

CE Mark of a novel reagent to detect RAS (KRAS and NRAS) gene mutations for testing of anti-EGFR therapeutic antibodies to colon cancer prior to treatment

Medical and Biological Laboratories Co., Ltd. (Nagoya, Aichi, Japan) and G&G Science (Fukushima, Fukushima, Japan), a subsidiary company, jointly developed a novel reagent to detect RAS (KRAS and NRAS) gene mutations for determination of anti-epidermal growth factor receptor (EGFR) therapeutic antibodies prior to treatment on the basis of a recent clinical finding. We submitted the application for CE mark for the reagent in Europe (Description : MEBGEN™ RASKET KIT) on June 13, and have also submitted the application for the manufacture and sales approval as an *in vitro* diagnostic to the Pharmaceuticals and Medical Devices Agency in Japan.

Anti-EGFR antibodies which target a specific molecule involved in tumor growth are often prescribed to patients with colorectal cancer. The mechanism of the antibodies has been reported to suppress tumor proliferation through competitive inhibition of EGFR-induced signal transduction. Multiple retrospective studies, however, demonstrated that the anti-EGFR antibodies cannot be clinically effective in patients with any mutation in KRAS exon 2 (codon 12 and 13). Therefore, we developed and have been providing “MEBGEN™ KRAS Gene Mutation Detection Kit” in the Japanese market since April 2011.

Recent clinical studies have reported that some patients having no efficacy even with KRAS exon 2 wild type have a mutation in KRAS exon 3 or 4, or NRAS exon 2, 3, or 4 and that prior to treatment diagnosis for these mutations as well as KRAS exon 2 mutations would be useful for therapeutic decision for anti-EGFR therapy. In Europe, the package inserts have already been revised to indicate treatment with anti-EGFR antibodies in patients with wild-type “RAS” including both KRAS and NRAS.

Since such *in vitro* diagnostics to detect variable RAS mutations have not existed in the market we have developed a “RAS mutations detection kit” and successfully demonstrated that test results of the new kit highly correlate with those of existing methods.

The MEBGEN KRAS KIT enables detection of RAS gene mutations rapidly and simultaneously in one well in a single assay using just a small amount of DNA through the PCR-rSSO method based on the xMAP technology by Luminex Corporation (Austin, TX, USA).

We are working toward the regulatory approval of the reagent in the Japanese market as well.

Glossary

- EGFR (epidermal growth factor receptor)

EGFR is a transmembrane protein which functions like a “switch” on cell growth through binding of growth factors such as EGF. EGFR is expressed in normal epithelial cells but is overexpressed in solid tumors and transmits signals for the proliferation and survival of the cancer cells. It has been a target molecule for cancer treatment.

- KRAS and NRAS genes

KRAS and NRAS are molecules which activate the downstream of the EGFR signaling to induce cell growth.

- CE marking

The CE Mark is an official conformity marking for certain products sold in the European Union. Especially for medical devices, the mark indicates that the devices conform to the EC directives.

- Exon

Genes include exons and introns. Exons are coding regions of genes, to be translated into proteins.

- Signal transduction

Signal transduction is the relaying of stimulations from a cell's exterior to its interior. Many intracellular molecules, by interacting with each other, transduce an extracellular signal to the nucleus modifying expression of specific genes and inducing cellular physiological phenomena, such as proliferation and apoptosis.

About Medical and Biological Laboratories Co., Ltd. (MBL)

MBL was established in 1969 as the first antibody manufacturer in Japan with a focus on providing high quality products and solutions for life science research and clinical diagnostics. In the last decade we have successfully expanded our scope of business to diagnostics in the fields of molecular biology and Immunology.

- Life science research business

MBL provides over 5,000 antibodies, mRNA identification kits, and custom manufacturing of antibodies, oligonucleotides, and artificial genes for the global market.

- Clinical diagnostic business

MBL develops diagnostics for autoimmune diseases, cancers, metabolic disorders, and molecular diagnostics. Leveraging our expertise in immunology, we developed a number of diagnostic reagents designed for difficult to diagnose autoimmune diseases thereby improving the tools available to clinicians.

- Cytology business

MBL provides an innovative system of liquid-based cytology for cervical cancer testing, including reagents for detection of Human papillomavirus (HPV) and a brush for collecting cells from the cervix.

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