

Tanaka Precious Metals succeeds in development of high-sensitivity in-vitro diagnostic kit

Expected to contribute to early discovery of prostate cancer

Tanaka Holdings Co., Ltd. (Holding company of Tanaka Precious Metals, Head office: Marunouchi, Chiyoda-ku, Tokyo; President & CEO: Hideya Okamoto) today announced that Tanaka Kikinzoku Kogyo K.K. (Head office: Marunouchi, Chiyoda-ku, Tokyo; President & CEO: Hideya Okamoto), which operates the Tanaka Precious Metals's manufacturing business, succeeded in the development of a "high-sensitivity in-vitro diagnostic kit using colloidal gold" which the Japan Science and Technology Agency (Headquarters: Kawaguchi-shi, Saitama; President: Koichi Kitazawa; JST) had established as a development theme for the Risk-Taking Fund for Technology Development.

JST commissioned the Company to work on this development theme from March 2007 until March 2010 based on the research by Professor Eiichi Tamiya of the Graduate School of Engineering, Osaka University (formerly Professor of the School of Materials Science, Japan Advanced Institute of Science and Technology), and seed development has been conducted with 300 million yen in developing funding.

In recent years, there has been a desire in the field of medicine for "in-vitro diagnostic agents enabling the simple and rapid early detection of disease" and examples of such diagnostic agents include immunochromatography^{*1)} used to diagnose influenza and pregnancy, and detect allergens. This uses the capillarity occurring in porous material to enable simple diagnosis of the presence of antigens in specimens (blood, etc.) in a short period of time. However, immunochromatographic agents have low sensitivity, and immunochromatographic kits for PSA (prostate specific antigen)^{*2)}, which is a marker for prostate cancer, are unsuitable for the early detection of prostate cancer because they are unable to detect PSA in concentrations of 0.2-2ng/ml (nanogram is 1 billionth of a gram), which is the level required for clinical tests of positive family history and recurrence tests.

The immunochromatographic diagnostic kit developed in this instance utilizes the color phenomenon caused by the plasmon effect^{*3)} of colloidal gold (gold particles with a diameter of approx. 60nm) to provide greater sensitivity than existing diagnostic agents. It also limits reactions with substances other than the targeted antigen (nonspecific reaction^{*4)}) and maintains a high level of sensitivity in case of using whole blood as specimen. As a result, it was possible to create a diagnostic kit able to detect PSA in concentrations of 0.2ng/ml within 15 minutes using whole blood.

In future, this technology is expected to be used in diagnostic kits for the early detection of prostate cancer. In addition to prostate cancer, it is expected to have applications in diagnostic kits for other diseases requiring a high level of sensitivity.

Details on the background, content and effects of this new technology can be found on the following page.

[Background] Until now, there has been a need for diagnostic kits able to provide early detection of diseases, etc. and enable easy and quick detection with high sensitivity.

Conventional primary screening in early diagnosis utilizes ELISA^{*5)} tests such as the enzymatic method, and in recent years immunochromatography has been utilized due to the ease and speed of detection. However, as ELISA tests take over 3 hours for results to be determined, this led to the problem in which doctors had to make patients wait instead of making a decision on the spot (Table 1). In addition, although immunochromatography is simple and fast, it can only be used in examination and primary screening because of its low sensitivity (lower detection limit), could not be used for early detection in clinical tests of positive family history and recurrence tests. In fact, whereas the detection threshold in a detection kit for detecting PSA, which is a prostate cancer marker, is 4ng/ml when using immunochromatography, that of 0.5-2ng/ml and 0.2-0.5ng/ml are required for clinical tests of positive family history and recurrence tests respectively, and this led to a need to increase the sensitivity of immunochromatography.

[Content] The Company has developed a highly sensitive diagnostic agent able to be used in early detection of prostate cancer in both clinical tests of positive family history and recurrence tests.

The diagnostic agent developed is an immunochromatographic kit using the color phenomenon caused by the plasmon effect of colloidal gold.

The following effects were obtained in this development:

- (1) Improving reproducibility of color by conjugated the colloidal gold particle size used;
- (2) Improving sensitivity by using a specific method to conjugated antibody to colloidal gold;
- (3) Repression of nonspecific reaction by addition of certain mouse antibodies to the running buffer.

(Figure 2)

- (4) Maintaining performance by the addition of mannitol (a type of sugar alcohol) for preventing the hemolysis^{*6)} and a detergent that has the effect of raising sensitivity in the running buffer (Figure 3).

Using these new technologies, the Company was able to develop a high-sensitivity diagnosis kit able to detect PSA in concentrations of 0.2ng/ml required for the clinical test of positive family history and recurrence test of prostate cancer.

[Effect] In future, it is expected to be used in diagnostic kits for the early detection of prostate cancer and detection kits for other diseases that require high sensitivity.

As this diagnostic kit can be used to easily and quickly detect PSA concentration as little as 0.2ng/ml, it is expected to be used in the early detection of prostate cancer.

Furthermore, this technology is also expected to be able to be used in diagnosis of other diseases requiring a high level of sensitivity.

<Reference Figure>

	ELISA	Immunochromatography
Measurement time	Approx. 3 hours	Approx. 15 minutes
Operation	Complex	Simple
Method of determination	Equipment required (Reading using plate reader)	No equipment required (Visual observation)
Measurement values	Quantitative	Qualitative
Samples	Serum	Blood, plasma, serum

Table 1: Comparison of ELISA and Immunochromatography

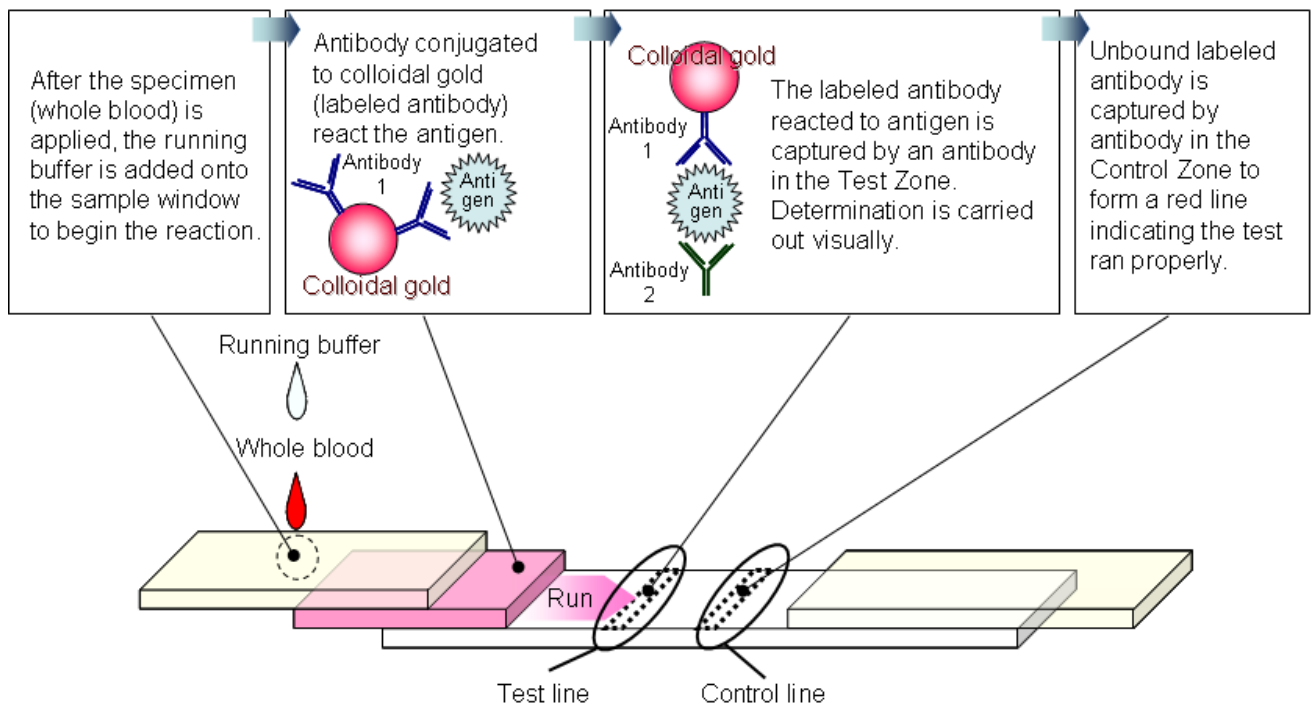


Figure 1: Principle of immunochromatography detection (when using colloidal gold)

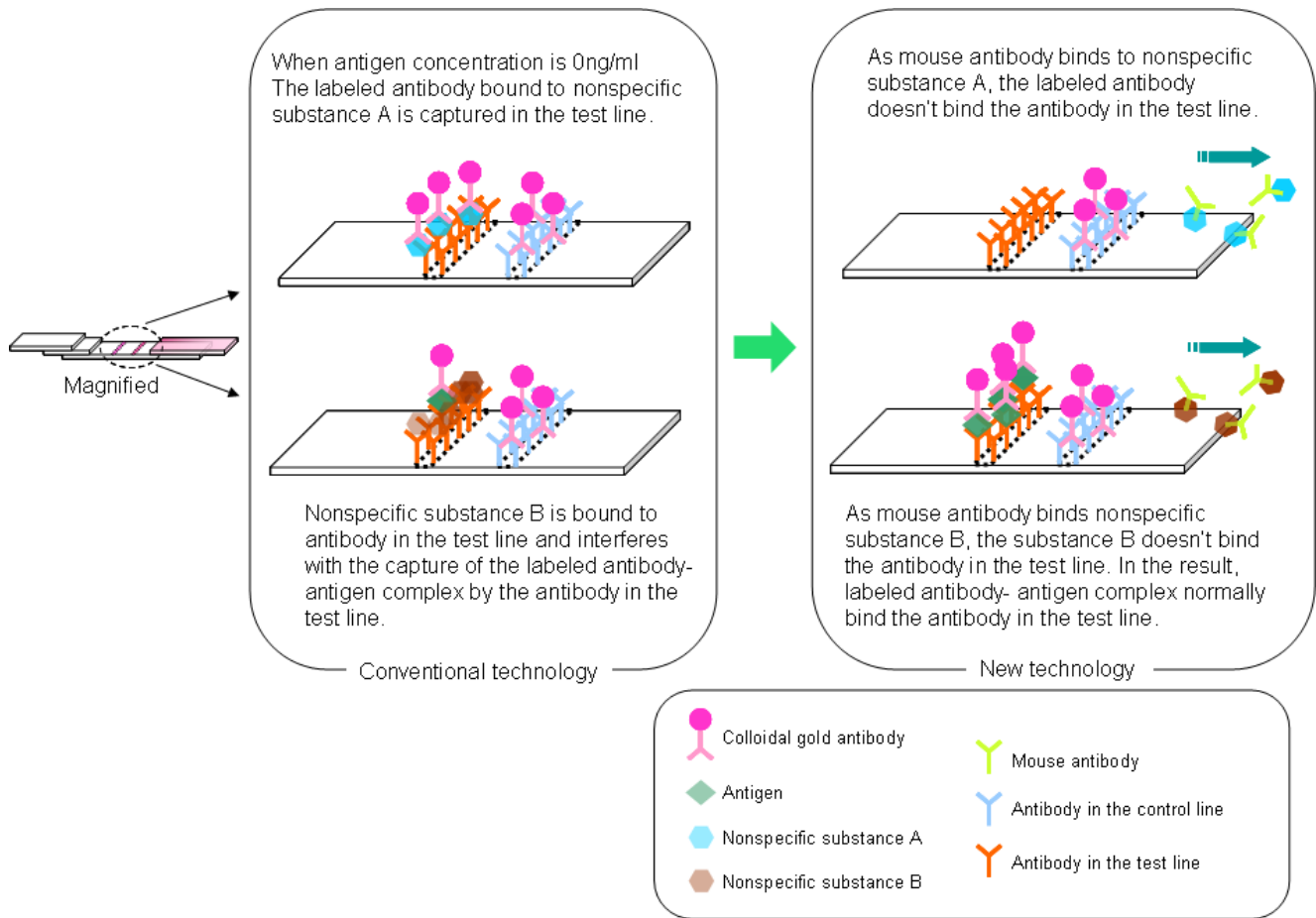


Figure 2: Technology for repressing nonspecific reactions

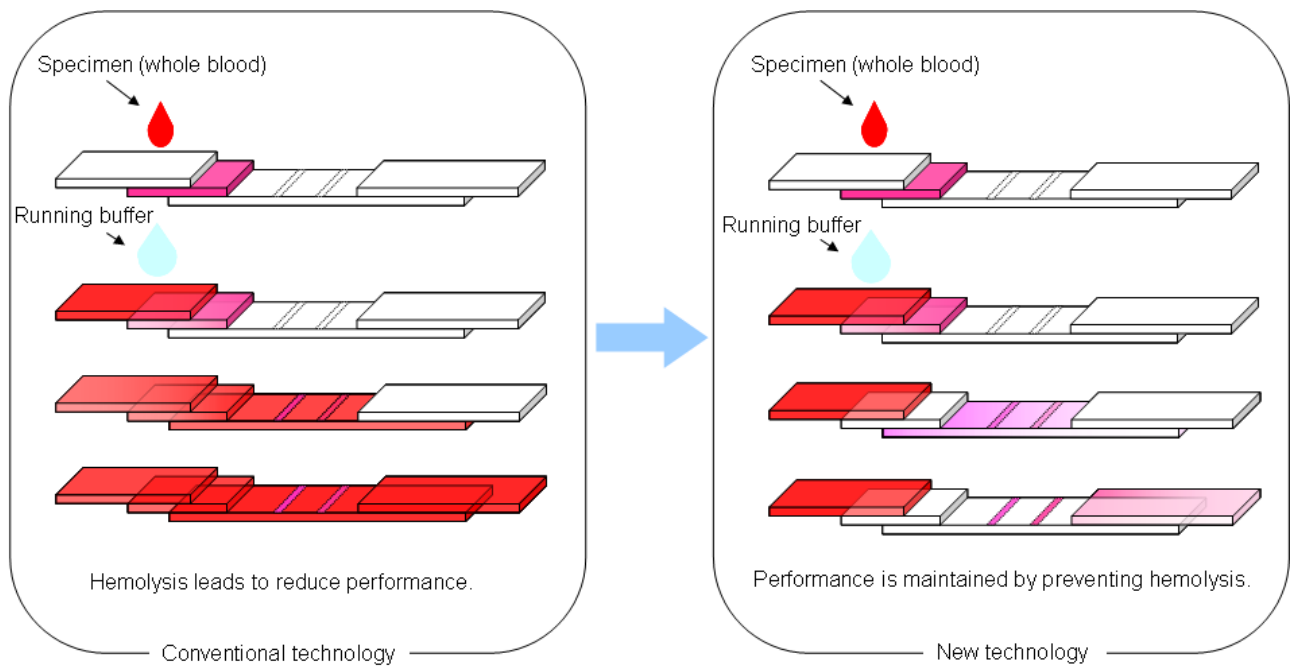


Figure 3: technology for maintaining performance even in whole blood

<Glossary>

*1) Immunochromatography

An analytical method enabling visual determination of the concentration of a target molecule is above or below a specified threshold of concentration by reacting colored- particle labeled antibodies immobilized on the test strip with a liquid sample which is drawn into the test strip by capillary action.

*2) PSA (Prostate Specific Antigen)

This is a substance secreted by the prostate, and its concentration in the blood increases in the event of prostate cancer, enabling it to be used as an indicator for diagnosing prostate cancer.

*3) Plasmon effect

A phenomenon in which the free electrons in a metal and incident light resonate on the surface of metal nanoparticles. This phenomenon causes colloidal gold to appear red.

*4) Nonspecific reaction

A reaction in which a substance other than the intended combination is bound. For example, where there is antibody a for antigen A, a reaction in which antibody a binds to another substance B instead of antigen A.

*5) ELISA (Enzyme Linked ImmunoSorbent Assay)

An immunoassay using enzymes as label in which the target molecule in a sample is quantified by measuring the strength of coloring in an enzyme-based reaction.

*6) Hemolysis

Burst of erythrocyte membrane

■Tanaka Holdings Co., Ltd. (Holding company of Tanaka Precious Metals)

Headquarters: 22F, Tokyo Building, 2-7-3 Marunouchi, Chiyoda-ku, Tokyo

Representative: Hideya Okamoto, President & CEO

Founded: 1885

Incorporated: 1918

Capital: 500 million yen

Employees in consolidated group: 3441 (FY2009)

Net sales of consolidated group: 710.2 billion yen (FY2009)

Main businesses of the group:

Manufacture, sales, import and export of precious metals (platinum, gold, silver, and others) and various types of industrial precious metals products. Recycling and refining of precious metals.

Website: <http://www.tanaka.co.jp>

■Tanaka Kikinzoku Kogyo K.K.

Headquarters: 22F, Tokyo Building, 2-7-3 Marunouchi, Chiyoda-ku, Tokyo

Representative: Hideya Okamoto, President & CEO

Founded: 1885

Incorporated: 1918

Capital: 500 million yen

Employees: 1,599 (as of March 2010)

Sales: 388.8 billion yen (as of the financial closing at the end of March 2010)

Businesses:

Manufacture, sales, import and export of precious metals (platinum, gold, silver, and others) and various types of industrial precious metals products. Recycling and refining of precious metals.

Website: <http://pro.tanaka.co.jp>

About the Tanaka Precious Metals

Established in 1885, the Tanaka Precious Metals has built a diversified range of business activities focused on the use of precious metals. On April 1, 2010, the group was reorganized with Tanaka Holdings Co., Ltd. as the holding company (parent company) of the Tanaka Precious Metals. In addition to strengthening corporate governance, the company aims to improve overall service to customers by ensuring efficient management and dynamic execution of operations. Tanaka Precious Metals is committed, as a specialist corporate entity, to providing a diverse range of products through cooperation among group companies.

Tanaka Precious Metals is in the top class in Japan in terms of the volume of precious metal handled, and for many years the group has developed and stably supplied industrial precious metals, in addition to providing accessories and savings commodities utilizing precious metals. As precious metal professionals, the Group will continue to contribute to enriching people's lives in the future.

The eight core companies in the Tanaka Precious Metals are as follows.

- Tanaka Holdings Co., Ltd. (pure holding company)
- Tanaka Kikinzoku Kogyo K.K.
- Tanaka Kikinzoku Hanbai K.K.
- Tanaka Kikinzoku International K.K.
- Tanaka Denshi Kogyo K.K.
- Electroplating Engineers of Japan, Limited
- Tanaka Kikinzoku Jewelry K.K.
- Tanaka Kikinzoku Business Service K.K.