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## Working Party on Biotechnology

# ANALYTICAL PAPER: FORMULATION OF THE BASIC GROUNDS FOR HEALTH INDUSTRY USING BIOMARKER DATABASE

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*This analytical paper was submitted for discussion at the workshop on Policy Issues in the Development and Use of Biomarkers in Health held on 6-7 October 2008 in Hinxton, United Kingdom. It is submitted for information to the WPB.*

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## NOTE BY THE SECRETARIAT

This analytical paper was submitted as background material for discussion at the expert workshop organised by the Biotechnology Division on "Policy Issues in the Development and Use of Biomarkers in Health" held in Hinxton, United Kingdom on 6-7 October, 2008. This workshop contributes to the fulfillment of Output Result 5 of the 2007-2008 PWB entitled "Analytical and policy reports on the impact of molecular markers and targeted therapies on Biomedicine".

This analytical paper, written by Dr. Junko Takahashi and Dr. Noboru Yumoto from AIST Japan, describes an example of a biomarker database currently under development in Japan.

This analytical paper, along with others developed for the Biomarker Workshop, will be used as input for the Policy Report entitled "Policy issues in the Development and Use of Biomarkers in Health" that will be submitted to WPB in early 2009.

Delegates to the Working Party on Biotechnology are invited to:

- **Note** the analytical paper.

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## I. Introduction

### Present state of life-science database in Japan

A promotion strategy for the life science research formulated by the Japan's Council for Science and Technology Policy aims to develop the world's highest infrastructure in the field of the Life Sciences in Japan as a part of the Focused Strategic Science and Technology Plan. The strategy is based on the Third-Stage Basic Plan for Science and Technology (2006-2011) approved by the Cabinet on March 28, 2006.

Under the present circumstances, the Integrated Database Project has been conducted by the Ministry of Education, Culture, Sports, Science and Technology. The Biomedicinal Information Research Center and the Research Center for Medical Glycoscience in our institute joined the project as a full and a supplementary member, respectively. One of the database open to the public is "Biomarker candidates for clinical omics and nutrigenomics"(http://omicspace.riken.jp/Biomarker/) developed by RIKEN, Japan. This database comprises a part of the PosMed (Positional Medline), a powerful web search site which deductively infers the relation between genes and their functions based on the existing expertise. Specifically, it is a powerful inference tool to relate the user-specified biomarker candidates to any functional keywords by connecting pieces of information appeared in multiple medical documents as Medline, OMIM, and PPIs.

### Features of biomarker data

The use of biomarkers will help refining diagnosis, prognosis, disease staging, disease extent, drug mechanism, effectiveness and toxicity. By their components, biomarkers may be classified into DNA, RNA, proteins, amino-acid sequence, sugars, lipids, and other physical quantities. By data type to be handled, they are classified into measurement data, annotation, documents, and images.

Thus, the biomarkers are associated with a multitude of pertinent information, unlike data on genes, proteins, or sugars alone. In order to describe these information and register in the database, a novel aggregating description method should be devised, a feature which is not yet incorporated in the RIKEN database possibly because it is an early stage of the construction of the life information database.

### Prospect of future healthcare system

Common view of the future is the increment of the longevity during which we will be able to work in good health and this will increase the social capital. In addition, this will make it possible to reduce medical expenses by preventing many cases of serious diseases and by improving the quality of life (QOL) even when ill.

We consider that the practical use of biomarkers will help personalized medicine available and serve as an essential part in preventive medicine. Then a few questions may arise; can we integrate the preventive medicine into the present healthcare system?; can the biomarkers be used for diagnosis at the preclinical stage?

To answer the above questions, our research center recently is preparing a shared platform for evidence based, knowledge sharing biomarker data, with a commitment to promotion of health industry through R&D in life sciences.

## II. Goals of biomarker database

The goal of our project is to develop the health monitoring biomarkers and present possible use of the health monitoring biomarkers in health industry, particularly in the scene of preventive medicine.

A comparison of the cost of "illness and treatment" shows that the cost of a quality lifestyle is justified by the results. Prediction and prevention of P4 (predictive, preventive, personalized, and participatory healthcare) are considered to be economically effective methods on the whole.

On the premise of expanding preventive treatment, the number of latent diabetes suffers is 7.4 million people and those at risk of diabetes number 8.8 million people (2002, Japan) while the number of people being treated is 2.5 million (2005, Japan). Conducting examinations will increase the opportunities to receive the necessary treatment, which may increase the cost of medical treatment. However, we will be able to provide those who stand at the border between diseased and non-diseased states with accurate healthcare information. This will also allow them to choose appropriate treatments for leading healthier lives at lower cost. On the other hand, medical care system may also be prompted to change in order to implement the P4 healthcare systems.

Our institute is committed to promotion of a health industry through R&D in life sciences, especially in health monitoring biomarkers as one of key technologies. The health monitoring biomarker of our interest consists of 1) a new set of non-specific biomarkers to be listed in health checks, 2) indicators of prevalence risk to a specific disease, 3) predictors of the onset of a disease, and 4) biomarkers indicating fatigue and stresses. Application of each health monitoring biomarker will differ depending on its delivery process. We need to establish a function to increase the effectiveness of the biomarkers and to translate them into industrial use and to make a consensus among stakeholders for its effectiveness while searching for novel biomarkers. Also, an optimal form of health industry to come should be identified and proposed based on the international differences and ethnic backgrounds.

More specifically, we need to define valid biomarkers applicable to the borderline between diseased and non-diseased states. To date, existing valid biomarkers have been approved with a consensus of experts through trials and errors for many years, together with accumulated medical and scientific evidence. However, establishment of the health monitoring biomarkers will require revision of their development process. To achieve our goals, we need to provide a new biomarker database to serve as a common ground for building a consensus to validate and qualify the potential health monitoring biomarkers still in research phase.

## III. Difficulties and challenges

Existing biomarkers available today are mainly used for choice of treatment, estimation of treatment effectiveness, and measurement of recurrence and prognostic implication. In this sense, our concept of advanced health monitoring biomarkers opens a new family. Disease biomarkers include diagnosis, prognosis, disease staging, and disease extent, while drug-discovery biomarkers include understanding of drug mechanism and evaluation of drug effectiveness and toxicity. Health monitoring biomarkers include advanced health checks, prevalence risk, prediction of the onset of a disease, and fatigue or stresses. Before

practical use, we expect several difficulties and challenges to overcome in the processes of selection, validation, qualification, and finally marketing such new biomarkers.

1. Selection of precise health definitions and predictions

2. Selection of high-precision, effective biomarkers is desired.

3. Institutional problems for validation and qualification

Although a multitude of potential novel biomarkers have been proposed, validation, qualification, and authentication have not been performed appropriately. For the health monitoring biomarkers, in addition to the research itself, methods of validation, qualification, and authentication should be simultaneously devised to improve their effectiveness.

4. Marketing

◇ Existing biomarkers

*Disease biomarker*

- diagnosis
- prognosis
- disease staging
- disease extent

*Drug-discovery biomarker*

- drug mechanism
- drug effectiveness
- toxicity

◇ Biomarkers to be developed

*Health monitoring biomarker*

- advanced health checks
- prevalence risk
- prediction of the onset of a disease
- fatigue, stresses

During the development of health monitoring biomarkers, we should define their purposes and applications, and estimate economic outcomes. Their introduction process should be also examined to gain a consensus between stakeholders.

## IV. Conclusion

R&D of disease biomarkers today mainly focuses on diagnosis in clinical practice, measurement of disease stage, and prognosis, while that of drug-discovery biomarkers concentrates on evaluation of efficacy in drug discovery, targeting, surrogate end point and toxicity assessment. In particular, biomarkers for early diagnosis of lethal diseases such as cancer and for reduction of drug-discovery cost have been actively pursued.

On the other hand, R&D of the proposed health monitoring biomarkers is still at its developing stage. Various necessary processes should be devised before these biomarkers are used in practice.

It is expected that the development of health monitoring biomarkers will help implementing personalized medicines, play a critical role in preventive medicine, and significantly contribute to the installation of P4 medicine. However, active involvement of public sector may be recommended to support their development in early stages while scientifically and institutionally inexperienced.

Without expansion of health industry, P4 medicine may not be self-sustaining by itself. Each necessary process should be executed in systematic and coordinated way based on common standards, without leaving entire decisions to individual participants.

As a first step, we consider that it is useful to provide an evidence-based, knowledge-sharing biomarker database which serves as a foundation to increase the effectiveness of the health monitoring biomarkers.