NicheVision Forensics, LLC

Technical Note on Typing DYS449

September 24, 2025

Background

DYS449 is included in the YFiler Plus (Thermo Fisher Scientific) CE kit as well as the mYSTR and CombiSTR (NimaGen) MPS kits. It is not included in the minimal set of markers for YHRD inclusion (1). DYS449 is considered a rapidly mutating locus, thereby making it potentially useful in differentiating among relatives. YSTR loci are components of YSTR haplotypes consisting of a series of linked allele numbers. Small databases of allele number-based haplotype frequencies are available (1), but sequence-based frequency databases have not yet been developed.

Nomenclature

Early reports described DYS449 as a [TTCT]n repeat motif (2). This nomenclature was updated in 2014 to a [TTTC]n repeat motif (3, 4) (**Table *1***). MixtureAce can be user-configured for either nomenclature. The [TTTC]n nomenclature results in an allele number one less than the [TTCT]n nomenclature for the same sequence. In either bracketing scheme, the count of nucleotides between the outermost bracketed motifs is the same (**Table *1***).

Location

The genomic location of the STR locus shifts one nucleotide in the 5′ direction when converting to the [TTTC]n bracketing convention. However, the number of nucleotides within the locus remains constant (**Table *1***) regardless of the bracketing for currently known alleles. This number is 166nt and 186nt for the GRCh38 and 2800M standard sequences respectively.

Allele Numbers

Allele numbers are defined in CE-based analysis (i.e., fragment length analysis) via the use of sizing standards, which typically are proprietary. Allele numbers are defined in MPS-based analysis (i.e., sequence analysis) by subtracting the nucleotides in a sequence that, by convention, do not contribute to allele number determination. Because current allele databases have been built based on CE-derived allele numbers, allele numbers assignments in MPS should seek concordance with CE-based allele numbers.

Table 1. Two different bracketing conventions used in literature applied to the GRCh38 reference sequence.

Bracket Scheme	Reference Sequence	STR Location	Repeat Count	Ref
[TTCT]n	[TTCT]15 N46 [TTCT]15	8349973 >>N_{166}<< 8350140	30	(2)
[TTTC]n	[TTTC]15 N50 [TTTC]14	8349972 >>N_{166}<< 8350139	29	(5)

Table 2. Genotype of standard DNA 2800M bracketed by two different conventions. Allele number 34 is concordant with the allele number reported by Robino et al. for 2800M (3)

Bracket Scheme	STR Region	Allele Number	
		Method 1	Method 2
[TTCT]n	[TTCT]16 N22 [TTCT]3 N12 [TTCT]19	186/4=46.2	(186-46)/4=35
[TTTC]n	[TTTC]16 N50 [TTTC]18	186/4=46.2	(186-50)/4=34

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U1-C08-2800M_S559
@M08352:108:000000000-M3MCP:1:2104:16435:8829 1:N:0:59
TGGAGTCTCTCAAGCCTGTTCTATGAATATTTTCCCTTAACTTGTGTGATTTTTTGTTTAAAAAGTTCCCCCATGTTTTTTTC
TTGCTCTTTTTCTTTTCTCTCTTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTC
TTTCTCTCTCTCCTCCTCTTTCTTTCCTTCTTTCTTTCTTTTCCTCTTTCCTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT
TTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTCTCTTTGTTTCTGTCTTACTCTTGTTGTCCAACCTAGAG
TGCAATGGT
+
CCCCCGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG#G#GGGGGGGGGGGGGG###GGGG#G#GG#GGGGGGGGGG
GG#GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG
GGFDGGGEGDEC#@,EF;GFFCFFGGCGGFGFGCFGGGGGGFCFGCGFFFCGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG
GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG
GGGGCCCCC
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Figure 1. A read record from 2800M standard DNA sequenced using the CombiSTR kit. [TTTC]n motifs are highlighted in green. The 50 nucleotides intervening between the two repeat motifs are not counted for allele numbering purposes: despite the presence of [TTTC] motifs inside this region (underlined).

Literature Cited

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