

# BLOOD-BASED BIOMARKERS OF ALZHEIMER'S DISEASE FOR DIAGNOSTICS AND CLINICAL TRIALS

<u>Cruchaga, Carlos, Dube, Umber, Ibanez, Laura</u>

Gill, John

T-019198

## **Technology Description:**

Researchers in Prof. Carlos Cruchaga's laboratory have identified a sensitive and specific panel of circular RNAs (circRNA) that could be used for diagnosing, screening or monitoring patients with Alzheimer's disease. The expression of these circRNAs tracks with the severity of the disease (both clinical dementia and neuropathological symptoms) and the analysis includes a series of custom models to predict Alzheimer's status. The circRNA can be detected in plasma using standard, inexpensive PCR-based assay, which could potentially enable population-based screening that identifies patients before the onset of clinical dementia. In addition, this technology could be particularly valuable in clinical trials for patient stratification or as surrogate biomarkers for efficacy.

## **Stage of Research:**

The inventors identified the panel of circRNA markers from transcriptome-wide analysis of circRNA differential expression in patients with Alzheimer's disease compared with healthy controls. Using two large and independent, brain derived, RNA-seq datasets, they validated these markers as significantly correlated with both neuropathological and clinical measures of AD severity.

**Publication:** Dube, U., Del-Aguila, J. L., Li, Z., Budde, J. P., Jiang, S., Hsu, S., ... & Gentsch, J. (2019). <u>An atlas of cortical circular RNA expression in Alzheimer disease brains demonstrates clinical and pathological associations. *Nature neuroscience*, 22(11), 1903-1912.</u>

#### **Applications:**

- Clinical trials for drugs to treat Alzheimer's disease:
  - o patient risk stratification and monitoring
  - potential for companion diagnostic because circRNA does not rely on measurement of drug targets (e.g., amyloid or tau)
- Diagnostics and screening for Alzheimer's disease:
  - diagnose, stage and monitor disease progression in patients with suspected Alzheimer's disease
  - pre-symptomatic screening of at-risk patients
  - potential for broad population-based screening

### **Key Advantages:**

- **High sensitivity and specificity**: AUC = 0.88; better than current methods with strong predictive ability for Alzheimer's disease status
- Inexpensive assay for blood-based markers:



- circRNA can be detected in unfasted plasma with standard PCR-based methods
- less invasive than testing cerebrospinal fluid and less expensive than PET-based amyloid imaging
- Stratification and presymptomatic testing:
  - circRNA expression tracks with both clinical and pathological severity for potential patient stratification
  - circRNA expression could identify pre-symptomatic individuals, potentially enabling early intervention or tracking in clinical trials for neuroprotective agents

Patents: Application pending

Related Web Links: Cruchaga Profile, NeuroGenomics and Informatics Lab