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Recent Update of Nanobiosensors Using Olfactory Sensing Elements and Nanomaterials

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Abstract

Various biomaterials such as antibody, aptamer, enzyme, DNA and sensory receptor can be used for recognizing ligands by nanobiosensor. Especially, olfactory sensing elements with olfactory receptor are most promising one to develop the nanobiosensor with high performance because they can discriminate target molecules with high selectivity and also detect numerous odorant molecules, for example over ten thousands of odorants at very low concentration can be detected by human nose. There have been increasing many efforts to develop the nanobiosensor using various olfactory sensing elements. Recently, several olfactory sensing elements were integrated with nanomaterials, which greatly improve the sensitivity of the nanobiosensor, to enhance the performance of nanobiosenor. In this paper, olfactory sensing elements were briefly introduced for the development of the nanobiosensor with high performance.

Keywords: Nanobiosensor; Olfactory sensing elements; Olfactory receptor protein; Olfactory nanovesicle; Olfactory receptor peptide

Nanobiosensors Using the Integration of Olfactory Sensing Elements with Nanomaterials

Various biomaterials have been applied for enhancing the performance of nanobiosensor [1-4]. These biomaterials have been used for the detection of target ligand by help of various detecting devices. Many efforts have been made to develop various sensing devices [5-7] and the rapid advances in nanotechnology have improved the technologies to design the nanobiosensor with high sensitivity and selectivity. Remarkable one of recent technologies for the development of nanobiosensor is the combination of biomaterials and nanomaterials such as carbon nanotube, conducting polymer nanotube, and graphene in order to enhance the selectivity and sensitivity of the sensor. Biomaterials as a primary transducer are the sensing elements which provide high recognition ability for nanobiosensor. Nanomaterials as a secondary transducer are non-biological part taking charge of the sensitivity and play a major role in transduction and amplification of signals from biological materials. Many biomaterials such as living cells, nucleotide, antibody, and enzyme have been introduced to nanomaterials for the development of nanobiosensing system [8-11]. Living cells such as neuron, cardiomyocytes and even cardiac tissue have been used as biomaterials for detecting cellular signalling [12,13]. Nucleotides such as single-stranded DNA, PNA (peptide nucleic acid) and aptamer have been interfaced with nanomaterials for the detection of DMMP (dimethyl methylphosphonate), DNA [14-16]. These biomaterials have the limitations such as low sensitivity, low reusability, and low range of detectable target molecules. Recently, olfactory sensing elements have been widely used as a biological recognition element to overcome the limitations of other biomaterials and so to enhance the performance of nanobiosensor. Since many kinds of nanobiosensors can be constructed using about 390 olfactory receptors or through the combination of olfactory receptors, olfactory sensing elements play a major role in recognizing and discriminating odorant molecules in nanobiosensing system. There are three types of olfactory sensing elements which can be integrated with nanomaterials by the covalent or noncovalent bonding for the construction of nanobiosensors with higher performance. They are olfactory receptor protein, olfactory nanovesicle, and olfactory receptor peptide. Binding of ligand induces the conformational change of the olfactory receptor and peptide resulting in the change in current of nanomaterials such as carbon nanotube, conducting polymer nanotube, and graphene. In case of olfactory nanovesicle, the binding event induces calcium influx into nanovesicle through calcium channels inducing the change in current of nanomaterials mentioned above. Finally, the changes in current can be measured.

As an olfactory sensing element, olfactory receptor proteins are useful biomaterials to be integrated with nanomaterials. Olfactory receptor proteins belong to G-protein coupled receptor and is seven-transmembrane protein containing many hydrophobic regions inserted into lipid membrane. Recently, olfactory receptor proteins were produced from *E. coli.* and directly functionalized on the single-walled carbon nanotube and graphene. In this study, functionalization of carbon nanotube was conducted by spreading membrane fraction of *E. coli* expressing olfactory receptors on the membrane and in case of graphene, functionalization was conducted by covalent bonding between the amine group of the olfactory receptor protein and the aldehyde group of the modified graphene with glutaraldehyde and 1,5-diaminonaphthalene. These nanobiosensors detected a specific odorant molecule at an extremely low concentration of 0.04 fM [17] and discriminated the difference of single carbon atom [18]. These data show a great enhancement of nanobiosensor performance by the combination of olfactory receptor proteins and nanomaterials. However, it is very difficult to solubilize, purify, and refold olfactory receptor proteins expressed in *E. coli* expression system because of their complicated structure and strong hydrophobic characteristic. So, some of purified olfactory receptor proteins do not have normal function and only 10% of whole olfactory receptor proteins were functional [17].

To provide olfactory receptor proteins with the condition for optimal structure, mouse olfactory receptor protein was inserted into

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nanodisc which is a self-assembling nanoscale membrane assembly and functionalized the carbon nanotube resulting in successfully detecting gaseous odorants at the concentration of 2 ppm [19]. As another approach for optimal structure, olfactory nanovesicle is derived from HEK-293 cells expressing the human olfactory receptor and contains signalling molecules as well as olfactory receptors on the lipid membrane. Nanovesicle is circular and formed with 200 nm of average size. In recent study, nanobiosensor was constructed using olfactory nanovesicle introduced to a single-walled carbon nanotube through the charge interaction between negative charges of nanovesicle membrane and positive charges of poly-D lysine coated carbon nanotube, and detected a target odorant with the detection limit of 1 fM concentration and single-carbon-atomic resolution like a human nose system [20]. In this sensing system, the binding of odorant to olfactory receptor is amplified by the signalling within olfactory nanovesicle related to the influx of calcium ions improving the sensitivity of the sensor since the nanovesicle contains calcium signal molecules as well as olfactory receptors. In more recent, nanovesicle-based bioelectronic nose (NvBN) has been applied to lung cancer diagnosis. In this study, nanovesicles containing human olfactory receptors on the membrane were functionalized with single-walled carbon nanotube in order to construct NvBN and the NvBN selectively detected heptanal, which is a lung cancer biomarker, at a concentration of 10 fM and even detected heptanal from human blood plasma without any pretreatment process [21]. The latest update of nanobiosensor using olfactory nanovesicle is the development of nanobiosensor for real-time monitoring of odor compounds in water pollution [22]. Nanovesicles containing two types of olfactory receptors were integrated with carbon nanotubes and geosmin and 2-methylisoborneol were selectively detected at concentrations as low as 10 ng/L at this nanobiosensing system. Thus, olfactory receptor protein showed a great function as a sensing element when it was incorporated into nanovesicle, however olfactory nanovesicle has a low reusability because of the depletion of signalling components and the saturation of calcium ions within it not allowing further calcium influx.

The most promising one of olfactory sensing elements is olfactory receptor peptide. Olfactory receptor peptide is derived from the olfactory receptor protein. Its size is much smaller than whole olfactory receptor protein since it is constructed using 10 to 20 amino acid residues contacting with odorant molecules in the pocket of active binding site of the olfactory receptor protein. Due to these structural characteristics of olfactory receptor peptide, it can be easily handled and also does not need to be incorporated into lipid bilayer membrane for their functional structure. Lim et al. have recently developed a peptide receptor-based bioelectronic nose (PRBN) [23]. The peptide receptor was designed on the basis of odorant binding sites in olfactory receptor and three phenylalanines were additionally attached to the end of a small peptide for the functionalization of single walled-carbon nanotube (SWNT) through π-π stacking. PRBN could determine the quality of seafood as well as selectively detect trimethylamine (TMA), which is produced from the decomposition of seafood, in real-time at concentration as low as 10 fM. Nanobiosensor using the peptide receptor was reusable many times and more stable compared to nanobiosensors using other kinds of olfactory sensing elements. Thus, olfactory receptor peptide is considered as the most promising biomaterial for the robust nanobiosensing system. However, a bottleneck still remains in use of olfactory receptor peptide. 3D structure of olfactory receptor protein should be identified using X-ray crystallography method in order to design olfactory receptor peptide by predicting the odorant binding sites in the main pocket of the receptor protein with high probability. Unfortunately, 3D structures of almost all olfactory receptor proteins have not been identified yet because of the difficulty in purifying and refolding olfactory receptor proteins expressed in various heterologous expression system including *E. coli* system. Therefore analysing 3D structure may be another challenge for the development of nanobiosensor with better performance. Thus, olfactory sensing elements of all biological materials are the most promising sensing elements for the nanobiosensor in that they can mimic the olfactory sense which is the best sensing device shaped by an evolutionary process.

Taken together, it is expected that various olfactory sensing elements derived from whole olfactory receptor proteins have a great potential for the development of supersensitive and superselective nanobiosensors by the integration with various nanomaterials, even though they still have some challenges.

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References

1. Beckera B, Cooper MA (2011) A survey of the 2006-2009 quartz crystal microbalance biosensor literature. J Mol Recognit 24: 754-787.
2. Lange K, Rapp BE, Rapp M (2008) Surface acoustic wave biosensors: a review. Anal Bioanal Chem 391: 1509-1519.
3. Pohanka M, Skladal P (2008) Electrochemical biosensors-principles and applications. J Appl Biomed 6: 57-64.
4. Rich RL, Myszka DG (2000) Advances in surface plasmon resonance biosensor analysis. Curr Opin Biotechnol 11: 54-61.
5. Zhang X, Guo Q, Cui D (2009) Recent advances in nanotechnology applied to biosensors. Sensors 9: 1033-1053.
6. Song HS, Park TH (2011) Integration of biomolecules and nanomaterials: toward highly selective and sensitivity biosensors. Biotechnol J 6: 1310-1316.
7. Lee SH, Sung JH, Park TH (2011) Nanomaterial-based biosensor as an emerging tool for biomedical applications. Ann Biomed Eng 40: 1384-1397.
8. Wang J (2005) Nanomaterial-based electrochemical biosensors. Analyst 130: 421-426.
9. Carrar S, Shumyantseva VV, Archakov AI, Samori B (2008) Screen-printed electrodes based on carbon nanotubes and cytochrome P450scc for highly sensitive cholesterol biosensors. Biosens Bioelectron 24: 148-150.
10. Lee CA, Tsai YC (2009) Preparation of multiwalled carbon nanotube-chitosanalcohol dehydrogenase nanobiocomposite for amperometric detection of ethanol. Sens Actuator B 138: 518-523.
11. Kharitonov AB, Zayats M, Lichtenstein A, Katz E, Willner I (2000) Enzyme monolayer-functionalized field-effect transistors for biosensor applications. Sens Actuator B 70: 222-231.
12. Patolsky F, Timko BP, Yu G, Fang Y, Greytak AB, et al. (2006) Detection, stimulation, and inhibition of neuronal signals with high-density nanowire transistor arrays. Science 313: 100-104.
13. Timko BP, Cohen-Karni T, Yu G, Qing Q, Tian B, et al. (2009) Electrical recording from hearts with flexible nanowire device arrays. Nano Lett 9: 914-918.
14. Hahm JI, Leiber CM (2004) Direct ultrasensitive electrical detection of DNA and DNA sequence variations using nanowire nanosensors. Nano Lett 4: 51-54.
15. Li Z, Chen Y, Li X, Kamins TI, Nauka K, et al. (2004) Sequence-specific label-free DNA sensors based on silicon nanowires. Nano Lett 4: 245-247.
16. Staii C, Chen M, Gelperin A, Johnson AT (2005) DNA- Decorated carbon nanotubes for chemical sensing. Nano Lett 5: 1774-1778.
17. Park SJ, Kwon OS, Lee SH, Song HS, Park TH, et al. (2012) Ultrasensitive flexible graphene based (FET)-type bioelectronic nose. Nano Lett 12: 5082-5090.

18. Kim TH, Lee SH, Lee J, Song HS, Oh EH, et al. (2009) Single-carbon-atomicresolution detection of odorant molecules using a human olfactory receptor-based bioelectronic nose. Adv Mater 21: 91-94.

19. Goldsmith BR, Mitala JJ, Josue J, Castro A, Lerner MB, et al. (2011) Biomimetic chemical sensors using nanoelectronic readout of olfactory receptor proteins. ACS Nano 5: 5408-5416.

20. Jin HJ, Lee SH, Kim TH, Park J, Song HS, et al. (2012) Nanovesicle-based bioelectronic nose platform mimicking human olfactory signal transduction. Biosens Bioelectron 35: 335-341.

21. Lim JH, Park J, Oh EH, Ko HJ, Hong S, et al. (2014) Nanovesicle-based bioelectronic nose for the diagnosis of lung cancer from human blood. Adv Healthc Mater 3: 360-366.

22. Son M, Cho D, Lim JH, Park J, Hong S, et al. (2015) Real-time monitoring of geosmin and 2-methylisoborneol, representative odor compounds in water pollution using bioelectronic nose with human-like performance. Biosens Bioelectron 74: 199-206.

23. Lim JH, Park J, Ahn JH, Jin HJ, Hong S, et al. (2013) A peptide receptor-based bioelectronic nose for the real-time determination of seafood quality. Biosens Bioelectron 39: 244-249.