Short Tandem Repeat Analysis in the Research Laboratory

ABSTRACT

Short tandem repeat (STR) analysis is an informative approach to genetic identification and is commonly associated with DNA testing in forensic laboratories, paternity disputes or missing persons cases. However, there are many other uses for STR analysis, such as verifying tissue sample origins, authenticating cell lines, detecting tissue or cell mixtures, determining twin zygosity and tracking genetic mutations in research studies of diseases such as cancer. This article highlights many of the research applications of human STR analysis.

Publication Date: 2012

Introduction

STRs are repetitive sequence elements 3–7 base pairs in length scattered throughout the human genome. By amplifying and analyzing these polymorphic loci, then comparing the resulting STR profile to that of a reference sample, the origin of biological samples such as cells or tissues can be identified and verified. The more loci that are amplified, the higher the statistical power of discrimination. For example, when analyzing the 15 STR loci amplified by the PowerPlex® 16 HS System, the power of discrimination is as high as 1 in 1.42×10^{18}, making it highly unlikely that two DNA profiles will match at random.

Authenticating Cell Lines

Cells lines are important tools in scientific research. Scientists can manipulate cultured cells and expose them to various stimuli under controlled conditions to provide answers to experimental questions. Information gathered in these experiments is often a foundation for further scientific advances. For this reason, cell line misidentification and contamination have become important concerns. A 2007 *Science* article reveals several cases where laboratories had invested substantial time and resources researching cell lines that were later revealed to be misidentified (1) . A specific example of misidentification is the esophageal adenocarcinoma cell line TE-7, which was later identified as a squamous cell carcinoma cell line (2) . As a result, scientists are being urged to authenticate cultured cells used in their laboratory, and standards are being developed for doing so (3) (4) (5) . Some scientists have as far as suggesting that research using unauthenticated cell lines should not be funded or published (6) .

As a result, an increasing number of scientists are performing STR analysis to confirm the identity of cell lines used in their labs.

Tracking and Confirming Tissue Provenance and Detecting Contamination

Tissues are also informative tools in the laboratory—researchers can dissect and characterize tissue samples to better understand normal or abnormal physiological or cellular events, such as cell differentiation. Anytime a tissue sample is collected, there is a risk that the sample was identified incorrectly (7) (8) . To minimize this risk, the laboratory or biobank that collects and stores the tissue must keep careful records. Any uncertainty as to a tissue's origin must be resolved before the sample can be used in an experiment. STR analysis is a fast and easy way to do this (9) (10) : Researchers can compare the STR profile of the tissue with that of a reference sample to determine the sample's identity.

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Likewise, STR analysis can be used to detect sample contamination, which appears as a mixed STR profile. Examples where tissue samples have been contaminated by extraneous tissue (also known as floaters) during the preparation of histological slides, have been reported in the literature (11) (12) . If undetected, such contamination can lead to incorrect results. The sensitivity of STR analysis, which can create full profiles from less than 100pg of DNA, allows detection of minute quantities of contaminating cells or tissue.

Detecting Maternal Cell Contamination and Fetal Aneuploidy

One specific example of tissue contamination is the presence of maternal cells in a prenatal sample. STR analysis can help ensure that a prenatal fetal sample is not contaminated with maternal cells prior to assaying the prenatal fetal sample. This can be important in situations where maternal DNA can interfere with the results. In addition to sample characterization, STR analysis can be used to detect fetal DNA in maternal blood samples during research and development of less invasive prenatal genetic tests (13) . Researchers also have used STR analysis to detect fetal chromosomal abnormalities, such as trisomies and other aneuploidies (14) , determine fetal gender using the sexually dimorphic Amelogenin locus, which can distinguish XX (female) and XY (male) individuals.

Cancer Research

Cancer is the unregulated growth of abnormal cells in the body brought about by genetic mutations, often in tumor suppressor genes or other proto-oncogenes. To better understand the disease's development and progression, researchers need to study the associated genetic changes. Cancer researchers can track determine genetic changes by examining STR loci (15) or single nucleotide polymorphisms (16) or performing whole genome sequencing (17) to detect DNA duplications, deletions or other mutations and use this information to calculate mutation rates of loci in response to a stimulus (18) . These types of analyses can help identify key chromosomal regions that are altered during pathogenesis.

Determining Twin Zygosity

STR analysis is commonly used to determine whether twins are monozygotic (identical) or dizygotic (fraternal) (19) (20) (21) (22) (23) (24) (25) (26) (27) . This information is useful in research with sets of monozygotic twins because they have the same genetic material, minimizing the effects of genetic differences in the test subjects that might confound the study results. Confirming zygosity also has been informative in studies that examine the rate of monozygotic twin or triplet births as a result of natural conception or assisted reproductive techniques (28) (29) .

Conclusion

Increasingly, researchers are turning to STR analysis to verify the origin of biological samples, detect sample contamination and track genetic changes. The sensitivity and high power of discrimination makes STR analysis an ideal choice for the types of applications discussed here.

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