

# About us

## Message from CEO

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### **Toward a healthy future in both body and mind**

I believe that health is the bedrock of a fulfilling life. As long as the body stays healthy, the mind naturally becomes optimistic. At Hirotsu Bio Science, we contribute to the development of revolutionary disease diagnostic technologies to lessen your concerns over health.

### **A future leveraging the capabilities of biology**

To stay healthy, technologies that catch and diagnose diseases in their early stages are essential. Since conventional diagnostics have primarily been conducted with man-made devices, the difficulty in striking a balance between high levels of sensitivity and low costs has been noted. The new concept of “biological diagnostics” will break through this barrier. Biological diagnostics deliver a high level of sensitivity by leveraging the astounding power of biology, surpassing the sensitivity of man-made devices, while enabling costs to be kept low by selecting organisms that cost nothing for upkeep. In light of the above, we at Hirotsu Bio Science are working towards the practical use of the world’s first ever biological diagnosis, a cancer test known as “N-Nose” that uses *Caenorhabditis elegans* (“roundworms,” or simply “c. elegans”). The test uses urine samples and is therefore non-invasive and simple, combining together numerous benefits including high sensitivity, low costs, and early detection. We are dedicated to pushing forward rigorously with our research and development to bring N-Nose to market at the earliest possible juncture.

### **A future where researchers shine**

Groundbreaking scientific innovations are brought about by the abundant ideas and untiring efforts of researchers. In recent years, however, there have been increasingly harsh circumstances and treatment of researchers in Japan. Hirotsu Bio Science values research and development above all else and aspires to become a company where researchers are the stars.

Hirotsu Bio Science Inc.  
CEO Takaaki Hirotsu

## Profile : Takaaki Hirotsu

April 25, 1972 Born in Suo-Oshima, Yamaguchi

1991 Graduated from Todaiji Gakuen private school

1991 Admitted to Tokyo University Department of Science Class II

1995 Graduated from Tokyo University Department of Science, Faculty of Biology

1995 Advanced to Master's Degree Program at Tokyo University Graduate School of Science, Research Department with a focus in Biochemistry

1997 Completed Master's Degree Program at Tokyo University Graduate School of Science, Research Department with a focus in Biochemistry

1997 Joined Suntory Inc.

1998 Left Suntory Inc.

1998 Entered Ph.D Program at Tokyo University Graduate School of Science, Research Department with a focus in Biochemistry

2001 Completed Ph.D Program at Tokyo University Graduate School of Science, Research Department with a focus in Biochemistry; Received Ph.D in Science

2001 Research Fellow at Japan Society for the Promotion of Science (Tokyo University Genetics Laboratory)

2004 Kyoto University Graduate School of Life Sciences, Research Department, Postdoctoral Research Fellow

2005 Kyushu University Graduate School of Science, Research Faculty, Life Sciences Department Assistant Professor

2016 Founded Hirotsu Bio Science Inc; Assumed office as CEO

## Awards

2002 Inoue Research Award (The Inoue Foundation for Science)

2016 Development Research Award (The Neurocreative Society)

2016 Nakayama Award (The Nakayama Foundation for Human Science)

2016 NISTEP Researcher (Japan Ministry of Education)

Dr. Hirotsu has focused consistently on research regarding the olfactory sense of *c. elegans* (also known as roundworms) since his doctorate program. Interested in mechanisms produced by preferences toward smells, he conducts analyses using *c. elegans* specimen. In March 2000, his first paper was published in the journal *Nature*. In March 2012 and April 2014, his research on changing preferences based on odor concentrations was reported in newspapers.

In July 2012, Dr. Hirotsu was the first in the world to successfully create a visual representation of single protein activation in *c. elegans* (reported in 10 newspapers). In May 2013, he began research on whether *c. elegans* can detect the smell of cancer cells, publishing his research in March 2015 (reported on numerous television networks and newspapers).

Company Name	Hirotsu Bio Science Inc.
Address	〒107-0052 Akasaka 5-Chome Building 3rd Floor, 5-4-9 Akasaka, Minato Ward, Tokyo
President & CEO	Takaaki Hirotsu
Capital	¥5,8850,000
Business Overview	Biological Diagnostics Research: Research, development, manufacturing, and sale of cancer diagnostic testing equipment utilizing c. elegans and c. elegans olfactory sensors.

## C. Elegans Cancer Test

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C. elegans (roundworms) have been thought of as laboratory specimen for analyzing the mechanisms of the olfactory system. We invented the “C. Elegans Cancer Test” based on the revolutionary new idea of leveraging the unrivaled olfactory senses of c.elegans for the benefit of society.

Deaths from cancer worldwide total 8.2 million people annually (as of 2012), and this number is expected to rise to 13 million by 2030. It has also been reported that the economic impact of cancer including social losses due to medical costs spent on cancer treatments, premature death, and disabilities reaches upward of 100 trillion yen.

In Japan, the effects of cancer are even more severe: cancer has been the leading cause of death since 1981, with one out of every two people experiencing cancer and one out of every three reportedly dying from cancer. The economic and social costs of cancer are enormous with medical care costs for cancer climbing to upward of 3.6 trillion yen annually (as of 2011).

The most effective way to prevent cancer deaths is early detection and early treatment. However, cancer screening rates in Japan lag at approximately 30%. This rate is low in comparison with other developed nations and is also a major factor underlying Japan’s high cancer mortality rate.

Reasons for the low screening rate include: the hassle associated with screening (requiring a trip to a medical care facility), the high costs, associated pain, the time taken until diagnosis, and the need to take different tests for each kind of cancer.

Accordingly, we set out to develop cancer screening technology that is simple, affordable, and capable of diagnosing all types of cancer at an early stage with high precision.

We first began investigating the reaction of c. elegans to cultures of cancer cells.

As a result of our research, we found that wild c. elegans worms demonstrated attraction to cancer cell cultures. This attraction was not observed in response to cultures of normal cells nor in c. elegans with olfactory mutations, therefore suggesting that the worms were responding to the smell of secretions unique to cancer cells.

So, do c. elegans respond to samples derived from humans? We decided to focus on testing urine samples since, compared with blood samples, it is simpler to make a diagnosis based on urine samples if possible. Upon studying the reaction of c. elegans to urine samples from 20 cancer patients and 10 healthy subjects, we found that the worms demonstrated attraction to the urine of all the cancer patients, whereas they demonstrated aversion to the urine of all healthy subjects.

The fact that the attraction toward the urine of cancer patients did not occur in *c. elegans* that had their olfactory nerves destroyed, coupled with the fact that the olfactory nerves of *c. elegans* reacted significantly to the urine samples of cancer patients, suggests that the worms sense the smell of cancer in urine.

We then conducted an experiment using urine samples from 242 test subjects (24 cancer patients and 218 healthy subjects) in order to test the precision of the cancer diagnostic test (N-Nose) using the olfactory sense of *c. elegans*. As a result, the worms identified 23 of the 24 cancer patients as testing positive for cancer and 207 of the 218 healthy subjects as testing negative for cancer.

That is to say, the sensitivity (the ratio at which cancer patients are successfully diagnosed with cancer) was 95.8% and the specificity (the ratio at which healthy subjects are successfully diagnosed as healthy) was 95.0%—an overwhelming level of sensitivity compared to other tumor markers tested simultaneously on the same subjects.

N-Nose, furthermore, featured the distinct characteristic that its sensitivity does not decline with respect to early-stage cancers.

(Hirotsu et al, PLOS ONE, 2015)

# **N-Nose is an unprecedented revolutionary technology with all of the following unrivaled benefits**

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## **① It is painless**

The test analyzes urine samples. All that is required is a single drop of urine.

## **② It is simple**

Urine sampling does not stipulate any special conditions such as diet restrictions, and urine taken at standard medical checkups can be used.

N-Nose does not require you to go to a medical care facility and thus does not present regional disparities.

## **③ It is fast**

It takes approximately an hour and a half for the results to come back.

## **④ It is affordable**

The cost of the testing system is inexpensive, raising prospectives for uptake in developing countries as well.

## **⑤ Cancer Screening**

N-Nose can detect all of the nearly 10 types of cancer we have investigated thus far, including pancreatic cancer for which early detection is problematic.

## **⑥ Early Detection**

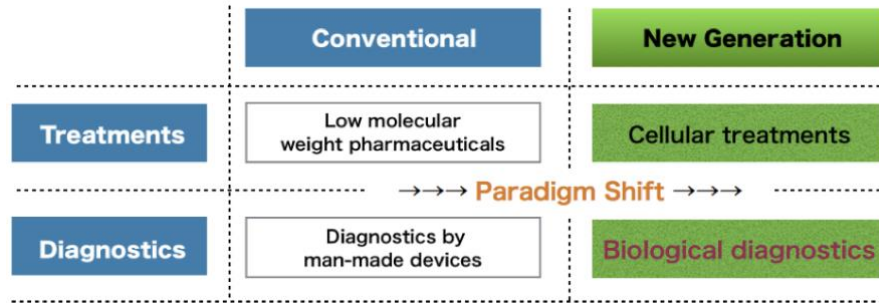
N-Nose has high sensitivity even in Stage 0 and Stage 1 early-stage cancer.

## **⑦ High Sensitivity**

The N-Nose test has a sensitivity rate of 93.8%

If N-Nose is introduced into society, we can expect dramatic improvements in cancer screening rates, thereby raising prospectives for a rise in early-stage cancer detection rates, a pronounced decline in cancer deaths, and significant reductions in health care costs. Furthermore, cancer would become recognized as a “curable disease,” raising expectations that it will lead to sweeping transformations throughout human civilization. As we push forward with development to bring the test to market at the earliest possible juncture, we continue to carry out fundamental research in an aim to produce an even better test.

# Bringing the Japanese-Derived Concept of “Biological Diagnostics” to the World



Early-stage diagnostics of diseases including cancer primarily feature diagnostic imaging and marker-based diagnostics; however, the majority of all existing technologies revolve primarily around detection with man-made devices (sensors and kits). Consequently, prioritizing sensitivity levels to detect trace amounts of disease-specific substances and small lesions (especially in early stages) leads to costly tests with expensive devices, while prioritizing affordability presents the problem of a loss in precision.

“Biological diagnostics” is a new concept set to break through this dilemma. Leveraging the abilities of biological organisms that far exceed the sensitivity of man-made devices and using organisms that cost nothing for upkeep enables tests to be made affordable.

Furthermore, there are oftentimes multiple substances present that characterize diseases and failure to detect these simultaneously has a negative impact on sensitivity. Man-made devices, however, are designed for detecting a single substance. On the other hand, living organisms perform best at detecting multiple signals and distinguishing them in combination (the olfactory sense distinguishes odors by sensing multiple kinds of odor at the same time), and are also superior on this front.

living organisms perform best at detecting multiple signals and distinguishing them in combination (the olfactory sense distinguishes odors by sensing multiple kinds of odor at the same time), and are also superior on this front. This corresponds with trends in the field of treatment as it undergoes a transition from low molecular weight pharmaceuticals to regenerative medicine leveraging the (biological) capabilities of cells, and a paradigm shift is also expected to occur in the field of diagnostics.

The “C. Elegans Cancer Test (N-Nose)” announced by Hirotsu Bio Science CEO Takaaki Hirotsu in 2015 was the world’s first report of biological diagnostics that can practically be brought to market. Using the unrivaled sense of smell of c. elegans to detect cancer odors not only delivers both high precision and low costs at the same time, it is also a technique that combines a variety of benefits.

It has been reported that diseases with distinct odors are not limited solely to cancer, promising the development of technologies to detect other illnesses at early stages through odor detection. With the exception of humans, sharpening the olfactory sense is a survival strategy for most animals, thus it may be possible to use other animals such as insects aside from c. elegans. In terms of other senses, there have been reports of using pigeons which have a sense of vision superior to that of humans for pathological diagnostics, promising great potential for further development of biological diagnostics moving forward.

Among diagnostics and treatment, the two axes of healthcare, Japan has pioneered the path for cellular treatments as a national technology with the advent of iPS cells, and in the field of diagnostics too, biological diagnostics promise to spread throughout the world as a technology derived in Japan.