including an anti-inflammatory agent, an anti-atherosclerotic agent, a statin, an anti-hyperlipidemic agent, a dysfunctional HDL-C lowering agent, a PCSK9 inhibitors, and a LAG3 mimetic.

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 LAG3 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 below 3400 pg/ml.
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 an 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 13, wherein the anti-hyperlipidemic agent is probucol.
15. The use of claim 14, wherein probucol is to be administered periodically within a range of from three to four months.

16. The use of claim 14, wherein probucol is to be administered periodically for a remainder of said subject's lifetime.

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

18. The use of claim 17, wherein said monitoring comprises monthly safety labs with comprehensive profiles and EKGs.