Lewy body disease biomarkers for risk assessment and treatment

This technology identifies a panel of biomarkers for Lewy body disease (LBD) that may enable risk assessment and the development of targeted therapeutics.

Unmet Need: Biochemical method for early detection of Lewy body disease

Diagnosis of Lewy body disease (LBD) currently depends on the presence of behavioral symptoms that only occur after disease onset and are hard to distinguish from other neurodegenerative diseases. Unfortunately, no reliable LBD biomarkers have been reported, preventing early diagnosis and treatment when the opportunity to slow disease progression is greatest. As such, the identification of LBD biomarkers could enable the early detection of LBD and provide targets for therapeutic development.

The Technology: Biomarkers for early detection and treatment of Lewy body disease

This technology presents new genes associated with Lewy Body Disease (LBD), a common form of dementia that remains untreatable. While mutations in the GBA gene were previously associated with LBD, how it contributed to disease progression was unknown, and the contribution of genetic variation in other lysosomal storage disorder genes in the same pathway was also unknown. To determine how the GBA gene affected LBD pathology, it was sequenced alongside other genes present in its signaling pathway, revealing new genetic variations in four lysosomal storage disorder genes analyzed. Following biochemical analysis, it was found that LBD brains carrying the new GBA variants exhibited lower GCase activity levels, providing a simple readout for disease progression. Additionally, lipodomic analysis revealed that mutant GBA brains had altered lipid compositions, which can be easily assessed using basic HPLC techniques. The initial sequence analysis implicated genetic variants in SMPD1 and MCOLN1 (in addition to GBA) with LBD pathology, a finding that could potentially lead to new therapeutic targets. The methods described by this technology have been shown to be highly robust and predictive, as the found variants in GBA, MCOLN1, and SMPD1 were significantly associated with Lewy Body formation and in the case of GBA, correlated well with disease progression.

Applications:

- Biomarkers for the early detection and prevention of LBD
• Diagnosis of LBD
• Therapeutic targets for the treatment and prevention of LBD
• Methods could be applied to biomarker identification in related diseases

Advantages:
• Early detection of LBD
• Non-behavioral screening method for LBD
• Simple readout in the form of genetic variants, lysosomal enzyme activity, and lipid HPLC profiles
• Complementary biomarkers reduce false positives
• Uses combined genetic, enzymatic, and lipidomic approach to validate new drug targets in LBD

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