DOWNLOAD PDF SHORT TANDEM REPEAT MARKERS

Chapter 1 : "Development of a Comprehensive Massively Parallel Sequencing Panel of " by David H. Wars

A short tandem repeat (STR or microsatellite) is a pattern of two or more nucleotides that are repeated directly adjacent to each other. The repeats can range in length from 2 to 6 base pairs/repeat.

History[edit] Although the first microsatellite was characterised in at the University of Leicester by Weller, Jeffreys and colleagues as a polymorphic GGAT repeat in the human myoglobin gene, the term "microsatellite" was introduced later, in , by Litt and Luty. Prominent early applications include the identifications by microsatellite genotyping of the 8-year-old skeletal remains of a British murder victim Hagelberg et al. Repeat units of four and five nucleotides are referred to as tetra- and pentanucleotide motifs, respectively. Most eukaryotes have microsatellites, with the notable exception of some yeast species. Microsatellites are distributed throughout the genome. Microsatellites in non-coding regions do not have any specific function, and therefore cannot be selected against; this allows them to accumulate mutations unhindered over the generations and gives rise to variability that can be used for DNA fingerprinting and identification purposes. They are thus classified as minisatellites. Similarly, insects have shorter repeat motifs in their telomeres that could arguably be considered microsatellites. Boxes symbolize repetitive DNA units. Arrows indicate the direction in which a new DNA strand white boxes is being replicated from the template strand black boxes. Three situations during DNA replication are depicted. Thus, the mutation rate at microsatellite loci is expected to differ from other mutation rates, such as base substitution rates. The actual cause of mutations in microsatellites is debated. One proposed cause of such length changes is replication slippage, caused by mismatches between DNA strands while being replicated during meiosis. Because microsatellites consist of such repetitive sequences, DNA polymerase may make errors at a higher rate in these sequence regions. Several studies have found evidence that slippage is the cause of microsatellite mutations. A study comparing human and primate genomes found that most changes in repeat number in short microsatellites appear due to point mutations rather than slippage. This is likely due to homologous chromosomes with arms of unequal lengths causing instability during meiosis. In the desert locust Schistocerca gregaria, the microsatellite mutation rate was estimated at 2. Others are located in regulatory or even coding DNA - microsatellite mutations in such cases can lead to phenotypic changes and diseases. In yeasts, the most common repeated amino acids are glutamine, glutamic acid, asparagine, aspartic acid and serine. Mutations in these repeating segments can affect the physical and chemical properties of proteins, with the potential for producing gradual and predictable changes in protein action. For example, microsatellite length changes are common within surface membrane proteins in yeast, providing rapid evolution in cell properties. For example, a GAA triplet expansion in the first intron of the X25 gene appears to interfere with transcription, and causes Friedreich Ataxia. This method of RNA splicing is believed to have diverged from human evolution at the formation of tetrapods and to represent an artifact of an RNA world. Microsatellites are widely used for DNA profiling , also known as "genetic fingerprinting", of crime stains in forensics and of tissues in transplant patients. They are also widely used in kinship analysis most commonly in paternity testing. Also, microsatellites are used for mapping locations within the genome, specifically in genetic linkage analysis to locate a gene or a mutation responsible for a given trait or disease. As a special case of mapping, they can be used for studies of gene duplication or deletion. Researchers use microsatellites in population genetics and in species conservation projects. Plant geneticists have proposed the use of microsatellites for marker assisted selection of desirable traits in plant breeding. Cancer diagnosis[edit] In tumour cells, whose controls on replication are damaged, microsatellites may be gained or lost at an especially high frequency during each round of mitosis. Hence a tumour cell line might show a different genetic fingerprint from that of the host tissue, and, especially in colorectal cancer , might present with loss of heterozygosity. Microsatellites have therefore been routinely used in cancer diagnosis to assess tumour progression. It is also used to follow up bone marrow transplant patients. Even shorter repeat sequences would tend to suffer from artifacts such as PCR stutter and preferential amplification, while longer repeat sequences would suffer more highly from environmental degradation and would amplify less well by PCR. Kinship analysis paternity testing [edit]

Autosomal microsatellites are widely used for DNA profiling in kinship analysis most commonly in paternity testing. Genetic linkage analysis[edit] During the s and the first several years of this millenium, microsatellites were the workhorse genetic markers for genome-wide scans to locate any gene responsible for a given phenotype or disease, using segregation observations across generations of a sampled pedigree. Although the rise of higher throughput and cost-effective single-nucleotide polymorphism SNP platforms led to the era of the SNP for genome scans, microsatellites remain highly informative measures of genomic variation for linkage and association studies. Their continued advantage lies in their greater allelic diversity than biallelic SNPs, thus microsatellites can differentiate alleles within a SNP-defined linkage disequilibrium block of interest. Thus, microsatellites have successfully led to discoveries of type 2 diabetes TCF7L2 and prostate cancer genes the 8q21 region. Created based on microsatellite markers. Their uses are wide-ranging. Microsatellites have been proposed to be used as such markers to assist plant breeding; [59] nevertheless, as of , "breeding programs based on DNA markers for improving quantitative traits in plants are rare". Therefore, microsatellites are normally analysed by conventional PCR amplification and amplicon size determination, sometimes followed by Sanger DNA sequencing. In forensics, the analysis is performed by extracting nuclear DNA from the cells of a sample of interest, then amplifying specific polymorphic regions of the extracted DNA by means of the polymerase chain reaction. Once these sequences have been amplified, they are resolved either through gel electrophoresis or capillary electrophoresis , which will allow the analyst to determine how many repeats of the microsatellites sequence in question there are. If the DNA was resolved by gel electrophoresis, the DNA can be visualized either by silver staining low sensitivity, safe, inexpensive , or an intercalating dye such as ethidium bromide fairly sensitive, moderate health risks, inexpensive , or as most modern forensics labs use, fluorescent dyes highly sensitive, safe, expensive. The Americans [64] increased this number to 13 loci. DNA is repeatedly denatured at a high temperature to separate the double strand, then cooled to allow annealing of primers and the extension of nucleotide sequences through the microsatellite. This process results in production of enough DNA to be visible on agaroseor polyacrylamide gels; only small amounts of DNA are needed for amplification because in this way thermocycling creates an exponential increase in the replicated segment. A number of DNA samples from specimens of Littorina plena amplified using polymerase chain reaction with primers targeting a variable simple sequence repeat SSR, a. Design of microsatellite primers[edit] If searching for microsatellite markers in specific regions of a genome, for example within a particular intron , primers can be designed manually. This involves searching the genomic DNA sequence for microsatellite repeats, which can be done by eye or by using automated tools such as repeat masker. Once the potentially useful microsatellites are determined, the flanking sequences can be used to design oligonucleotide primers which will amplify the specific microsatellite repeat in a PCR reaction. Random microsatellite primers can be developed by cloning random segments of DNA from the focal species. These random segments are inserted into a plasmid or bacteriophage vector , which is in turn implanted into Escherichia coli bacteria. Colonies are then developed, and screened with fluorescentlyâ€”labelled oligonucleotide sequences that will hybridize to a microsatellite repeat, if present on the DNA segment. If positive clones can be obtained from this procedure, the DNA is sequenced and PCR primers are chosen from sequences flanking such regions to determine a specific locus. This process involves significant trial and error on the part of researchers, as microsatellite repeat sequences must be predicted and primers that are randomly isolated may not display significant polymorphism. More recent techniques involve using oligonucleotide sequences consisting of repeats complementary to repeats in the microsatellite to "enrich" the DNA extracted Microsatellite enrichment. The enriched DNA is then cloned as normal, but the proportion of successes will now be much higher, drastically reducing the time required to develop the regions for use. However, which probes to use can be a trial and error process in itself. The complementary sequences to two neighboring microsatellites are used as PCR primers; the variable region between them gets amplified. The limited length of amplification cycles during PCR prevents excessive replication of overly long contiguous DNA sequences, so the result will be a mix of a variety of amplified DNA strands which are generally short but vary much in length. Since an ISSR may be a conserved or nonconserved region, this technique is not useful for distinguishing individuals, but rather for phylogeography analyses or maybe delimiting species ; sequence

diversity is lower than in SSR-PCR, but still higher than in actual gene sequences. In addition, microsatellite sequencing and ISSR sequencing are mutually assisting, as one produces primers for the other. Limitations[edit] Repetitive DNA is not easily analysed by next generation DNA sequencing methods, which struggle with homopolymeric tracts. Therefore, microsatellites are normally analysed by conventional PCR amplification and amplicon size determination. Occasionally, within a sample of individuals such as in paternity testing casework, a mutation in the DNA flanking the microsatellite can prevent the PCR primer from binding and producing an amplicon creating a "null allele" in a gel assay , thus only one allele is amplified from the non-mutated sister chromosome , and the individual may then falsely appear to be homozygous. This can cause confusion in paternity casework. It may then be necessary to amplify the microsatellite using a different set of primers. In species or population analysis, for example in conservation work, PCR primers which amplify microsatellites in one individual or species can work in other species. However, the risk of applying PCR primers across different species is that null alleles become likely, whenever sequence divergence is too great for the primers to bind. The species may then artificially appear to have a reduced diversity. Null alleles in this case can sometimes be indicated by an excessive frequency of homozygotes causing deviations from Hardy-Weinberg equilibrium expectations.

Chapter 2 : STR Searchable Database

Short Tandem Repeats (STRs) The human genome is full of repeated DNA sequences. These repeated sequences come in various sizes and are classified according to the length of the core repeat units, the number of contiguous repeat units, and/or the overall length of the repeat region.

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Chapter 3 : Microsatellite - Wikipedia

Microsatellites are often referred to as short tandem repeats (STRs) by forensic geneticists and in genetic genealogy, or as simple sequence repeats (SSRs) by plant geneticists. [4] Microsatellites and their longer cousins, the minisatellites, together are classified as VNTR (variable number of tandem repeats) DNA.

Chapter 4 : STR Markers â€“ Short Tandem Repeat | Devyser

By themselves, Y-chromosome DNA (Y-DNA) short tandem repeat (STR) markers from a Y-DNA test do not have any particular meaning. The value of testing Y-DNA STR markers comes from creating a Y-DNA signature (haplotype) with them and comparing that Y-DNA signature to others in a database.

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Chapter 5 : Y-STR - Wikipedia

Start studying Chapter 5 Commonly Used STR Markers. Learn vocabulary, terms, and more with flashcards, games, and other study tools. STR - short tandem repeat 2.

Chapter 6 : STR - Forensic DNA Testing System

Variable nucleotide tandem repeats (VNTRs) are repeating sequences of multi-base segments of DNA. If the repeat is equal to or less than 6 bases, NTRs are named microsatellites, also known as short tandem repeats (STRs). One common example of a microsatellite is a (CA) n repeat, where n varies.

Chapter 7 : Short Tandem Repeat Test â€“ NGeneBio

This database is an information resource for the forensic DNA typing community with details on commonly used short tandem repeat (STR) DNA markers. STRBase consolidates and organizes the abundant literature on this subject to facilitate on-going efforts in DNA typing.

Chapter 8 : Short tandem repeat - ISOGG Wiki

Short tandem repeat (STR) markers are the DNA marker of choice in forensic analysis of human DNA. Here we extend the application of STR markers to Cannabis sativa and demonstrate their potential for forensic investigations.

Chapter 9 : Y-STR - ISOGG Wiki

Abstract. The chapter describes the use of capillary array electrophoresis (CAE) for the detection of triplet repeat expansion at the huntingtin locus associated with autosomal dominant Huntington disease (HD), an adult-onset neuro-degenerative disorder.