A new blood test, ADtect®, has been developed that can aid the early detection of Alzheimer’s Disease (AD). The test is based on measuring the expression of selected genes in blood and is kit and quality assessed by NanoDrop spectrophotometer and Agilent 2100 Bioanalyzer. Samples are manufactured instructions. Total RNA is extracted from blood samples using PAXgene™ Blood RNA biomarker result and true pathology. The implications of using an imperfect reference standard when diagnosis and true pathology can vary significantly and may mask a good agreement between a biomarker result and true pathology. The developments of biomarkers for early detection of AD clinical diagnosis is most often used as the management strategies which may delay the onset of the more debilitating symptoms of AD. In the development of biomarkers for early detection of AD clinical diagnosis is most often used as the standard of truth. However, it has been shown in several studies that the agreement between clinical diagnosis and true pathology can vary significantly and may mask a good agreement between a biomarker result and true pathology. The implications of using an imperfect reference standard when assessing biomarker performance have to be taken into consideration.

The ADtect® test procedure

Whole blood is collected from individuals in PAXgene™ Blood RNA tubes and processed according to manufacturer instructions. Total RNA is extracted from blood samples using PAXgene™ Blood RNA kit and quality assessed by NanoDrop spectrophotometer and Agilent 2100 Bioanalyzer. Samples are prepared using the high-capacity cDNA reverse transcriptase kit and the Universal PCR Master Mix reagent from Applied Biosystems. Up to 4 individual samples are applied to the ADtect® multi-fluidic card. The test procedure is outlined in Box 1.

Results

During calibration of the ADtect® test, the disease algorithm was developed using partial least square regression on a balanced set of samples from Alzheimer’s disease patients (N=103) and cognitively healthy controls (N=105) recruited from Norwegian and Swedish hospitals. The final disease algorithm was built into the ADtect® software for patient reporting.

Two independent validation studies of the ADtect® separated in time with 1 year was performed (Box 2). The first validation included blood samples collected at 4 sites in Norway. All samples (N=74, 32 AD, 42 cognitively healthy controls) were independent from the calibration study, and 3 of the recruitment sites were independent from the calibration. The second and extended validation study included blood samples collected at 11 sites in Norway and Sweden. All samples (N=130, 68 AD, 62 cognitively healthy controls) were independent from the calibration, and 6 of the recruitment sites were independent from the calibration. The validation studies showed a 71.6% and 71.5% agreement of the ADtect® test with the clinical diagnosis (Box 2).

28 AD cases and 2 controls where CSF biomarkers also were included were investigated. 22 of the AD subjects and both controls were correctly predicted using the 96-gene array.

Conclusions

- A novel blood test has been developed that can aid the early detection of Alzheimer’s Disease using a peripheral blood sample.
- The accuracy of the ADtect® is likely significantly higher than its agreement with clinical diagnosis indicate.
- The test is a relevant biomarker for early detection of Alzheimer’s disease.
- An agreement of 80% was observed when comparing ADtect® with CSF biomarkers.

References


Acknowledgements

The following sites contributed to clinical samples:
Norway:
- Ullevål University Hospital, Oslo
- Haraldsplass Deaconesses Hospital, Bergen
- Stavanger University Hospital, Stavanger
- Sykehuset Innlandet, Sanderud and Hamar
- Haugesund University, Haugesund
- Eldercare center, Oslo

Sweden:
- Lund University Hospital, Lund
- Upptalia Academic Hospital, Upptalia
- Stockholm’s Hospital, Stockholm
- Karolinska University Hospital, Huddinge