ADx neurosciences mind your brain

Session

Session 6: biomarkers
Time: Thursday, 14/Apr/2022: 10:00am - 10:40am
Session Chair: Wolfgang Oertel
Session Chair: Wilma D.J. Van de Berg
Location: Lecture Hall (Promotiezaal)
University Halls, Naamsestraat 22, Leuven

Abstract Session

15 min presentations + 5 min Q&A

Presentations

10:00am - 10:20am
Luis Oliveira, MJFox Foundation (US)
'Building the Toolkit for Alpha-Synuclein Biomarkers in Parkinson's Disease'

10:20am - 10:40am
Erik Stoops, ADx NeuroSciences NV, Ghent (Belgium)
'The added value of immunoassay in α-Synuclein Amplification Assays; from qualitative to quantitative measurement'

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Background: Clinical diagnosis is a challenge in α-synucleinopathies with regard to early diagnosis and discrimination (eg. PD vs PDD). α-Synuclein Amplification Assays (SAA) have proven high specificity and sensitivity over several studies for PD diagnosis [1]. A further use of SAA assays is hampered by the absence of quantitative interpretation and ease of use. We have explored the potential of combining SAA with an oligomeric alpha synuclein immunoassay as a tool that eventually can report quantitative results.

Methods: An exploratory cohort of 28 subjects (8 healthy controls, 14 PD, 2MSA and 4 DLB) was included for the clinical assessment. The clinical diagnosis of probable DLB, PD, MSA was established according to international criteria. The clinical history, neurological evaluation and diagnostic investigations, including brain magnetic resonance imaging, cerebral 129I-ioflupane SPECT (DaTSCAN) were obtained for each patient. Furthermore an in house SAA assay was developed at the University of Verona to obtain qualitative output of the assay.

Immunoassay: Antibody clone A17183B (BioLegend, Cat# 865001) was generated using aggregated recombinant α-synuclein and was used as capture antibody. The detector antibody Syn 211 is reactive towards the C-terminal region of α-synuclein and was used in biotinylated form. This pair of antibodies was further used in ELISA and Simoa platform. Amplified material from the SAA assay was applied in both assays including a calibrator curve based upon oligomeric α-synuclein. In addition, the analytical performance parameters were assessed (eg. specificity and selectivity).

Result: Both platforms ELISA and Simoa were capable to quantify the amplified material into the samples. For ELISA the concentration ranged between 322 ng/mL and 1014 ng/mL for healthy controls while in the disease groups the concentration was between 9092 ng/mL and 51934 ng/mL for those samples where the SAA assay resulted in a positive interpretation. In addition,

the analytical performance revealed high specificity towards oligomeric forms and not monomeric forms of α-synuclein. With regard to selectivity the ELISA method was able to discriminate oligomeric from monomeric form of α-synuclein up to a concentration of 5 ng/mL monomeric α-synuclein.

Conclusion: Our study shows that amplified material from Synuclein amplification assays can be used as sample in immunoassay with a quantitative readout that is comparable to SAA result. The necessary analytical performance parameters were verified and found acceptable.

References:

[1] Russo, Marco J et al. "High diagnostic performance of independent alpha-synuclein seed amplification assays for detection of early Parkinson's disease." Acta neuropathologica communications vol. 9,1 179. 6 Nov. 2021

Keywords: Synuclein, immunoassay, amplification