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Editorial

Peptidome and Peptide Aptamer: Key Players for the New Age of Smart Bio Electrochemical Sensors

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Editorial

Individual biomarker has been unsuccessful in defining the disease pathology, progression and thus early diagnosis. For example, Amyloid-β peptide (Aβ) in Cerebrospinal Fluid (CSF) is commonly thought to represent as a potential biomarker for Alzheimer's Disease (AD), however, very recent studies on misprocessing of proteins in the brain of patients with AD suggested that the diagnostic performance of Aβ is suboptimal and thus single biomarkers are often of limited diagnostic value [1]. Few surrogate markers (e.g., APLβ28) for amyloid-beta production have recently been identified in CSF at a concentration of near 4.5 nM as a novel and highly sensitive biomarker for early detection of sporadic AD [2]. In addition, no significant differences of Aβ in blood between patients with AD and early AD types and no correlation between time-linked blood plasma and cerebrospinal fluid Aβ hampers the diagnostic utility of the Aβ as biomarker [3]. In a recent report, the course of AD that begins more than 20 years before first clinical signs emerge is estimated with full of changes in the concentration and/or localization of AD associated low-molecular-weight biomarkers in human Peptidome [peptidome represents a total set of endogenous peptides that are naturally generated by proteolytic degradation of human proteins in a specific cell or tissue] [4]. Therefore, a more comprehensive characterization of bioactive peptides in peptidome can reveal more AD-specific patterns. Recently, peptide fingerprinting of AD in CSF is reported and a discriminative 57 low-molecular-weight endogenous peptides were identified as new synaptic biomarkers [5]. However, in order to realize the full power of peptidome, we need to measure and compare the peptidome patterns in the course of disease of many individuals. Mass Spectrometry (MS)-based approaches that have been used as a primarily tool for peptidome analysis, however, impractical for clinical diagnosis of peptidome and thus an innovative approach need to be developed for a simple, sensitive, and specific diagnosis and monitoring of peptidome-based disease progression.

This indicates to deal two major challenging issues: First, development of novel bio-probes that can binds to low-molecular-weight peptide biomarker for affinity-based biosensing [selectivity issue]. The conventional antibody-based sandwich Enzyme-Linked Immunosorbent Assay (ELISA) requires the target to be measured must be large enough to have at least two epitopes (binding sites) to be captured. Therefore, antibody-based probe has a fundamental limitation (unobtainable issue) to detect low-molecular-weight biomarkers such as peptidome, which has only one epitope, i.e., one available binding site. In this context, mimicking and accelerating the evolution process at the molecular level using evolutionary molecular engineering has been arisen and powered by adding Man-made skills to it. This resulted in creation of aptameric reagents as a new bio-recognition element that are engineered on-demand through an in vitro selection procedure to selectively bind with a substrate which have recently emerged as a 'superior and smart class of versatile building blocks in the construction of novel biosensor with respect to their potential use in biomedical diagnostics [6]. In particular, peptide-based aptamers, which are comparatively smaller in molecular weight, exhibit a smaller binding footprint allowing for a more thorough and precise interrogation of the target than that afforded by nucleic acid-based aptamers. A small surface area of the scaffold peptide aptamer should result in higher molar binding densities and lower background signals arising from nonspecific interactions with regions that are not directly involved in target recognition. Because of these properties, peptide aptamers are potential candidates to recognize low-molecular-weight smaller target molecules with a sensitivity that can compete with antibodies. Development of in vitro selection technologies, such as cDNA display [7] which improves

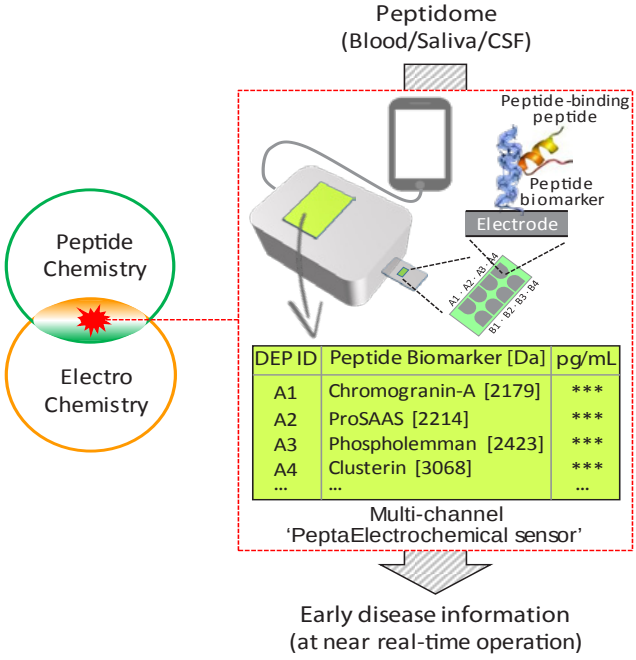

Figure 1: Pepta electrochemical sensor.
A schematic illustration of the peptide-binding peptide aptamer-based multi-channel electrochemical biosensor to detect multiple biomarkers in parallel using a competitive binding assay.

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efficiency and stability, facilitated the high-throughput in vitro selection of peptide aptamers [8]. Using cDNA display, high-binding affinity (with KD nM to pM range) peptide aptamers for neurological disease-associated biomarker, e.g., Aβ42 [9]; cancer biomarker, e.g., cathepsin E [10]; cardiovascular risk biomarker, e.g, renin [11] have recently been identified. Additional key characteristic of peptide aptamers includes smaller (few kDa) in size than antibodies (150 kDa), production is easier (in vitro, no animal use, stable at ambient temperature, less-expensive, no lot-to-lot variation issue) and they have minimal restrictions for targets.

Second challenging issue is the identification of low- to medium-abundance biomarkers in a complex biological sample by lowering the limit of detection [sensitivity issue]. For example, human serum contains over 100,000 different protein molecules of which 99% is made up by the 22 most abundant proteins. Therefore, it is a very challenging issue how to improve sensitivity while specifically recognizes targets in the presence of thousands-fold excess of non-targeted identical analytes within a complex biological sample for clinical diagnostics. To delve this, an important goal is to develop in vitro multiplex selection approach that retain the favorable and rapid molecular recognition of specific aptamers against multiple targets in parallel and in the presence of non-targeted (background) peptides/proteins by facilitating '*interspecies* over *intraspecies* selection force'. Next, these target-aptamer binding event can be detectable sensitively using a transducer such as electrochemical signals. Electrochemistry offers a simple alternative to traditional analytical methods and provides a high degree of sensitivity, and it has been shown to be highly effective for device miniaturization. The introduction of screen-printing electrode technology (called Disposable Electrode Printed (DEP)-chip) and multi-channel potentiostat have further widened the scope of available electrochemical sensors for large-scale applications [11]. As shown in Figure 1, fabrication of a multiplex probe panel by the integration of peptide chemistry and electrochemistry can open exciting new possibilities for ultra-sensitive biosensing where the rich sensing of electrochemistry is merged with the outstanding binding properties of aptamers with excellent specificity. Furthermore, since peptides participate in many physiological events, the extension of proteomics to peptidomics, i.e., global analysis of low-molecular-wright peptides, can provide valuable information to the underlying pathobiology and future treatment of AD and other diseases. Overall, it is clear that the early knowledge on these peptide-based biomarkers through peptide-based aptamers and portable electrochemical devices can make a significant role in the development of a broad class of 'smart' biosensors with improved specificity and high sensitivity which can receive more interest from pharmaceutical companies.

References

1. Toledo JB, Shaw LM, Trojanowski JQ. Plasma amyloid beta measurements - a desired but elusive Alzheimer's disease biomarker. Alzheimers Res Ther. 2013; 5: 8.
2. Yanagida K, Okochi M, Tagami S, Nakayama T, Kodama TS, Nishitomi K, et al. The 28-amino acid form of an APLP1-derived Abeta-like peptide is a surrogate marker for Abeta42 production in the central nervous system. EMBO Mol Med. 2009; 1: 223-235.
3. Le Bastard N, Aerts L, Leurs J, Blomme W, De Deyn PP, Engelborghs S. No correlation between time-linked plasma and CSF Abeta levels. Neurochem Int. 2009; 55: 820-825.
4. Bateman RJ, Xiong C, Benzinger TL, Fagan AM, Goate A, Fox NC, et al. Clinical and biomarker changes in dominantly inherited Alzheimer's disease. N Engl J Med. 2012; 367: 795-804.
5. Jahn H, Wittke S, Zurbig P, Raedler TJ, Arlt S, Kellmann M, et al. Peptide fingerprinting of Alzheimer's disease in cerebrospinal fluid: identification and prospective evaluation of new synaptic biomarkers. PLoS One. 2011; 6: 26540.
6. Zhou W, Huang PJ, Ding J, Liu J. Aptamer-based biosensors for biomedical diagnostics. Analyst. 2014; 139: 2627-2640.
7. Yamaguchi J, Naimuddin M, Biyani M, Sasaki T, Machida M, Kubo T, et al. cDNA display: a novel screening method for functional disulfide-rich peptides by solid-phase synthesis and stabilization of mRNA-protein fusions. Nucleic Acids Res. 2009; 37: e108.
8. Mochizuki Y, Biyani M, Tsuji-Ueno S, Suzuki M, Nishigaki K, Husimi Y, et al. One-pot preparation of mRNA/cDNA display by a novel and versatile puromycin-linker DNA. ACS Comb Sci. 2011; 13: 478-485.
9. Ghimire Gautam S, Komatsu M, Nishigaki K. Strong inhibition of beta-amyloid peptide aggregation realized by two-steps evolved peptides. Chem Biol Drug Des. 2015; 85: 356-368.
10. Biyani M, Futakami M, Kitamura K, Kawakubo T, Suzuki M, Yamamoto K, et al. *In Vitro* Selection of Cathepsin E-Activity-Enhancing Peptide Aptamers at Neutral pH. Int J Pept. 2011; 834525.
11. Biyani M, Kawai K, Kitamura K, Chikae M, Biyani M, Ushijima H, et al. PEP-on-DEP: A competitive peptide-based disposable electrochemical aptasensor for renin diagnostics. Biosens Bioelectron. 2016; 84:120-125.

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