Fusion of Biotechnology and Nanotechnology: What It Brings

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Nanotechnology breaking fresh ground in medicine

To advance the creation of new technologies through a combination of nanotechnology and biotechnology, we have undertaken research on the basic technologies shown in Figure 1 (single-molecule DNA analysis, diagnostic nano-bio devices, and single-cell diagnosis), and the combination of them. This research provides a foundation for the practical application of new systems that enable us to comprehend physical conditions, and diagnose diseases based on individual genetic information. Mobile or wearable devices for evaluating an individual’s condition at home are the fruition of these research efforts. In addition, our recent invention to fuse semiconductor nanoparticles and biomolecules has attracted attention. This innovation has produced encouraging results and provided a new perspective on nanotechnology. It may lead to “super” early diagnosis, as well as new cancer treatments. In the future, these research efforts will contribute to the development of the predictive diagnostic technology, facilitate the transformation of treatment-oriented health care into a prevention-oriented one, and realize an active aging society.

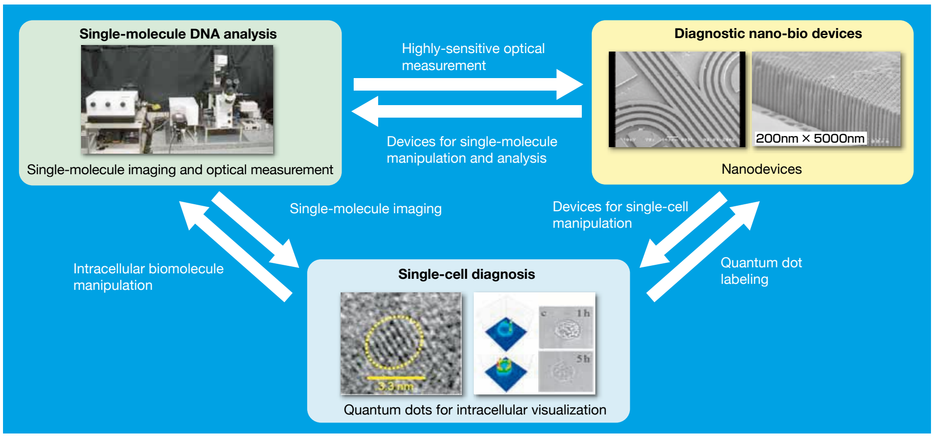

Figure 1 : Research objectives to develop the predictive diagnostic technology
New technologies for predictive health diagnosis will be developed by combining three basic technologies cultivated at the Health Technology Research Center.

Development of a genetic diagnostic device requiring only a fraction of the blood

Using our semiconductor technology, and in collaboration with Kyoto University and Starlite Co. Ltd., we have developed a technology for producing plastic chips for genetic diagnosis at a lower cost. An electromicrograph of the chip is shown in Figure 2. This extremely small chip possesses 10 microchannels, with a width and depth of 50 μm, which allows the simultaneous analyses of blood samples from 10 individuals. We have succeeded in placing 10 channels within a 1-mm width. By expanding this technology, one chip with a size of several centimeters will be sufficient to analyze the genes of more than 1,000 individuals. Moreover, a highly sensitive device that can rapidly analyze genetic information on chips and make diagnosis has been contrived.

Figure 2 illustrates the genetic diagnosis of lung cancer. Conventional genetic tests require 1-2 days to obtain the results. Our device has successfully shortened the diagnostic time, requiring approximately 10-20 minutes. In addition, the amount of blood necessary for testing has been reduced to 1/100 or less. Our technologies will also lower the cost of genetic testing to 1/10-1/100 or less, relative to previous tools. These improvements are believed to reduce the burden on patients. The system is roughly the size of a desktop computer at present, but will be downsized to the size of a laptop computer,

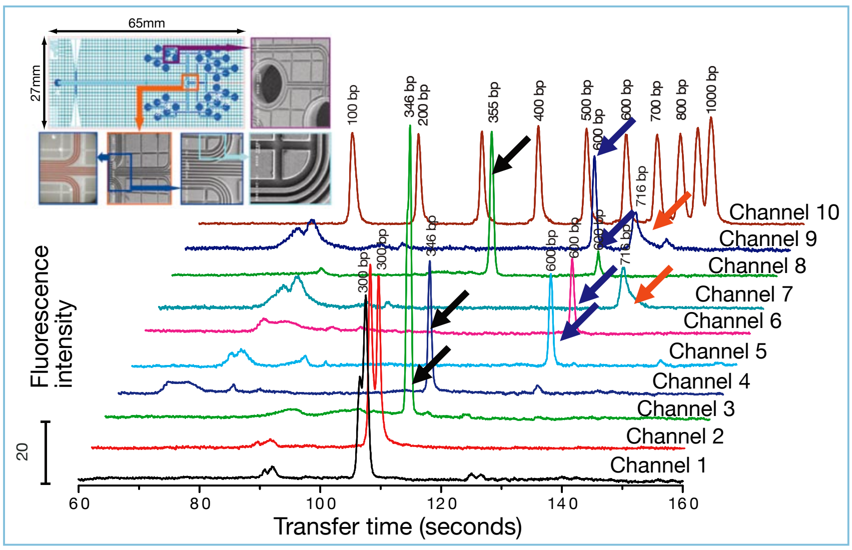

Figure 2 : Development of a genetic diagnostic device and its application to lung cancer
We have collaborated with a university and a private company to develop a technology for producing diagnostic biodevices at low cost, and with a university hospital to apply the resulting device to lung cancer. Blue arrows indicate normal genes, while red and black arrows indicate potentially pathogenic genes of altered size.

or even to a mobile or wearable size.

Development of single-cell diagnostic technology that realizes "super" early diagnosis

A single-cell diagnostic device using nanotechnology and its application to cancer diagnosis are illustrated in Figure 3. This device enables us to manipulate single cells freely, and perform highly sensitive analyses for trace quantities of intracellular genes and proteins. Additionally, a new reagent named as quantum dots can be used for cell imaging instead of conventional organic fluorescent dyes or fluorescent proteins. Quantum dots are an inorganic semiconductor material with a diameter of 2-5 nm. When irradiated with ultraviolet rays, they emit fluorescent light ranging from violet to red, according to diameters. Although quantum dot performance is excellent, their application to biotechnology had been limited because they are not compatible with proteins and other biomolecules. To overcome this problem, we have developed a new technology to fuse quantum dots with proteins. Using this technology, quantum dots can be fused to lectin molecules that specifically recognize cancer cells, or to antibodies that recognize specific proteins. These fusion quantum dots, together with single-cell diagnostic chips, are employed in the cytopathological diagnosis of cancer. As shown in Figure 3, the addition of quantum dots to cancer cells followed by irradiation with ultraviolet rays produces a bright green fluorescence resulting from the binding of quantum dots to the surface of cancer cells. In contrast, no fluorescence was observed in normal cells, due to the absence of an interaction between the quantum dots and normal cells. The presence of disease is revealed using this technology, which may detect cell populations as small as a few to several dozens of cancer cells. Cutting-edge diagnostic imaging systems, including magnetic resonance imaging and positron emission tomography are costly and do not detect cancer tissues smaller than 1 millimeter in size. Considering the above, the improvement of the sensitivity and accuracy of quantum-dot technology will lead to "super" early diagnosis and more effective cancer treatment.

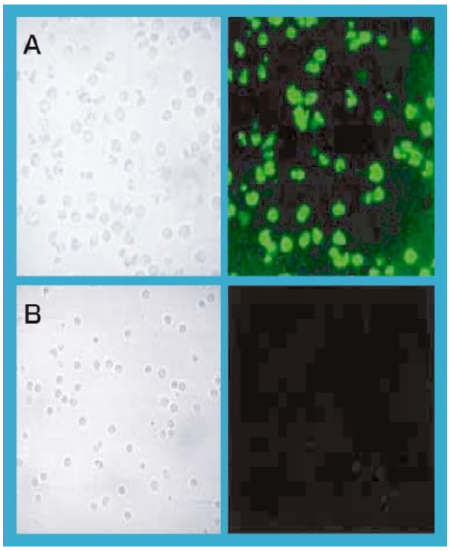

Figure 3 : Development of single-cell imaging and its application to cancer cell detection
Cancer cells were selectively detected by integrating a nanodevice technology and single-cell imaging. Cancer cells, but not normal cells, emitted fluorescence.
(A) A mixture of cancer cells and normal cells. Dozens of cancer cells were detected in groups. (B) Normal cells. No signal was detected.

Novel applications of nanotechnology to medicine

The devices and quantum dots mentioned above, as well as other technologies utilizing nanostructures can introduce new physical phenomena into the field of biotechnology, and allow us to invent unimaginable revolutionary technologies. For example, very small amounts of disease-related proteins present in cells will be detected using different types of quantum dots. Though fluorescence diminishes when conventional fluorescent reagents are used in combination, such an effect is not observed in quantum dots, which facilitate the highly sensitive detection of target proteins.

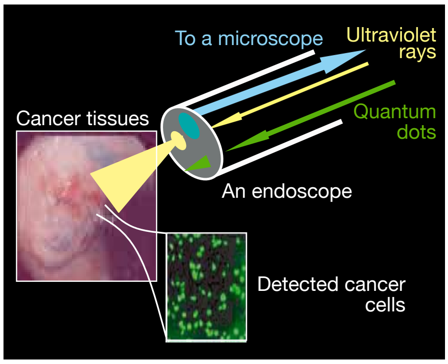

Figure 4 : Invention of a quantum dot-based technology in the biomedical field
Our aim is to develop modalities for the simultaneous diagnosis and treatment of cancer.

Furthermore, it has been elucidated that approximately 60 minutes of ultraviolet irradiation induces apoptosis in cancer cells, but not in normal cells, following the diagnostic test described above. Quantum dots absorb ultraviolet energy, a portion of which reacts with oxygen to generate noxious oxygen species, including the radical oxygen that causes apoptosis in cancer cells. Such an event may occur only when nanomaterials are used. Combining these technologies with an endoscopic approach, not only "super" early diagnosis, but also the treatment of detected cancer cells by inducing apoptosis will become practical. The development of technologies that integrate diagnosis with treatment is not fantasy (Figure 4).

Future perspectives

The application of nanodevices and quantum dots to the biomedical field has just begun. Further research will lead to the development of technologies that make the early diagnosis of diverse diseases possible. The fusion of nanotechnology and biotechnology will realize health care that has been considered impossible with conventional diagnostic tools and treatment measures.