Washington University in St. Louis
Office of Technology Management

CERAMIDE PROFILING FOR BLOOD-BASED PREDICTIVE SCREENING FOR CARDIOVASCULAR DISEASE, HEART FAILURE AND DEATH

Ory, Daniel, Peterson, Linda, Schaffer, Jean

Zou, Dianxiong

T-014627

Technology Description

A team of researchers has developed a high throughput, FDA-compliant assay to predict coronary heart disease and mortality in the general population 6-10 years before the onset of disease. This fully validated two-dimensional liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay measures the levels of ceramide species in plasma. Ceramide analysis is a very strong prognostic indicator, independent of other risk factors (e.g., smoking, cholesterol levels). Therefore, it can be added to traditional screening to improve overall predictive value.

A simple blood test to measure ceramide species, akin to widely used lipid profiles, could potentially be incorporated into standard clinical care to assess risk of both cardiovascular and non-cardiovascular death. This could lead to improved patient monitoring, treatment decisions and disease prevention.

Stage of Research

The inventors analyzed plasma samples from two large, community-based studies (Framingham Heart Study and Study of Health in Pomerania) and validated very long chain and long chain ceramide species as biomarkers for coronary heart disease (HR 0.8, CI 95%, p=0.0006), heart failure and all-cause mortality (HR 0.6, CI 95%, p=0.0001).

Applications

- **Routine cardiovascular screening –** expansion of current lipid panel/cholesterol screening to predict risk for heart disease or death in the general population and potentially prevent cardiovascular disease
- **Patient monitoring and stratification** to manage treatment of cardiovascular disease

Key Advantages

- **Early detection:** provides predictive information about coronary heart disease and mortality in the general population years before the actual onset of disease
- **Robust, high throughput, FDA-compliant assay** with little barrier to widespread adoption
    - fully validated two-dimensional liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay
    - simultaneously quantifies the three most abundant very long chain and long chain ceramide species in human plasma
- **Independent risk factor for improved prediction:**
    - improves the C-statistic when added to conventional tests (e.g., cholesterol screening) or standard coronary risk factors (e.g., smoking, diabetes)
    - equally predictive for men and women

Publications

- Peterson, L. R., Xanthakis, V., Duncan, M. S., Gross, S., Friedrich, N., Völzke, H., ... & Jiang, X. (2018). Ceramide remodeling and risk of cardiovascular events and mortality. *Journal of the American Heart Association*, 7(10), e007931.
- Jiang, H., Hsu, F. F., Farmer, M. S., Peterson, L. R., Schaffer, J. E., Ory, D. S., & Jiang, X. (2013). Development and validation of LC-MS/MS method for determination of very long acyl chain (C22: 0 and C24: 0) ceramides in human plasma. *Analytical and bioanalytical chemistry*, 405(23), 7357-7365.

Patents

- Methods of detecting ceramide (U.S. Patent Application, Publication No. 20180306797; WUSTL T-017009)
- Ceramides for evaluating risk of cardiovascular disease (U.S. Patent Application, Publication No. 201901015500; WUSTL T-014627)