

Supplementary information

Potentiometric Biosensor based on Artificial Antibodies for an Alzheimer Biomarker detection

Sónia C.S. Ribeiro¹, Rúben Fernandes^{4,5}, Felismina T. C. Moreira^{1,3*}, M. Goreti F. Sales²

Table S1. Log KPOT for different interfering species in MOPS pH 8.0.

Interfering	Log K _{POT}
	MIP
Creatinine	-0.018
Albumin	-0.016
Urea	-0.016

Table S2. Electrochemical biosensors for the detection of AD peptide biomarkers using nanomaterials as electrode modifiers or as labels published over the lastten years.

Biorecognition element	Biomarker	LOD	Linear Range	Selectivity Tested	Real Sample Tested	Ref
Antibody	A β	22 fM	0.22 pM–2.22 nM	Not tested	Serum samples	[1]
Antibody	A β	1.15 pM	2.22–221.6 pM	Not tested	Not tested	[2]
Antibody	p53	0.05 nM	2–50 nM	Not tested	Real plasma samples of MCI and AD patients	[3]
Antibody	A β	22.2 pM	111 pM–111 nM	Not tested	Not tested	[4]
Antibody	A β	100 fM	100 fM–25 pM.	HSA, IgG and other AD	Serum and plasma samples	[5]
Antibody	A β	10 pM	0.02–1.50 nM	Artificial CSF	Not tested	[6]
MIP	A β o	88.6 fM	22 pM–14.6 nM	Not tested	Serum samples	[7]
MIP	A β o	0.3 fg mL ⁻¹	1.0 fg mL ⁻¹ - 100.0 fg mL ⁻¹	A β 42	plasma samples for A β 42 analysis.	[8]
MIP	A β o	0.27 pM	1.1 pM–2.2 nM	A β 40-42 monomers,	Human serum samples	[9]
Aptamer	A β o	100 pM	0.5–30 nM	A β 40-42 monomers, CSF A β (40–42)o, A β (40–42)f		[10]]
cellular prion protein (PrPC)	A β o	10–2 fM	10–8–104 nM	A β f and monomers	AD mice tissue	[11]
PrP(95-110)	A β o	8 pM	20 pM–100 nM	A β f and monomers	Human serum samples	[12]
membrane capturing A beta aggregates 1	A β	2.21 pM	2.21 pM–221 nM.	A β monomers, peptides	Human blood serum	[13]
Gelsolin-HRP	A β	28 pM	0.1–50 nM	Not tested	CSF and rat brain tissues	[14]
ferrocene-encapsulated Zn zeolitic imidazole framework (ZIF-8	A β o	10–5 μ M	10–5–102 μ M	A β f and monomers and artificial CSF	Not tested	[15]

References:

1. Wu CC, Ku BC, Ko CH, Chiu CC, Wang GJ, Yang YH, et al. Electrochemical impedance spectroscopy analysis of A-beta (1-42) peptide using a nanostructured biochip. *Electrochimica Acta*. 2014;134:249-57. doi: 10.1016/j.electacta.2014.04.132.
2. Carneiro P, Loureiro J, Delerue-Matos C, Morais S, Pereira MD. Alzheimer's disease: Development of a sensitive label-free electrochemical immunosensor for detection of amyloid beta peptide. *Sensors and Actuators B-Chemical*. 2017;239:157-65. doi: 10.1016/j.snb.2016.07.181.
3. Amor-Gutierrez O, Costa-Rama E, Arce-Varas N, Martinez-Rodriguez C, Novelli A, Fernandez-Sanchez MT, et al. Competitive electrochemical immunosensor for the detection of unfolded p53 protein in blood as biomarker for Alzheimer's disease. *Analytica Chimica Acta*. 2020;1093:28-34. doi: 10.1016/j.aca.2019.09.042.
4. Rama EC, Gonzalez-Garcia MB, Costa-Garcia A. Competitive electrochemical immunosensor for amyloid-beta 1-42 detection based on gold nanostructurated Screen-Printed Carbon Electrodes. *Sensors and Actuators B-Chemical*. 2014;201:567-71. doi: 10.1016/j.snb.2014.05.044.
5. Diba FS, Kim S, Lee HJ. Electrochemical immunoassay for amyloid-beta 1-42 peptide in biological fluids interfacing with a gold nanoparticle modified carbon surface. *Catalysis Today*. 2017;295:41-7. doi: 10.1016/j.cattod.2017.02.039.
6. Liu L, Zhao F, Ma F, Zhang L, Yang S, Xia N. Electrochemical detection of beta-amyloid peptides on electrode covered with N-terminus-specific antibody based on electrocatalytic O-2 reduction by A beta(1-16)-heme-modified gold nanoparticles. *Biosensors & Bioelectronics*. 2013;49:231-5. doi: 10.1016/j.bios.2013.05.028.
7. Moreira FTC, Rodriguez BAG, Dutra RAF, Sales MGF. Redox probe-free readings of a beta-amyloid-42 plastic antibody sensory material assembled on copper@carbon nanotubes. *Sensors and Actuators B-Chemical*. 2018;264:1-9. doi: 10.1016/j.snb.2018.02.166.
8. Ozcan N, Medetalibeyoglu H, Akyildirim O, Atar N, Yola ML. Electrochemical detection of amyloid-beta protein by delaminated titanium carbide MXene/multi-walled carbon nanotubes composite with molecularly imprinted polymer. *Materials Today Communications*. 2020;23. doi: 10.1016/j.mtcomm.2020.101097.
9. Cabral-Miranda G, Cardoso AR, Ferreira LCS, Sales MGF, Bachmann MF. Biosensor-based selective detection of Zika virus specific antibodies in infected individuals. *Biosensors & Bioelectronics*. 2018;113:101-7. doi: 10.1016/j.bios.2018.04.058.
10. Zhou YL, Zhang HQ, Liu LT, Li CM, Chang Z, Zhu X, et al. Fabrication of an antibody-aptamer sandwich assay for electrochemical evaluation of levels of beta-amyloid oligomers. *Scientific Reports*. 2016;6. doi: 10.1038/srep35186.
11. Qin J, Cho M, Lee Y. Ultrasensitive Detection of Amyloid-beta Using Cellular Prion Protein on the Highly Conductive Au Nanoparticles-Poly(3,4-ethylene dioxythiophene)-Poly(thiophene-3-acetic acid) Composite Electrode. *Analytical Chemistry*. 2019;91(17):11259-65. doi: 10.1021/acs.analchem.9b02266.
12. Xia N, Wang X, Zhou BB, Wu YY, Mao WH, Liu L. Electrochemical Detection of Amyloid-beta Oligomers Based on the Signal Amplification of a Network of Silver Nanoparticles. *Acs Applied Materials & Interfaces*. 2016;8(30):19303-11. doi: 10.1021/acsami.6b05423.
13. Wustoni S, Wang SF, Alvarez JR, Hidalgo TC, Nunes SP, Inal S. An organic electrochemical transistor integrated with a molecularly selective isoporous membrane for amyloid-beta detection. *Biosensors & Bioelectronics*. 2019;143. doi: 10.1016/j.bios.2019.111561.
14. Yu Y, Sun X, Tang D, Li C, Zhang L, Nie D, et al. Gelsolin bound beta-amyloid peptides((1-40/1-42)): Electrochemical evaluation of levels of soluble peptide associated with Alzheimer's disease. *Biosensors & Bioelectronics*. 2015;68:115-21. doi: 10.1016/j.bios.2014.12.041.
15. Qin J, Cho M, Lee Y. Ferrocene-Encapsulated Zn Zeolitic Imidazole Framework (ZIF-8) for Optical and Electrochemical Sensing of Amyloid-beta Oligomers and for the Early Diagnosis of Alzheimer's Disease. *Acs Applied Materials & Interfaces*. 2019;11(12):11743-8. doi: 10.1021/acsami.8b21425.