BioNano Health Guard Research Center

by **Bong Hyun Chung** and **Taejoon Kang**

Introduction

Global frontier program is Korean government representative research program funded by the Ministry of Science, ICT and Future Planning (MSIP). The vision of this program is the development of world-class core technologies and the creation of an economic growth. Global frontier program started from 2010 and currently 10 research centers are onto vigorous research work. BioNano Health Guard Research Center was established as one of the research arms of *Korea Research Institute of Bioscience and Biotechnology* (KRIBB) in 2014. Dr. Bong Hyun Chung is appointed as the director of BioNano Health Guard Research Center (photo above).

For the last decade, we had pandemic occurrences of emerging diseases from new strands of influenza viruses ranging from foot-and-mouth disease to H1N1 influenza. In 2003, world economic loss of severe acute respiratory syndrome was ~50 billion USD. In 2008, Korean economic loss of avian influenza was estimated at 530 million USD. In 2015, middle east respiratory syndrome (MERS) outbreak in Korea resulted in 36 deaths. There are also concerns on super bacteria with resistance to antibiotics. These biohazardous substances are some of the factors that are threats to our society. Early detection, monitoring of biohazardous substances and early diagnosis of the disease are crucial for the health and safety of the population. The BioNano Health Guard Research Center at KRIBB Institute has achieved a significant number of research findings and novel solutions to solve health-threatening diseases that are prevalent in Asia; shown in the next section.

BioNano Health Guard Research Center aims to develop new technologies which are capable to detect new mutant viral and super bacteria strains. It is anticipated that the new developments in BioNano Health Guard will reduce the economic burden from infectious and chronic diseases in the population.

Figure 1. A brief illustration of social impacts from respiratory infectious diseases.

Novel Technologies and Health Solutions by BioNano Health Guard Research Center at KRIBB

1. Development and Validation of a Rapid Immunochromatographic Assay for Detection of Middle East Respiratory Syndrome Coronavirus Antigen in Dromedary Camels

We developed a rapid immunochromatographic assay for the detection of MERS-coronavirus (MERS-CoV) antigen in the nasal swabs of dromedary camels. The assay is based on the detection of MERS-CoV nucleocapsid protein in a short time frame using highly selective monoclonal antibodies at room temperature. The relative sensitivity and specificity of the assay were found to be 93.90% and 100%, respectively. The results suggest the immunochromatographic assay is a useful tool for rapid diagnosis and epidemiological surveillance of MERS-CoV infection in dromedary camels. [1]

2. Massively Parallel and Highly Quantitative Single-Particle Analysis on Interactions between Nanoparticles on Supported Lipid Bilayer

Observation of individual single-nanoparticle reactions provides direct information and insight for many complex chemical, physical, and biological processes, but this has shown to be a challenge with conventional high-resolution imaging techniques. Here, we developed a photo-stable plasmonic nanoparticle-modified supported lipid bilayer (PNP-SLB) platform that allows for massively parallel in situ analysis of the interactions between nanoparticles with single-particle resolution on a two-dimensional (2D) fluidic surface. Each particle-by-particle PNP clustering process was monitored in real time and quantified via analysis of individual particle diffusion trajectories and single-particle-level plasmonic coupling. Importantly, the PNP-SLB-based nanoparticle cluster growth kinetics result was fitted well. As an application example, we performed a DNA detection assay, and the result suggests that our approach has very promising sensitivity and dynamic range (high attomolar to high femtomolar) without optimization, as well as remarkable single-base mismatch discrimination capability. The method shown herein can be readily applied to detect different types of intermolecular and interparticle interactions and, provide convenient tools and new insights for studying dynamic interactions on a highly controllable and analytical platform. [2]

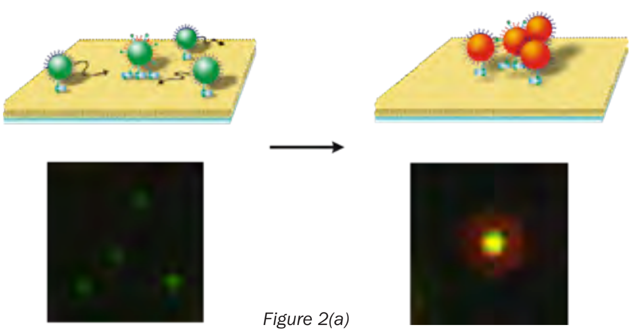

Figure 2(a)

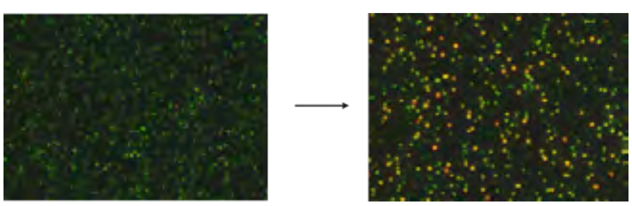

Figure 2(b)

Figure 2 (a) Single-nanoparticle-level in situ parallel imaging and analysis of dynamically tethered nanoparticles on a supported lipid bilayer. (b) Multi-parallel in situ observation and analysis of supported lipid bilayer-tethered plasmonic nanoprobes via dark-field microscopy with single-nanoparticle resolution. (Left) before target DNA hybridization. (Right) after target DNA hybridization. (Adapted with permission from Ref. [2]. Copyright (2014) American Chemical Society)

3. Scalable Nanopillar Arrays with Layer-by-Layer Patterned Overt and Covert Images

Transferring flexible and scalable nanopillar arrays on a variety of unconventional substrates, including fabric, paper, and metals, was achieved by a single-step replication process using UV-curable polymers. Local alteration of the contact angle on the nanopillar arrays by layer-by-layer (LBL) assembly films creates selectively hidden images. Balancing the adhesion and mechanical strength of the curable polymer matrix allowed us to develop a new method of nanopillar arrays production that is scalable and universally adhesive on various substrates. It can be accomplished by using a special polyurethane blend that enables their single-step replication with high fidelity. Moreover, the technique affords the transfer of nanopillar arrays onto a variety of substrates, including fabric, paper, and metals via intermolecular bonds. The nanopillar arrays maintains its structure, flexibility, and wettability even after rubbing with various materials, including a finger, a brush, and fabrics. nanopillar arrays is also demonstrated to be a suitable structure for inkjet nano-patterning and replication systems using the property of LBL films to form thin conformal coatings. [3]

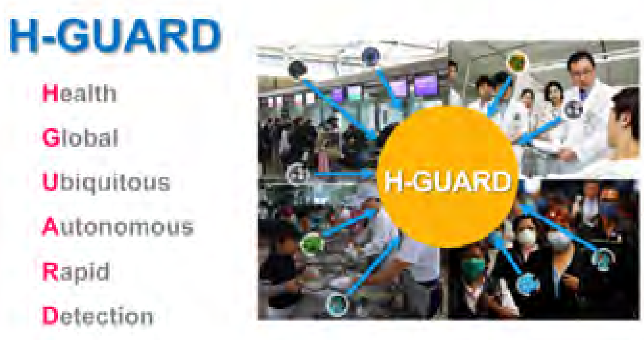

Figure 3. H-GUARD

New Directions for BioNano Health Guard Research Center: H-GUARD

The goal of BioNano Health Guard Research Center is to develop Health-Global Ubiquitous Autonomous Rapid Detection (H-GUARD) system (Figure 3) and world-class platform technologies for the detection and monitoring of biohazardous substances including new and mutant viruses, super bacteria, etc.

H-GUARD is a real-time monitoring system of biohazardous substances (virus, super bacteria, etc.) with sample collection, processing, detection, and signal transfer modules. The following Figure 4 shows the concept for H-GUARD that we would like to develop. We intend to develop complete system that can collect and separate samples, and detect biohazardous substances. Only from the convergence in research, H-GUARD will be successfully developed.

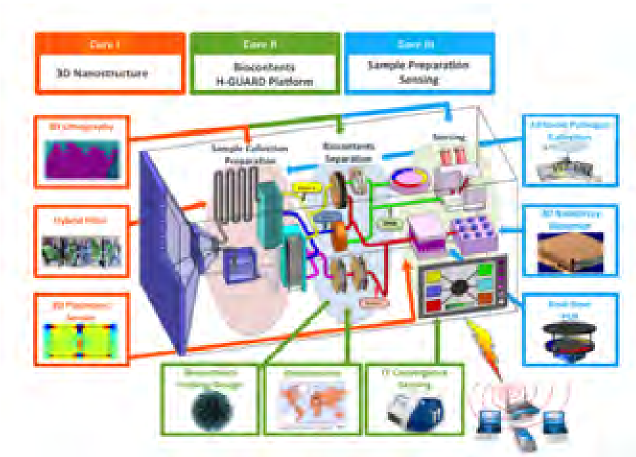

Figure 4. An illustration of H-GUARD platform in three cores (Core I to III).

Core Research Projects

The core research projects of BioNano Health Guard Research Center are as follows:

- [Core I] Development of 3D nano-micro hybrid structures which enable to detect biohazardous substances with increased speed and sensitivity
- [Core II] Prediction of virus mutations and development of technologies for rapid detection/diagnosis of super bacteria
- [Core III] Development of integrated H-GUARD system which enables rapid field detection of biohazardous substances

In core project I, we are developing the lithography technologies for 3D nano-micro hybrid structures and mass-production technology for nano-bio devices. We are also developing and optimizing the organic-inorganic nano-hybrid structured probes and materials for lysis of captured virus and multiplexed detection of target DNA at a molecular level in a single platform. Moreover, commercial applications of single biomolecule detection method based on nanopolyhedron assembly still require further research work.

In core project II, we are developing the technologies for acquisition and application of bio-contents for H-GUARD. The highly sensitive- and selective-antigen receptor is undergoing developments in this project. We are trying to develop the diagnostic techniques for multi-drug resistant bacteria, viral recombination prediction and validation technique using bioinformatics.

In core project III, we are developing an on-site diagnosis system for the real-time monitoring of pathogens by combining pre-treatment, sensors, and polymerase chain reaction systems. For the development of pre-treatment technique, we are trying to develop a pre-treatment technique that can capture, separate, and concentrate harmful pathogens in the air. We will integrate this pre-treatment system with 3D nano-structure based biosensors to develop diagnosis system for the real-time monitoring of pathogens. Figures 5(a) to 5(d) below illustrate the three core research projects of BioNano Health Guard Research Center.

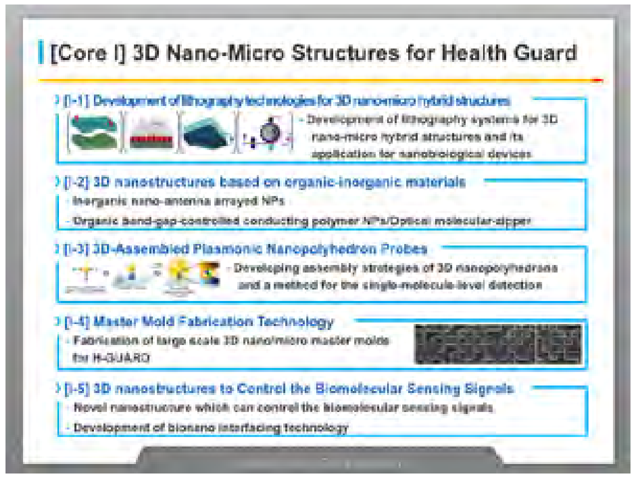

Figure 5(a). Description of Core Project I

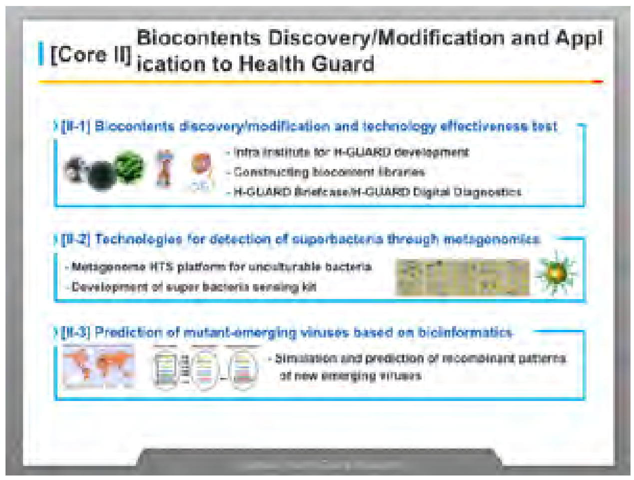

Figure 5(b). Descriptions of Core Project II

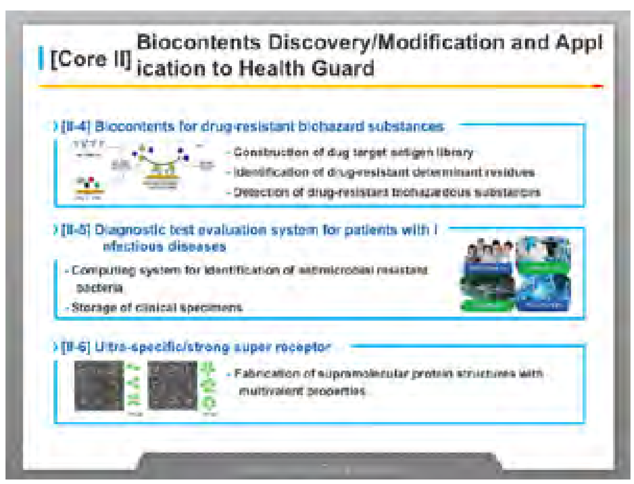

Figure 5(c). Descriptions of Core Project II

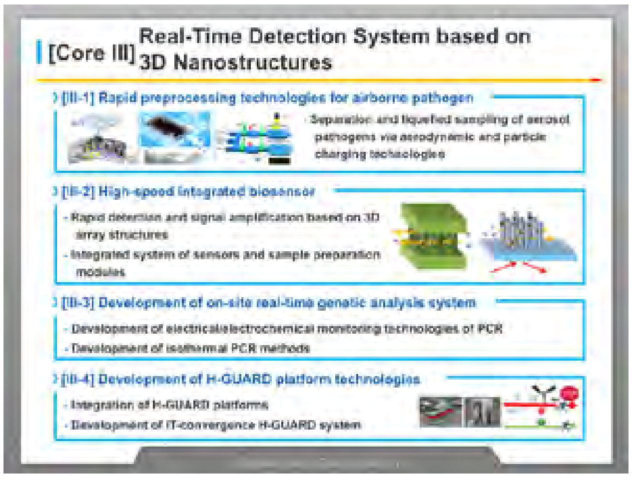

Figure 5(d). Descriptions of Core Project III

Global Network

We are cooperating with various organizations over the world to practice our research successfully. We believe they can offer us great help on H-GUARD system development. We also hope to proceed our research further and on a global scale by expanding out networks to more international organizations.

Figure 6. Global Network of BioNano Health Guard Research Center.

Future Society with H-GUARD

H-GUARD system we intend on developing will be applied to and made into many different forms and they will be installed in every possible correlating areas. H-GUARD can be utilized in various areas such as monitoring in public building like airport and subway, it can be used for early diagnosis of infection diseases, and in hospitals. We can also use H-GUARD as on-site monitoring method and it can also use in transportation systems for rapid detection of biohazardous substances. This will bring us life-changing experiences with significant improvement on our lifestyle in the future. We strive to develop H-GUARD system and we firmly believe in success of our researches.

Figure 7. Functions of H-GUARD

References

[1] Song, Daesub, et al. "Development and Validation of a Rapid Immunochromatographic Assay for Detection of Middle East Respiratory Syndrome Coronavirus Antigen in Dromedary Camels." *Journal of clinical microbiology* 53.4 (2015): 1178-1182.

[2] Lee, Young Kwang, et al. "Massively Parallel and Highly Quantitative Single-Particle Analysis on Interactions between Nanoparticles on Supported Lipid Bilayer." *Journal of the American Chemical Society* 136.10 (2014): 4081-4088.

[3] Lee, Kyoung G., et al. "Scalable Nanopillar Arrays with Layer-by-Layer Patterned Overt and Covert Images." *Advanced Materials* 26.35 (2014): 6119-6124.

About the Authors

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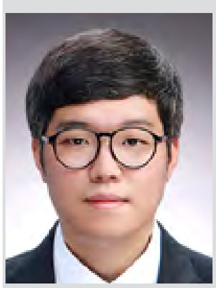

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