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17<sup>th</sup> July 2002  
Hitachi, Ltd.

### Development of a compact, inexpensive and highly sensitive DNA analysis system for SNP typing

- Opening the way for “tailor-made medicine” -

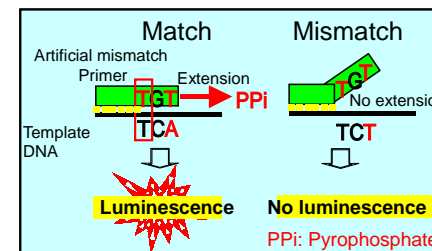
Hitachi Ltd., Central Research Laboratory (General Manager; Dr. Toshikazu NISHINO) announced today that it has developed a compact, inexpensive and highly sensitive DNA analysis system for typing of single nucleotide polymorphisms (SNPs); SNPs are thought to affect susceptibility to disease and receptivity to drugs in individuals. SNP typing can be carried out within tens of seconds easily by adding a reagent to the sample solution. As the developed system is compact and portable, it can be used in various locations such as laboratories, hospitals, etc. The way for “tailor-made medicine”, which supports individualized healthcare such as therapy and medical prescriptions tailored to individual constitutions, will be opened by SNP databases in the future. This work was performed as a part of a research and development project of the Industrial Science and Technology Program supported by New Energy and Industrial Technology Development Organization in Japan (NEDO).

The human genome project to clarify the human genome sequence has been successfully carried out. The next stage in the field of genomic research is to understand gene functions and to use the genome information in diagnosis and medical treatment. In the case of drug treatment, the performance of the drug, such as the effect or side effect on patients is differentiated by differences in each individual constitution and the disease. The differences are controlled by SNPs in individuals. In the field of tailor-made medicine, the most effective therapy will be realized by SNP typing. For example, optimum medical treatment could be realized if the detection and analysis of an allergic disease and disease susceptibility could be measured by SNP typing easily and rapidly on the medical treatment site. In the human genome project, as it was necessary to read long DNA sequences to clarify all of the human genome, measurements were performed at special facilities such as analytical centers, with complex and time-consuming procedures by large sophisticated expensive instruments. Tailor-made medicine would require low-cost and rapid DNA analysis based on SNP typing of individuals. Further, a portable and compact system would be more suitable for use at various locations and in the field. Thus the methods used in the human genome project would not be suitable for tailor-made medicine.

Hitachi has developed new and simple SNP typing method, and a compact and highly sensitive DNA analysis system using this method. The technologies developed are as follows.  
(1) Easy and inexpensive SNP typing by bioluminescence assay: SNP typing is carried out as

follows. Inorganic pyrophosphates (PPi) are released and bioluminescence caused when double-stranded DNA (*i.e.* the primer extends by nucleotide incorporation) formation takes place by adding a reagent to the sample solution. The bioluminescence is detected with a high sensitivity optical sensor. Thus, SNP typing can be easily carried out within tens of seconds by simply adding the reagent to the sample solution on the medical treatment site.

- (2) High sensitivity and high accuracy SNP typing: Primers having an artificial mismatch base at the 3rd position from the 3'-terminus are used to prevent the false positive signal by a primer mismatched to a target at the 3'-terminus. The modified primers work very well for SNP typing. As a result, the background noise by the mismatch extension was greatly decreased, and highly sensitive detection of two orders or more compared with previous methods, was achieved (*cf.* figure below).
- (3) Development of a compact and inexpensive DNA analysis system: As this system utilizes bioluminescence detection, it does not require the expensive laser used in the fluorescence detection method. Further, a compact DNA analysis system was realized by incorporating micro-fluidic technologies, that enable solutions of less than 0.1  $\mu$ L (1/10,000,000 liter) to be easily handled, and integrated optical sensor technologies, that enable the luminescence from the reaction to be detected with the efficiency of 7%.



#### Principle of DNA analysis method by bioluminescence detection

As this system is portable and easily operated, it can be widely used not only in the medical field but also in food and environmental analysis. By using this system, simple and low cost DNA analysis of individuals can be performed. This system will help to clarify the difference in the genetic variations influencing the susceptibility to disease, and effects or side-effects of drugs in individuals. This system can thus contribute to achieving “tailor-made medicine”, supporting individualized healthcare for a healthier and safer life in the future.

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