

Basic Stage

(Fiscal Year 2004-2006)

# Foot of Mt. Fuji Area

Development of Diagnostic Agents and Diagnosis Equipments for Cancers by Applying Genomics and Proteomics

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**Project Promotion**

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**Core Research Organizations**

Research Organization of Information and Systems - National Institute of Genetics, Shizuoka Cancer Center, Tokai University School of High-Technology for Human Welfare, Numazu National College of Technology

**Major Participating Research Organizations**

Industry... KYOWA MEDEX Co., Ltd., ABLE Corporation Mishima Branch, BL Co., Ltd., Yanaiara Institute Inc., Effector Cell Institute, Inc.  
Academia... Research Organization of Information and Systems - National Institute of Genetics, Shizuoka Cancer Center, Tokai University School of High-Technology for Human Welfare, Numazu National College of Technology, Tokyo Institute of Technology  
Government... Numazu Industrial Research Institute of Shizuoka Prefecture, Fuji Industrial Research Institute of Shizuoka Prefecture

**Aim of research and development**

In Mt. Fuji area, there are a lot of laboratories and factories of the enterprise related to biotechnology including the medical manufacture enterprise, and the medical treatment-allied industry is one of the key industries. Based on these situations, Shizuoka Prefecture settled on "Pharma-Valley Center Project", established basic strategies for promotion of an up-to-date research and development, improvement of quality of medical treatments and creation of new industries and activation of pre-existing industries, and promoted creation and accumulation of health-related industries in cooperation and collaboration with industries, institutes and universities. In this business, diagnostic reagents and equipments to detect the early stage cancers will be developed by establishing basic techniques effective for cancer diagnostics through genetic approaches and also by searching for tumor markers and developing diagnostic systems for cancers through proteomics approaches. In the future, this business aims the formation of a large accumulation hub of medical treatment-allied industries by creating bio-medical venture companies based on proper diagnostic techniques for detection of the early stage cancers.

**Contents of research**

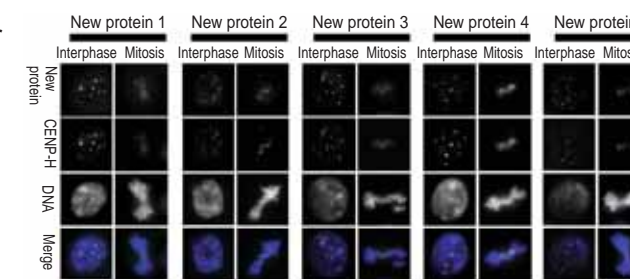
1. Development of a basic technology for cancer diagnostics by applying genomics  
A basic technology of the cancer diagnostics is developed through the application of the visualization of transcription-coupled negative DNA supercoiling and the mutation identification technique of centromeric proteins that play an important role in the chromosome segregation, and through clarifying the specific phenomena caused by cancer cells.
2. Tumor marker searches based on application of proteomics technique and development of cancer diagnostic system.  
Construction of specific diagnosis system for cancer using analytical data such as cancer specific structure changes and expression levels of genes and proteins, CTL activity arisen by cancer antigen peptides, metabolite of porphyrin in cancer cells. These diagnosis systems were applied for tumor maker searches, which are effective for development of the diagnosis medicines and equipment.

**The main study results**

1. Development of cancer diagnostic techniques based on the higher order structure of chromatin DNA.  
Focusing on the potent transcription activities of the genome DNA in cancer cells, we have succeeded in detection of cancer cells by visualization of transcription-coupled negative supercoiling of DNA. Using the same technique, we have also demonstrated the importance of two proteins in the boundary function of chromatin domains

2. Chromosome segregation studies, which lead cancer diagnosis and therapy.

We identified new centromere proteins, which are essential for chromosome segregation and analyzed these proteins. We found that these proteins are important during centromere assembly and that these are highly expressed in cancer cells. Furthermore, we developed a method by which we measured a centromere activity. Using this method we identified 2 chemical compound that cause mislocalization of CENP-H.



Centromere localization of proteins, which associate with CENP-H and CENP-I. As these proteins colocalize with CENP-H throughout the cell cycle, we confirm that these are centromere proteins

3. Development of cell-based cancer immunotherapy using novel tumor antigens:

Utilizing the 2-dimensional differential gel electrophoresis (2D-DIGE) method, the 13 proteins specific for a highly metastatic gastric cancer cell line were identified. Additionally, novel T cell receptor (TCR) gene specific for melanoma-associated antigen (MART1) was determined using TCR genetic analysis of melanoma-specific CTL line.

4. Development of cancer diagnosis system targeted to peptide, protein and genes

Among the protein secreted from cultured cancer cell lines, marker candidate was selected. It also succeeded to identify two proteins; one is from human small cell lung carcinoma cell lines, and the other is from highly metastatic human stomach cancer cell lines respectively.

