## [Cover]

## The Center of Healthy Aging Innovation

Development of an innovative strategy for disease prediction and prevention by combining neuroscience research and analysis of "big health" data

## [P.1]

Our dream today: common sense after a decade. Creating a whole new future.

In November 2013, the Ministry of Education, Culture, Sports, Science and Technology (MEXT) adopted the theme proposed by Hirosaki University entitled "Development of an innovative strategy for disease prediction and prevention", and selected Hirosaki University as one of 12 Innovation Centers in Japan. It is truly a great honor to Aomori Prefecture, Hirosaki University and the participating companies. I was elated when I first heard the news.

"COI STREAM" (<u>Center of Innovation S&T</u> based <u>Radical Innovation and</u> <u>Entrepreneurship Program</u>) is a program designed to imagine and achieve an "Ideal society after a decade" through innovation, by implementing a new method (including novel method of disease prediction and prevention) established from backcasting research.

A goal of our COI program is to propose, verify, and implement a new method for prediction and prevention of diseases, such as dementia and stroke, by analyzing the big data obtained from health examinations that Hirosaki City has been conducting over the past 9 years. The analysis makes it possible to detect dementia or stroke early. Beyond our goal awaits the realization of a healthy aging society and Aomori Prefecture redeeming itself from being dubbed "the shortest-life prefecture", which is the ideal society we have been imagining for a decade.

There are many age-related diseases, ranging from cancers to cardiovascular disease, and among them our main target is dementia. This is because in a country like Japan, where both men and women live an average of 80 years, the national focus is shifting gradually from "How to live a long life" to "How to age healthily". The important factor is to prevent dementia and its progression.

To establish our goal, industry-academia-government cooperation is indispensable. In

Aomori Prefecture, where industry, academia, government and the citizens share the same goal of extending the average lifespan, many activities to improve one's health are promoted individually or cooperatively. Our COI is determined to establish the goal and spread Aomori-based health-promoting activities both at home and abroad.

## [P.2]

## Greeting

Shingo Mimura: Governor of Aomori Prefecture

Looking forward to the project that breathes new life into the field of preventive medicine.

The COI STREAM at Hirosaki University involving industry–academia–government cooperation seeks to invigorate the field of preventive medicine, with Hirosaki University's up-to-date research on dementia and analysis of the big data obtained from the Iwaki Health Promotion Project. Its social implications are significant, and I am looking forward to Aomori residents having a healthier and richer lifestyle and to the revitalization of the Prefecture's industry as the project progresses. I hope for innovation and improvement of the quality of life (QOL) not only in Japan, where aging is progressing rapidly, but also worldwide.

## Kei Sato: President of Hirosaki University

What we must challenge is to make innovation happen in the field of preventive medicine.

The field of preventive medicine has played an important role throughout the formation of modern society. Still, it is easy to imagine that establishing practical precautionary measures is difficult for lifestyle diseases such as stroke or vascular disorders, which involve many kinds of factors for a long period. Hirosaki University has been and will continue focusing on neuroscience research. We are striving for innovation in the field of preventive medicine, by combining our research and the cohort study through the creation of the COI.

Toshihiko Kudo: Project Leader and Executive Director of the Maruman Computer Service Expanding one's healthy life expectancy and spreading the social implementation model from Aomori to the world.

The vision we aim for is the creation of a healthy city living for an average of 90 years, as well as achieving social implement of preventive medicine based on risk. We set our sights on structuring methods for detecting disease symptoms and developing precautionary measures by making full use of the cohort study Hirosaki University has been carrying out through the Iwaki Health Promotion Project and research results from the Institution of Brain Science. Through this course of action, we will achieve social implementation at an early stage and spread the Aomori-borne model throughout Japan and the world.

Shigeyuki Nakaji: Research Leader, Dean of the Hirosaki University Graduate School of Medicine

Setting our sights to redeem Aomori from being dubbed the shortest-life prefecture, and make conclusive innovations happen to expand one's healthy life expectancy.

Hirosaki University has been selected to be a part of a national project, the "COI STREAM", as one of 12 Innovation Centers in Japan. This project is aimed at sparking innovation by imagining the innovation, conducting backcasting research, obtaining new results, and then implementing the results socially. We are eager to connect our research to a conclusive innovation; expanding Aomori Prefecture's healthy life expectancy, by targeting residents that show symptoms of lifestyle disease such as stroke or dementia.

## [P.3-4]

## Purpose of Hirosaki "COI"

Vision: Creating the healthy city where residents enjoy a healthy life span of 90 years Preventive medicine based on risk  $\rightarrow$  improving QOL and GNH Symptom-detecting algorithm/Software for disease prediction

<Figure-Left side>

Disease prediction service: Analyzes future risks of dementia or stroke and warns the user

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Depending on the risk levels

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Various software applications

 ${\scriptstyle (1)}$  Estimation of your health condition according to the symptoms

② Guidance to improve your health according to the symptoms

③ Health-promoting educational program

<Figure-Center Top>

Symptom analyzing factors: Health examination data, Additional data (genetic data)

Results from analyzing symptoms  $\rightarrow$  Health examination center; Local government, Health insurance association

Symptom analyzing factors: Medical information (including MRI, PET)  $\rightarrow$  Medical institution

Results from analyzing symptoms  $\rightarrow$  Supporting early diagnosis

## <Figure-Right side>

Service for precautionary measures

- ① Lifestyle service: Service to prevent brain diseases by supporting your lifestyle
- ② Exercise service: Service to prevent diseases through exercise
- ③ Nutrition service: Service to prevent diseases by warning of excessive consumption of salt content and so on.
- ④ Anti-aging service: Service to prevent diseases by anti-aging methods that use foodstuffs and medicines.

## <Figure-Center>

Regional Cooperation ① Health Examination Center Cooperation; Local government, Medical institutions, Health insurance association ② Area Comprehension Identifying disease

<Figure-Center Bottom> Medical examination center; Local government; Health insurance association Medical facilities Early Detection (preliminary group) → Early Action (prophylaxis) Identifying disease → Early treatment: Implementing precautionary measures afterward

Improved QOL, Health promotion, Reduced medical expenses  $\rightarrow$  Let's make our GNH the best in the world

\*GNH = Gross National Happiness

Project name of Hirosaki COI: Development of an innovative strategy for disease prediction and prevention by combining neuroscience research and analysis of "big health" data

# The state of the nation: Society is aging and age-related diseases are increasing

While Japanese society ages at an unprecedented rate, our nation's focus is shifting from "How to live a long life" to "How to age healthily". Thus, creating a society where seniors can spend their life energetically is one of our primary goals.

Notably, three out of every four deaths in Japan are due to an age-related disease (such as a lifestyle disease), and the social implications are becoming more and more important. While slowing somatic aging (e.g., via anti-aging methods) may delay the onset of age-related diseases, there is currently no definitive way of preventing them. One major anti-aging method these days is living a good lifestyle (by not smoking, not drinking excessively, and by exercising and eating properly). Still, there are many undiscovered fields in anti-aging research. In particular, precautionary measures for dementia, a disease most associated with aging (lifestyle does not have much influence on dementia when compared with the influence from aging), have yet to be found.

#### Project Summary of our "COI"

Aomori Prefecture is not only an aging society, but is also the prefecture in Japan with the highest prevalence of medical problems. The high death rate of Aomori residents from age-related disease such as stroke is one of the reasons why residents of this prefecture have the shortest lifespan in Japan.

Hirosaki University has been researching the pathology of brain disease, such as stroke, ever since the research facility for brain disease was opened in the Hirosaki University Medical Department, in 1965. For the past 9 years, we have been working on the "Iwaki Health Promoting Project", which is a cohort study of health-promoting and research activities involving residents in Hirosaki City (formerly Iwaki district), in hopes of shedding the notorious distinction of being "the shortest-life prefecture". A large database including data from both healthy and unhealthy individuals is essential for developing precautionary measures for age-related diseases, in which many factors intricately interact. Up until now, however, no studies had been conducted that collected enough social, environmental, and personal data on residents that were sufficient for analysis. This was because of the many problems concerning the protection of patient privacy, and because citizens were unconcerned about their health condition. Our "COI" has a large database of residents' conditions, obtained from the Iwaki Health Promotion Project, and this will allow us to develop brand-new precautionary measures for

age-related diseases.

Summarizing the above, our goal is to revitalize local economies by using the big data obtained from the Iwaki Health Promotion Project and extend Aomori residents' life expectancy to decrease medical expenses and improve Japan's GNH. We are attempting to overcome age-related diseases, such as dementia and stroke. We are striving to develop a method to detect early signs of these diseases, develop precautionary measures, and implement these measures socially. Implementation will involve not only the creation of health-related products (such as software), but also all kinds of health-promoting activities taking place in local areas, workplaces, and educational facilities. Beyond the implementation, we await the increase in health awareness in Aomori Prefecture, which is key to redeeming itself from being known as the shortest-life prefecture. We believe this Aomori-borne innovation will surely spread not only nationwide, but also worldwide.

Specifically, we are working on the following projects:

① A method for early detection of brain disease: By analyzing the big data obtained from the Iwaki Health Promoting Project, we plan to develop an algorithm and software for predicting disease risks.

(2) Precautionary measures for brain disease: From the precautionary measures established, we aim to develop new ways of spreading and teaching health promotion, and also to foster guidance for individual lifestyles, exercise, and diet. Next, we plan to develop software that offers warnings and guidance in stages to each user, depending on their risk level. We also plan to develop an innovative anti-aging method, to combine it with other methods and software thoroughly, and make them interact synergistically.

#### The attempt for social implementation

The model case our "COI" is working on for social implementation is a model that cooperates with medical examination centers and medical institutions, and offers a service, which includes early detection of brain disease and advice for its prevention, to the residents (and local governments) or company health insurance associations.

From the residents' perspective, having a medical checkup tells the residents not only their health condition on that day, but it also tells them whether there is a possibility of falling ill in the future. Especially when it comes to stroke or dementia, our model warns residents whether they should have a medical checkup right away, or otherwise how they should live their life to prevent the disease. For those residents who wish, our model can give them their genetic information and specific risk. Moreover, the model lets residents choose private services to practice precautionary measures, depending on their risk level and lifestyle. The combination of foresight on someone choosing private services to practice precautionary measures, depending on health condition, enhances individual health literacy.

Furthermore, if we could implement the precautionary measure service in medical examination centers and medical institutions, we can expect income from sources outside of insured medical services, and to that end the possibility of establishing a "health-promoting center (for outpatients)" will increase. This not only means an increase of options that can be taken to prevent the disease, but also innovation in the clinical flow, which involves all the main stakeholders (residents, local governments, health care providers, and medical examination centers).

What we mentioned above is a concrete example mostly targeting stroke or dementia, but our "COI" targets are all age-related diseases. If the model could be applied to other diseases similarly, extending healthy life expectancy, improving QOL, and creating that healthy city with an average lifespan of 90 years will not be very difficult.

Our attempts mentioned above are strongly supported by Aomori Prefecture, which aims to create a cluster of Life Innovation industries by 2030, according to the Aomori Life Innovation Strategy. With the industry–academia–government collaboration involving health care providers, we are collectively striving for the COI STREAM.

## [P.5]

#### The "application" that a "COI" produces

1. Developing a disease-predicting algorithm

We are developing a system that enables analysis of an individual's risk level, by finding predicting factors from the individual's health data and diagnosis. The system is assumed to make use of the domestic database and feed the results back to the individual (fee-based service).

2. Developing a system that cooperates with the medical examination center or medical facility

We are developing a system that integrates health data (obtained at medical examination centers) and diagnoses (obtained at medical institutions) into a cloud database per local governments and companies (health insurance associations included). The cloud database and disease prediction center work together and form an overall system for detecting disease risks. We are planning on the cloud database to be

fee-based, and assume that the local governments and companies will bear the expense.

We also are developing a system to send the results of examinations and health guidance details to users. Our final goal will be the development of a "health literacy device". Health-promoting activities that the cooperating companies practice will be accumulated in a cloud database, and will be accessible for a fee. We assume that the local governments and companies will bear this expense as well.

#### [Paragraph #3 is not here ("予兆発見のアプリケーション開発").]

#### 4. Creating a model for precautionary measures

For precautionary measures, we plan to create three services. To make the measures more effective, our goal is to combine the three services and create a synergistic model.

#### 1) Development of the Exercise Service

Investigate the best way to exercise based on the individuals' examination results, and test the exercise program's effectiveness to develop an ideal exercise program.

#### 2) Development of the Medical Diet Service

Investigate the best way to diet based on the individuals' examination results, then test the diet program's effectiveness to develop an ideal dietary cure as well as produce a lunch menu best suited for the individual.

#### 3) Development of the Anti-Aging Service

Investigate a new oral health care method that takes into consideration lifestyle disease, to establish the molecular basis of an anti-aging method to produce <u>a</u> preventive product.

#### Specific model of the product offer and overall flow of people and information

 $\rightarrow$  The flow of an individual  $\rightarrow$  The flow of information

<Figure-From Left side>

A local government/health insurance association  $\rightarrow$  Incentive to have a periodic health examination  $\rightarrow$  Screening while the residents undergo a medical examination  $\rightarrow$  For those who need to see a doctor  $\rightarrow$  Give them a diagnosis at a medical institution  $\uparrow$  For the preliminary group of a type of disease  $\rightarrow$  Precautionary measures put into practice

#### <Figure-From Bottom>

Data obtained from medical examination; Additional data (genetic data)  $\rightarrow$  Database for health data and genetic data  $\rightarrow$  Give warnings and advice/symptom-detecting <Figure-Right Side>

Identify the disease and treat it early  $\rightarrow$  A Merit to Each of the Stakeholders • Residents, Patients, and their Families

Preventing or delaying the onset of illness, improving the QOL via effective connections, combining the three services that an individual needs for care by recognizing symptoms and carrying out precautionary measures

Health Care Provider

Alleviate the patients' symptoms and carry out precautionary measures by treating the disease early and realizing the clinical flow from an early stage

·Local government and health insurance association

Medical expenses lowered through early treatment and intervention

Service Provider

Refine the algorithm's accuracy by combining each database and expanding the inputs

<Figure-Bottom>

Implementing "preventive medicine based on risk" by recognizing symptoms and starting early treatment

# [P.6]

# Figure of project summary Overall summary

<Figure-Left side>

Detecting the symptoms of dementia using big data

- ① Develop software for detecting symptoms
- 2 Analyzing and using the cohort study data

**O** Hirosaki University: Behavior and pathology analysis, making use of 10 years of residential health data from an early stage, effectively combining the three services, and

gathering new data such as genomic data

- O Maruman Computer Service: Structure the system
- **O** GE Healthcare Japan: Develop the algorithm and software
- **O** Claro: Develop pathological image apparatus
- **O TOHOKU CHEMICAL:** Omics analysis

**O** Aomori Prefectural Government and Hirosaki City Hall: Support the project generally

<Figure-Right side>

Prophylaxis system based on symptoms

① Educating new health promotion, investigating a way to popularize it, implementing health-promoting activities

2 Structure a warning system based on symptoms

Develop an innovative anti-aging method

**O Hirosaki University:** Large-scale cohort study, forefront analysis of stress response, technology for improving breeds, analysis of functional ingredients, and study of food function

O Maruman Computer Service: Structure the system for regional cooperation

O (Now coordinating): Develop functional foods

**O** Aomori Prefectural Industrial Technology Research Center: Analysis of functional ingredients

**O** Aomori Prefectural Government and Hirosaki City Hall: Support the project generally

<Figure-Center>

University – Residents – Finance – Local government – Companies Innovative "Health-power promoting center" (tentative)

Innovation  $\rightarrow$  By making the best use of health and medical data, we are striving to extend the healthy life expectancy to reduce medical expenses, for improving residents' GNH and developing the health care industry.

From "Advanced medical care depending on convalescence"; to "Risk concerning preventive medicine"

From Aomori to Japan, then to the World

Change the social environment in hopes of social implementation

To implement our "COI's" results, we think that it is necessary to change the social environment gradually. We are not sure if the results will be welcomed just because of their quality. This is because improving health is thought to be achieved only when individuals make an effort on their own initiative. Our "COI's" most unique point is that we are trying to simultaneously change the social environment for the results to be welcomed socially.

1. Cultivate an environment for local governments and companies to promote health easily

We will encourage the leaders of local governments and companies to issue a "health declaration". By encouraging the leader of an organization to issue a health declaration, other members would recognize that the declaration involves the entire organization. In this way, we will cultivate a health-promoting environment gradually throughout the entire prefecture.

2. Foundation of an innovative "Health-power promoting center" (tentative)

We plan to establish an institution that transmits and offers guidance on health-related activities based on the data and test results we obtain from the COI. This institution will also provide a platform for meetings or training on health promotion.

As described above, the cultivation of a health-promoting environment is the foundation of our project, and we will develop an appealing "software application" and spread our project from Aomori Prefecture to the nation and the world.

#### [Back Cover]

#### Access to the Bunkyo-cho District

Bunkyo-cho 1, Hirosaki, Aomori

- From JR Hirosaki station or Hirosaki bus terminal
  - O On foot/Takes about 20 minutes

**O** By bus/Takes about 15 minutes

Get on the bus of the "Koguri-yama/Oinomori" or "Gakuen-cho" line at [Platform No. 3] in front of JR Hirosaki station. Then get off the bus at Hirosaki University mae" station

- O By taxi/Takes about 5 minutes
- By Konan railways

- **O** On foot after getting off the train at Hiroko-shita station/Takes about 5 minutes
- O On foot after getting off the train at Hirosaki Gakuindai-mae station/Takes about 7 minutes

## Access to the Honcho District

Zaifu-cho 5, Hirosaki, Aomori

- From JR Hirosaki station or Hirosaki bus terminal
  - O On foot/Takes about 35 minutes
  - O By bus/Takes about 20 minutes
    - •Get on the bus of the Komagosi line at [Platform No. 6], in front of JR Hirosaki station. Then get off the bus at "Daigaku Byouin mae" station.
    - •Get on the bus of Kinzokudanchi-Sakuragaoka line at [Platform No. 8], JR Hirosaki station. Get off at "Hon-cho" station.
  - O By taxi/Takes about 10 minutes
- From Hirosaki central station, Konan Railways
  - O On foot after getting off the train at "Hirosaki Chuo" station/Takes about 7 minutes