proceedings

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Abstract

Innovative Silicon-Based Sensing Strategy for the Alzheimer's Disease Detection by Phage Display †

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† Presented at the XXXV EUROSENSORS Conference, Lecce, Italy, 10–13 September 2023.

Abstract: An innovative biosensing strategy for the diagnosis of Alzheimer's disease (AD) in human sera has been developed. The technology relied on a silicon flat substrate that was functionalized to perform a phage display detection of anti-amyloid beta (Aβ) antibodies, as AD markers, among the pool of IgGs of human sera. The substrate was derivatized with an interface able to bind and orient the IgGs for the detection operated by an engineered selective probe phage. The interface chemistry and its discrimination activity of healthy and AD sera have been fully characterized.

Keywords: biosensing; silicon technology; functionalization; phage display; Alzheimer's disease

Citation: Calorenni, P.; Rizzo, M.G.; De Plano, L.M.; Leonardi, A.A.; Paratore, V.; Condorelli, G.G.; Irrera, A.; Sciuto, E.L.; Oddo, S.; Conoci, S. Innovative Silicon-Based Sensing Strategy for the Alzheimer's Disease Detection by Phage Display. *Proceedings* **2024**, *97*, 65. https://doi.org/10.3390/proceedings2024097065

Academic Editors: Pietro Siciliano and Luca Francioso

Published: 21 March 2024

1. Introduction

The conventional diagnosis of Alzheimer's disease (AD), a neurodegenerative disorder of people of an advanced age, is based on imaging techniques that are too invasive, expensive and lab constrained for a massive screening. Biosensors based on the phage display technique solved these issues proposing a diagnostic method that allows the direct detection of the anti-Aβ IgGs of a patient's serum by the selective binding with engineered phages, making the diagnosis faster and cheaper [1]. However, phage display-based biosensors are, mostly, assembled on plastic surfaces, and their thermal properties and low level of integration make them unsuitable for massive biosensing applications. In this study, we proposed an innovative PoC silicon biosensing strategy for the selective detection of anti-Aβ antibodies in human sera by phage display. The combination with silicon technology allowed an improvement in the sensing performances due to silicon's low heat capacity, good thermal conductivity and high level of nanostructuring [2,3]. The sensing activity hinged on a silicon interface that was functionalized to expose anti-Aβ IgGs to the selective recognition by a M13 probe phage exposing Aβ-mimics peptides on its capsid, allowing the discrimination by phage display of healthy and AD affected sera.

2. Materials and Methods

The silicon interface (Figure 1a) was functionalized by a (GOPS) silanization, followed by the anchoring of the immunoglobulin-binding protein G (**1b**). Once spotted on the interface, all IgGs of the tested human sera, including the anti-Aβ IgG of AD serum (**1c**),

were bound to the protein array and exposed to an engineered M13 probe phage (**1d-I**) for the anti-Aβ phage display. The functionalization was characterized by SEM analysis, while the sensing activity was immunologically validated by using an anti-M13 HRP-conjugated antibody (**1d-II**) and its MTT substrate in the Enzyme-Linked Immunosorbent Assay (ELISA) test.

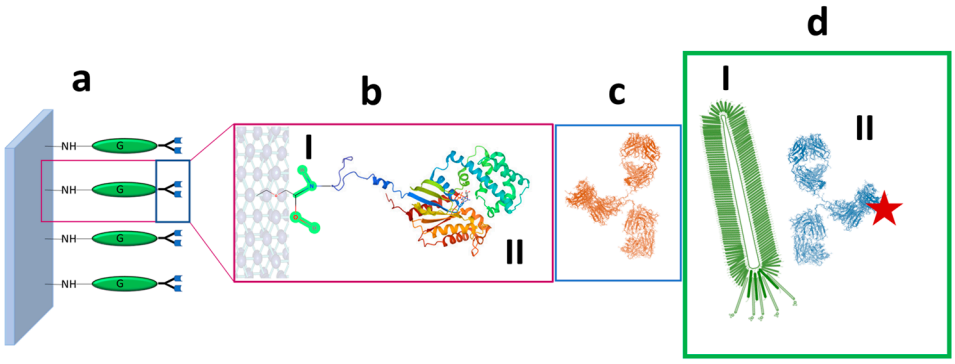

Figure 1. Silicon interface: (**a**) complete view; (**b**) detail of interface derivatization with (**I**) GOPS layer bound to (**II**) protein G array; (**c**) anti-Aβ IgG target; and (**d**) detection system based on (**I**) probe M13 phage and (**II**) anti-M13 HRP-conjugated antibody.

3. Results

The SEM data reported the IgGs exposure on silicon interface (Figure 2a). Figure 2b, instead, shows the ELISA test and spectroscopic validation of the phage-display sensing activity.

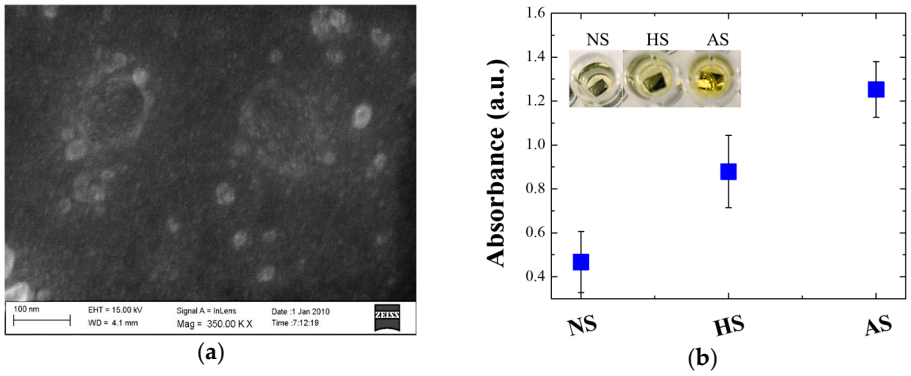

Figure 2. (**a**) Silicon interface SEM characterization. (**b**) Sensing activity validation by ELISA test on Abs450nm signal of no serum (NS), healthy serum (HS) and AD serum (AS) sample.

The test produced a colorimetric signal whose intensity, measured by the spectroscopic analysis of 450 nm absorbance, was enhanced in the AD serum-treated silicon interface, where the probe phage selectively interacted with the exposed anti-Aβ IgGs. Brought together, these results show that the proposed silicon interface is a promising tool for innovative AD sensing applications and diagnosis.

Author Contributions: Investigation, P.C.; writing—original draft preparation, E.L.S.; writing—review and editing, M.G.R., L.M.D.P., A.A.L., V.P., G.G.C., A.I., S.O. and S.C.; supervision, S.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was approved by the Ethics Committee of the "Policlinico Vittorio Emanuele" of Catania.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

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