

We Claim

1. A method of detecting Alzheimer's disease (AD) in a human subject without amyloid Positron Emission Tomography (PET) imaging, the method comprising the steps of:
 - a. obtaining a sample from the subject;
 - b. comparing normalized measured level of at least four biomarkers from the subject's sample to a reference level of each AD diagnosis biomarker, wherein the four biomarkers are CD69, tau, phosphorylated-tau proteins and amyloid- β peptide; and wherein the reference level of each AD diagnosis biomarker comprises a normalized measured level of the AD diagnosis biomarker from one or more samples of patients with confirmed AD and wherein levels of tau proteins is lesser in the subject's sample than the reference level, and the level of p-tau and amyloid- β peptide is greater in the subject's sample than in the reference level.
2. The method of claim 1, wherein the diagnosis of AD in the subject is confirmed by amyloid PET imaging.
3. The method of claim 1, wherein CD69 protein is measured in mitogenic lymphocytes from peripheral blood samples.
4. The method of claim 1, wherein tau, p-tau protein and amyloid- β peptide levels are measured in cerebrospinal fluid (CSF) sample.
5. The method of claim 3, wherein there is high inverse correlation between the positive PET imaging result of AD and expression of CD69 protein in mitogenic lymphocytes.
6. The method of claim 4, wherein there is high inverse correlation between positive PET imaging result of AD result and expression of tau protein.
7. The method of claim 2, wherein there is high positive correlation between the positive PET imaging result of AD result and expression of p-tau protein.
8. The method of claim 2, wherein there is high positive correlation between the positive PET imaging result of AD result and expression of amyloid- β peptide.

9. The method of claim 1, wherein is used to determine the risk of developing AD.
10. The method of claim 1, wherein it is used for selecting subjects for AD treatment.
11. The method of claim 1, wherein the method is used for determining treatment efficacy in subjects undergoing treatment for AD.
12. The method of claim 1, wherein it is used for severity assessment of AD in a subject by determining correlation between PET imaging results and expression of CD69 protein in mitogenic lymphocytes from a subject.
13. The method of claim 1, wherein it is used to distinguish AD-associated dementia from other forms of dementia.
14. The method of claim 1, wherein it is used to discover novel therapeutic agents to reverse cell cycle dysfunction as measured by CD69 expression.
15. The method of claim 1, wherein the method is used for determining AD progression in a human subject.
16. The method of claim 1, wherein the CD69 levels in mitogenic lymphocytes are assessed by the lymphocyte activation score in the LymPro® assay.
17. The method of claim 13, wherein the method comprises multivariate analysis of five variables including the LymPro® activation score, expression of tau protein in CSF, expression of phosphorylated-tau protein in CSF, expression of amyloid- β peptide in CSF, and amyloid-PET imaging.
18. The method of claim 1, wherein it is used to enrich for rare mitogenic lymphocyte subsets to assess the level of cell cycle dysfunction as measured by CD69 expression.