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e4Quant
A new, simple and cost-effective method to quantify the apolipoprotein E4 in plasma

CLINICAL SIGNIFICANCE

- Apolipoprotein E4 (ApoE4) is a glicoprotein involved in lipid transport. It is encoded in the ε4 allele of *APOE* gene (*APOE* ε4). Carriage of ε4 allele has been extensively described as a major risk factor for non-dominantly inherited Alzheimer's Disease (AD)[1, 2], one of the most devastating and prevalent forms of neurological disease. Similarly, it is very well established that *APOE* ε4 is an important risk factor for cardiovascular disease (CVD) [3], which is the most common cause of death worldwide.
- However, if ApoE4 blood concentration can be used as a predictor for those diseases have not been established yet, mainly because available techniques for measuring ApoE4 concentration in blood are complex, time-consuming and difficult to implement in the clinic.
- Biocross has adapted a proprietary and patented technology to create a quantitative test that allows the precise quantification of ApoE4 in human plasma. This technology is based in turbidimetry, a technique widely used in clinical routine for the analysis of other biomarkers. Therefore, e4Quant implementation in the clinical routine is easy, since it can be used in the chemistry analyzers already available in hospitals and clinical laboratories.

PUTATIVE APPLICATIONS OF e4Quant

Alzheimer's Disease

ApoE4 plasma concentration as a predictor of pathological concentrations of AD biomarkers (Aβ, Tau and p-Tau) in the cerebrospinal fluid or brain. Currently, the analysis of these biomarkers requires invasive and/or expensive techniques. **e4Quant** could be used as a cost-effective and non-invasive approach for estimation of the concentration of Aβ, Tau and p-Tau in patients with symptoms of dementia.

ApoE4 plasma concentration as a predictor of disease progression. AD starts earlier and progress faster in *APOE* ε4 carriers. ApoE4 plasma concentration could be a good predictor of the risk for progression to the first stages of the disease (mild cognitive impairment, MCI) or from MCI to more severe stages of the disease within *APOE* ε4 carriers.

ApoE4 plasma concentration as companion diagnostic. It is well reported that *APOE* ε4 carriers respond differently, both in terms of efficacy and side effects, to the most promising experimental treatment against AD, anti-Aβ antibodies, one of which is currently evaluated by the FDA for approval as treatment for AD. It is possible that the response to anti-Aβ treatment is dependent on the ApoE4 plasma concentration. Therefore, **e4Quant** could be used to select patients with best response or more prone to side effects within *APOE* ε4 carriers.

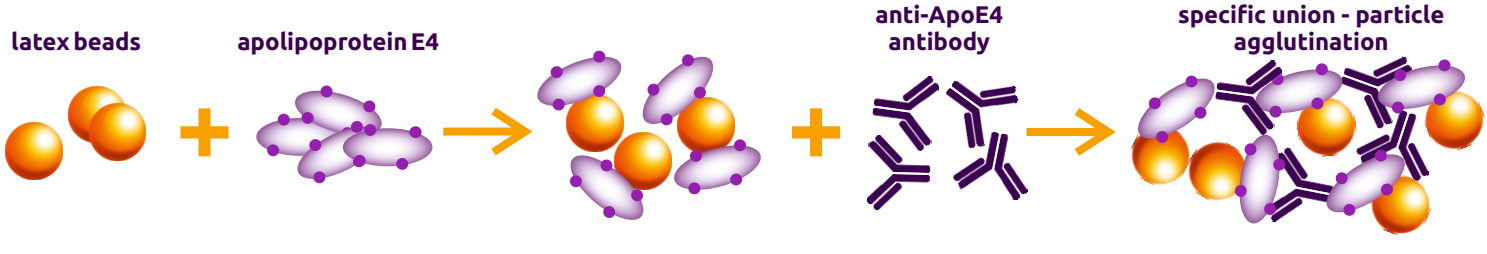
Discrimination between *APOE* ε4 homozygous and *APOE* ε4 heterozygous. The quantitative nature of **e4Quant** allows the normalization of ApoE4 to total ApoE, an strategy that has been proven successful to differentiate people with only one ε4 allele from people with two ε4 alleles without the need of a genetic test [4]. This information is very relevant for AD risk, since *APOE* ε4 homozygous have a significantly increased risk (12X than *APOE* ε4 non-carriers) than *APOE* ε4 heterozygous (3-5X than *APOE* ε4 non-carriers).

Cardiovascular Disease

Apoe4 plasma concentration as a predictor for CVD risk. e4Quant offers the possibility to investigate if ApoE4 can be a risk biomarker with the same or higher performance than the biomarkers currently used such as cholesterol, LDL or ApoB/ApoA1 ratio).

PRINCIPLE

e4Quant consists on one reagent with latex particles and another reagent with a mouse anti-ApoE4 antibody, which induces the latex particles agglutination when ApoE4 is present in the plasma sample. This agglutination can be measured with a photometer. The degree of turbidity is proportional to the sample concentration of ApoE4.



SPECIFICATIONS

Format	**Reagents (2)**	R1: Liquid. Buffer with anti-ApoE4 antibody.	
		R2: Liquid. Buffer with polystyrene beads.	
	Calibrators (5)	Freeze-dried human plasma spiked with rApoE4	
		0 (water) µg/mL	
		4,6 µg/mL	
		8,2 µg/mL	
		17,2 µg/mL	
		34,9 µg/mL	
	Controls (2)	Freeze-dried human plasma spiked with rApoE4	
		9,7 µg/mL	
		19,2 µg/mL	
Specifications	**Detectability**	Limit of Blank (LoB)	1,13 µg/mL
		Limit of Detection (LoD)	1,73 µg/mL
		Limit of Quantification (LoQ)	3,69 µg/mL
	Linearity	4 - 40 µg/mL	
	Precision	Repeatability	CV (%): 1,41-6,20
		Reproducibility	CV (%): 2,86-9,34
	Interferences	Haemoglobin (0-500 mg/dL)	No
		Bilirrubin (0-18 mg/dL)	No
		HAMA (0-40 ng/mL)	No
		Rheumatoid factor (0-450 UI/mL)	No
	Prozone	No prozone at 200 µg/mL	
	Stability	R1 and R2 (2-8°C)	≥18 months
		Calibrators (2-8°C)	≥6 meses
	Performance	Cut-off of 4,72 µg/mL	
		APOE ε4 discrimination	Specificity: 100% Sensitivity: 100%
Set up parameters	**Reaction (min)**	10	
	Volumes (µL)	R1: 110 / Plasma: 5 / R2: 110	
	Secuence (sec)	t=0; R1 + sample / t=300: R2 / t=320: A_1 / t=600: A_2	
	Calculation [ApoE4]	A_2-A_1	

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