New Protein Truncation Test Kit Simplifies Mutation Detection

Protein Truncation Test detects mutations at the protein level

The Protein Truncation Test (PTT) is a mutation-screening method that allows researchers to detect mutations at the protein level rather than the DNA level (1). The PTT detects “nonsense” or “stop” mutations, the most prevalent mutations in several disease-related genes, which prematurely terminate translation and produce a truncated protein unable to function like the normal protein.

The Protein Truncation Test has proved particularly useful in the study of human disease genes. For example, nonsense mutations account for up to 98% of the mutations in the APC (Adenomatous Polyposis Coli) gene associated with an inherited form of colon cancer (2) and up to 86% of the mutations in the BRCA1 gene linked to breast cancer (3). Faster and more convenient than mutation screening by DNA sequencing, the Protein Truncation Test has also successfully detected truncated proteins encoded by genes linked to Duchenne Muscular Dystrophy (1) and Hereditary Non-Polyposis Colon Cancer (4).

New kit provides safety, convenience, and reliability

Boehringer Mannheim’s new Protein Truncation Test, increases the convenience of PTTs with optimized reagent premixes for in vitro transcription and translation reactions following PCR (Figure 1). These reagent premixes improve the reliability of PTTs by minimizing the number of pipetting steps and avoiding the optimization of reaction mixtures. In addition, the translation premix employs biotin as a protein label, which eliminates the safety concerns, disposal hassles, and record keeping required by radioactive PTTs using 35S-methionine.

Detection of the biotinylated translation products in a chemiluminescent reaction (Figure 2) produces results much more quickly than the day-long film exposures required by radioisotopic PTTs. The complete PTT procedure, from PCR product to chemiluminescent detection, takes less than 6 hours.

Each lot of kits is function tested (with the provided control DNA and control primers) in an actual Protein Truncation Test, ensuring success from PCR through translation and detection. In addition, the kit’s convenient biotinylated molecular weight marker facilitates accurate determination of protein size.

The Protein Truncation Test is now available

Order the Protein Truncation Test, non-radioactive, (Cat. No. 1 888 439) from your local Boehringer Mannheim Biochemicals representative. Or, for additional information, visit http://biochem.boehringer-mannheim.com on the Internet.

References

This product is sold under licensing arrangements with Roche Molecular Systems and The Perkin-Elmer Corporation. Purchase of this product is accompanied by a license to use it in the Polymerase Chain Reaction (PCR) process in conjunction with an authorized thermal cycler.

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Applicants are encouraged to submit abstracts for poster presentation.

Application deadline: September 30, 1997

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Our cover features Stanley J. Korsmeyer, who is the recipient of the 20th Annual Bristol-Myers Squibb Award for Distinguished Achievement in Cancer Research for his work in identifying key genetic mechanisms that govern programmed cell death and survival and defining their role in causing lymphomas and other cancers.

Dr. Korsmeyer is Professor of Medicine and Pathology at Washington University School of Medicine in St. Louis, MO, and Chief of the Division of Molecular Oncology. He also is an Investigator of the Howard Hughes Medical Institute at the University. His work has focused on cancers that result from chromosomal translocations—genetic mix-ups in which the DNA of one chromosome within a cell inadvertently snaps off and becomes fused to that of another. By creating transgenic mice, he showed that a specific translocation of genes on chromosomes 14 and 18 gives rise to human follicular lymphoma, the most common of all lymphomas. This translocation is the molecular hallmark of follicular lymphoma throughout the world. To date, scientists have identified 125 distinct chromosomal abnormalities that lead to different forms of cancer. This translocation that prevents normal cell death also appears to confer the ability to resist chemotherapy.

More broadly, Dr. Korsmeyer has established a new paradigm in cancer research, one that holds that the overall wellbeing of an organism is dependent on a homeostasis of cell death and cell division. Dr. Korsmeyer has identified a large family of proteins that mediate the struggle to maintain this homeostasis, functioning as agonists or antagonists of death. He has delineated the complex signaling sequences between the different proteins and described the process by which cell death actually contributes to disease states.

Dr. Korsmeyer graduated from the University of Illinois at Urbana in 1972 and received his M.D. from the University of Illinois at Chicago in 1976. He did his internship and residency in the University of California Hospitals in San Francisco from 1976 through 1979 and then spent seven years in the Metabolism Branch of the National Cancer Institute, first as an Associate, then as a Senior Investigator. He came to Washington University and the Howard Hughes Medical Institute in 1986, was named Professor of Medicine and Molecular Microbiology in 1990, and Professor of Pathology and Investigator at the Institute in 1993.

Dr. Korsmeyer has published more than 175 scientific papers and is a member of the Editorial Boards of *Cell Growth & Differentiation* (CG&D), the molecular biology journal of the American Association for Cancer Research (AACR), *Journal of Cell Biology, Leukemia Research, and Genes, Chromosomes and Cancer*. In addition, he serves on the Board of Scientific Counselors of the National Cancer Institute, and he is a member of the National Academy of Sciences, the American Society for Clinical Investigation, the Association of American Physicians, as well as the AACR, to which he has contributed actively.

Besides his aforementioned service as an Associate Editor for *CG&D*, Dr. Korsmeyer served on the AACR Board of Directors for a term that began in 1994 and ended in April 1997. He was also instrumental in two very successful AACR Special Conferences, serving on the Program Committee for “Cell Death in Cancer and Development,” which was held in Chatham, MA, in 1993, and as Co-Chairperson for “Programmed Cell Death,” which took place in Bolton Landing, NY, in 1996. Also, for the 1997 AACR Annual Meeting in San Diego, he chaired the Cell Growth and Death Section of the Program Committee, and he was the recipient of the G. H. A. Clowes Memorial Award given at that meeting.

Dr. Korsmeyer has been widely honored for his contributions to cancer research. In addition to his receipt of the Clowes Award and the Bristol-Myers Squibb Award, he has been honored with the Pasarow Medical Research Award, the CIBA-Drew Award in Biomedical Research, and the E. Donnall Thomas Prize given by the American Society of Hematology.

Sidney Weinhouse