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To whom it may concern:

Announcement of the Adoption of  
*the Development of the Genome Biomarker Probing Device for  
Cellular Diagnostics*  
by the New Energy and Industry Technology Development Organization (NEDO)  
as a Subsidized Project

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We are pleased to announce that the New Energy and Industry Technology Development Organization (NEDO) has adopted the *Development of the Genome Biomarker Probing Device for Cell Diagnostics*, proposed by PSS, as part of its Second Series of Industrial Technology Research and Development Projects for 2005.

PSS has been providing unique automated systems in various fields of bioscience. To date, we have sold over 3,000 fully automated DNA extractors, which feature internationally patented Magtration<sup>®</sup> technology, through our worldwide sales network including OEM supply.

The *Genome Biomarker* project can be accomplished by combining all of our accumulated technology for automated systems, with a unique comprehensive analysis methodology for genomic DNA methylation, called MONIC analysis.

In cooperation with the inventor of MONIC analysis, Dr. Naomi Yamakawa of the Tokyo Metropolitan Institute of Gerontology, in this project we aim to develop a DNA biomarker probing device that uses a typing technology for Genomic DNA methylation. This will enable the construction of a genome-diagnostic database, and hence facilitate early detection of cancer and quality assessment of future cell transplants.

Two-thirds of the estimated project expenses will be provided by NEDO subsidies, and so the project will have minimal effect on our finances.

The details of the project are as follows:

- Outline of the subsidized project

Although each cell making up the human body carries an identical genetic background, the methylation patterns of cytosines in genomic DNA vary, and so the cells can express diversity. In transformed cells, for example, they exhibit an aberrant methylation pattern of cytosine residues which is not observed in normal cells. Therefore, these patterns have attracted attention in recent years as a biomarker for early detection of cancer.

Thus, we aim to develop a DNA biomarker probing device utilizing the methylation typing technology for genomic DNA, and to construct a genome-diagnostic database, which will facilitate early detection of cancer and quality assessment of future cell transplants.

- Background and objective of development

As the elderly population continues to grow in Japan, the medical expenses paid by the government are rising exponentially. To reduce such medical expenses, it is crucial to extend the length of healthy life, which means improving the recovery rate from diseases through early detection and developing regenerative medicine as a basic remedy for illness. The mortality rate by cancer in Japan is worsening contrary to other advanced nations, mainly because of the low rate in Japan of detecting cancer at an early stage.

The DNA methylation analysis, which is one of the key technologies of this project, is expected to be a potent weapon for cancer diagnoses, identification of cell types, and also for cellular diagnostics. Therefore, the construction of a fully automated analysis device will ultimately help reduce medical expenses.

- Target areas for development

The major areas targeted in this project are *early detection of cancer*, and *safety evaluation of cells* in the field of cell transplants.

- (1) Early detection and diagnosis of cancer

Most of the somatic cells in the human body are constantly renewed. Consequently, DNA from dead cells can be found in the blood (or more accurately, in the serum). When cancer grows in the body, DNA is also released, flows out of the cancer cells, and then circulates in the blood stream. Since DNA molecules originating from solid tumor exhibit a characteristic methylation pattern, analysis of the patterns of circulating DNA in serum can yield information on whether it is derived from normal tissue or tumor. Furthermore, it may be

possible to predict the primary tumor location because the characteristics of the originating normal tissue are partially retained. One of the goals of this project is to search for markers valid in the diagnosis of cancer by utilizing this mechanism.

It should be emphasized that the DNA biomarkers in the blood can be easily amplified by conventional PCR techniques, which is a major advantage for DNA processing. Therefore, the DNA in blood is a good candidate as a diagnostic biomarker with higher sensitivity. Moreover, a similar detection system can be applied to all types of cancer, even if they do not express valid protein markers for early detection.

(2) Safety evaluation of cells in regenerative medicine

In the realm of regenerative medicine, it is essential to establish a method for *evaluating the safety of transplanting cells*, which identifies cell types and examines the risk of post-transplant transformation. Moreover, since the diversity of genomic DNA methylation patterns produces different cell types, analysis of those will also enable accurate identification of the cell type produced *in vitro*.

(3) Screening candidates for administration of anti-cancer drugs

In recent years, anti-cancer drugs targeting specific molecules have been introduced, but serious side effects of such drugs have also been reported. Therefore, the safe administration of these drugs has become a critical issue. Thanks to comprehensive analyses of DNA methylation patterns, it would be possible to make even more detailed classifications of cancer types. In other words, this will enable investigation of what types of treatment were valid in the past for specific types of cancer, thereby identifying beforehand which patients should receive specific anti-cancer medications. This in turn would significantly reduce the risk of patients aimlessly undergoing various treatments without hope of favorable effects.

(Reference)

(MONIC analysis)

MONIC is an acronym for *modified nucleotides immunocapturing method*.

MONIC analysis is a new method for analyzing DNA methylation, which enables the comprehensive methylation analysis of genomic DNA. The Japan Science and Technology Agency and Tokyo Metropolitan Foundation for Research on Aging and Promotion of Human Welfare have filed a patent application for the technique, which is characterized by far lower cost of analysis per gene and faster analysis of a single assay compared to competing technologies.