

News Release

Ricoh Company., Ltd.
DNA Chip Research Inc.

Reference DNA plate for genetic testing in lung cancer
Launch of RICOH Standard DNA Series EGFR mutation Type001
– Contributing to improvement of the accuracy of highly sensitive genetic testing using blood –

TOKYO, August 20, 2020 - Ricoh Company., Ltd. (President and CEO Yoshinori Yamashita) and DNA Chip Research Inc. (President Ryo Matoba) announced that today they will launch “RICOH Standard DNA Series EGFR mutation Type001”, a reference DNA plate^{*1} jointly developed as reference material^{*2} for use in accuracy control of blood-based genetic testing for lung cancer. This product contributes to improving the accuracy of testing by making it possible to confirm the accuracy of highly sensitive genetic testing that detects the very small amounts of DNA molecules from cancer cells that are contained in blood from lung cancer patients. Currently, these are only available in Japan.

Personalized medicine is beginning to be used more widely as a means of discovering and treating cancer. This is a type of precision medicine in which the genes in patient’s cancer tissue are tested to predict the effects of therapeutic agents. Genetic testing investigates mutations in genes that are related to oncogenic transformation and the effects of therapeutic agents against cancer. In genetic testing for lung cancer, a number of therapeutic agents (molecularly targeted drugs^{*3}) tailored to changes (mutations) in genes have been developed and have come into practical application early on.

The EGFR (Epidermal Growth Factor Receptor) gene^{*4} test is one of the typical genetic tests related to lung cancer. When patients are considering pharmacotherapy for lung cancer, they are tested for EGFR-activating mutants in order to decide upon a therapeutic agent. They are also tested for EGFR-resistant mutants in order to investigate what kinds of drug resistance might develop after administration of the therapeutic agent. Methods such as PCR^{*5} and NGS (next-generation sequencing)^{*6} are used in these kinds of genetic testing.

The samples used in genetic testing of lung cancer consist of resected tissue harvested during surgery or tissue harvested with a bronchoscope (biopsy), but these methods of harvesting are invasive and impose a heavy burden on the body of the patient. In recent years, attention has been focused on the liquid biopsy,^{*7} which reduces the burden on the patient by using blood, which can be harvested with minimal invasiveness.

“EGFR Liquid”,^{*8} developed by DNA Chip Research, is a minimally invasive testing method that uses blood, and it

makes it possible to perform highly sensitive genetic testing by the NGS method. Cell-free DNA (cfDNA) released by various cells is present in the harvested blood, but most of it comes from normal cells. This test can detect the EGFR-activating mutants that locate on small amounts of circulating tumor DNA (ctDNA), together with the even less common resistant mutants.

“RICOH Standard DNA Series” is a family of products based on reference DNA plate technology, which uses Ricoh’s own bioprinting technology to dispense a prespecified number of DNA molecules in 1-molecule units, so that accuracy control and quality control of genetic testing equipment, genetic testing methods, and reagents can be performed rigorously even in the low-concentration area with fewer than 100 molecules, where variation tends to develop if dilution is performed by hand.

Ricoh developed “RICOH Standard DNA Series EGFR mutation Type001”, a reference material for confirming the accuracy of genetic testing as a model for the cell-free DNA in the blood of lung cancer patients. The number of cancer cell–derived cell-free DNA molecules in the blood differs from one patient to another, but in over half of patients, there are fewer than 100 molecules with EGFR-activating mutants in the blood sampled for one test, and the number of resistant mutants is even smaller (according to an investigation by DNA Chip Research). “RICOH Standard DNA Series EGFR mutation Type001” was modeled on this, with 10 to 100 cancer cell–derived DNA molecules (including genetic sequences of both EGFR-activating mutants and resistant mutants) per 10,000 normal DNA molecules, dispensed into each well of 8 tubes, so it is expected that this product will be used as a reference material with a mutant allele frequency*⁹ of 0.1% to 1.0% in the evaluation of testing systems at medical institutions, testing centers, and research institutes that perform lung cancer testing. We aim to contribute to making precision medicine more accurate and improving the efficacy of treatments for lung cancer by providing this product for use in the confirmation of test accuracy in advance.

Product Name

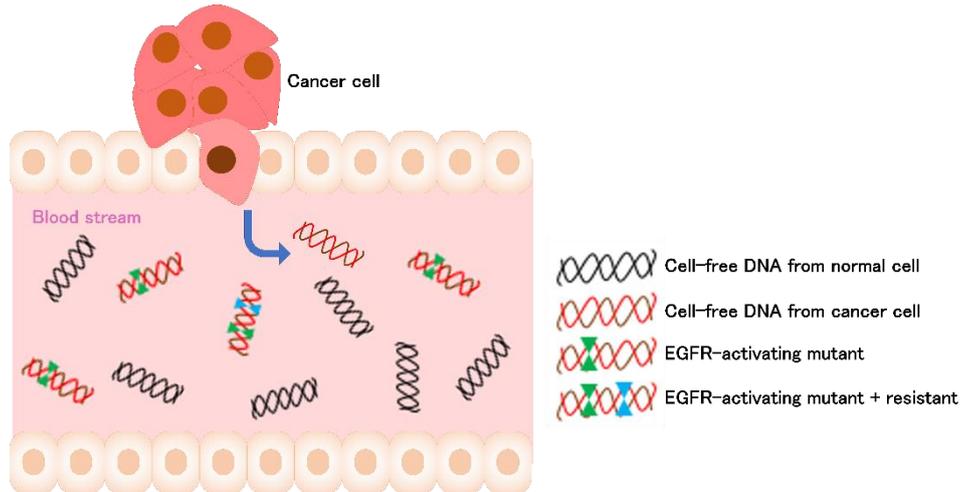
RICOH Standard DNA Series EGFR mutation Type001

Product Code	256771
Gene	EGFR
Mutation*⁸	G719A, E19_del, T790M, C797S, L858R, L861Q
Allele	0.1%, 0.3%, 0.5%, 1.0%
Frequency	
Content	8-tube strip x 5 strips
Storage	-20 degrees or less
Temperature	

	1	2	3	4	5	6	7	8
Allele Frequency	0.1%	0.1%	0.3%	0.3%	0.5%	0.5%	1.0%	1.0%
Mutant (Number of copies)	10	10	30	30	50	50	100	100
Wild type (Number of copies)	10000							

*The cap of the No. 1 well has a round black seal.

Product information



Schematic diagram of cell-free DNA in blood of lung cancer patient



RICOH Standard DNA Series EGFR mutation Type001

※This product is a reagent for research use only.

*1 Reference DNA plate

Reference DNA plate is the result of joint research by Ricoh Company, Ltd., the National Agriculture and Food Research Organization (NARO), and FASMAC of the Nippon Flour Mills Group

*2 Reference material

A substance with a clearly specified content of an ingredient, which is used as a standard of measurement.

https://www.ricoh.com/release/2018/0604_1.html

*3 Molecularly targeted drug

A therapeutic agent that exerts its effect by attacking specific molecules that are peculiar to cancer cells in a targeted manner.

*4 EGFR (Epidermal Growth Factor Receptor) gene

EGFR gene mutations are found in approximately 30% of lung cancer patients. They are the most frequently found mutation in lung cancer patients, and tens of thousands of tests for these mutations are performed annually.

*5 PCR method

A DNA amplification method using the Polymerase Chain Reaction.

*6 NGS.

An abbreviation for Next Generation Sequencing. This is a method that can simultaneously read multiple DNA sequences.

*7 Liquid biopsy

Test using blood or other body fluids, mainly to diagnose and treat cancer.

*8 “EGFR Liquid”, developed by DNA Chip Research

Official name: “EGFR Liquid” Gene Analysis Software

A test that can be used in liquid biopsies, developed with the aim of performing EGFR gene testing in a minimally invasive manner (can use both tissue and blood). Application for regulatory approval submitted in July 2019. Among cancer-related mutations, known as an activating mutant, which plays a part in oncogenic transformation. Activating mutants are found among EGFR genes as well, and it is possible to test for 2 types of activating mutants (exon 19 deletion and L858R) with “EGFR Liquid”. “EGFR Liquid” is a test that performs companion diagnostics. An application was made in July, last year to the Ministry of Health, Labor, and Welfare for manufacture and sales approval of the product, and the approval has been issued on July 31st, 2020.

ANNOUNCEMENT OF SPECIALLY-CONTROLLED MEDICAL DEVICE MANUFACTURING AND SALES APPROVAL FOR THE "EGFR Liquid" GENE ANALYSIS SOFTWARE, AS A DISEASE DIAGNOSIS PROGRAM.

https://www.dna-chip.co.jp/en/common/press_en_148.pdf

*9 Allele frequency

Ratio of mutant DNA to non-mutant DNA

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Relevant Information

(News Release) RICOH launches RICOH Standard DNA Series of reference DNA plates that overcome challenges in PCR testing

https://www.ricoh.com/release/2020/0415_1/

(News Release) Bioprinting Technology to Control the Number of DNA Molecules in Units of One

https://www.ricoh.com/release/2018/0604_1.html

(Technical page) The Manufacturing of reference DNA plates

https://www.ricoh.com/technology/institute/research/tech_dna_reference_plate.html