Supplementary Material - Mousavi, *et al.*

1 Supplementary Note: GangSTR Model

1.1 Class probabilities

Class probability describes the probability of a read pair belonging to a specific class, considering uniform coverage. For any value of underlying allele length A, this probability can give an intuition for the relative abundance of different classes of reads **(Supplementary Figure 1)**.

Derivation of class probabilities for each read pair class are given below. Notation corresponds to that used in the main text and depicted in **Figure 2**.

1.1.1 Class Probability of Enclosing Reads

Without loss of generality, we assume the first mate in the pair is enclosing. The calculation is similar for the other mate (Equation (1)). Assuming uniformity of coverage, we use a uniform distribution to find the probability of a TR region being enclosed by a read.

$$\begin{aligned} P(c_i = E; A) &= P(S_1 < F, S_1 + r > F + A \cdot m) \\ &= P(F + A \cdot m - r < S_1 < F) \\ &= \frac{(F) - (F + A \cdot m - r)}{2F + A \cdot m - 2r} \\ &= \frac{(r - A \cdot m)}{2F + A \cdot m - 2r} \end{aligned} \tag{1}$$

1.1.2 Class Probability of Spanning Reads

1.1.3 Fragment Length Distribution

We model the observed fragment length δ with a limited Gaussian random variable Δ with the following distribution:

$$f_\Delta(\delta) = \frac{1}{C\sqrt{2\pi}\sigma} e^{-\frac{1}{2\sigma^2}(\delta-\mu)^2} \qquad ; r \leq \delta \leq \infty \tag{2}$$

In this equation μ is average fragment length, σ is the standard deviation of the fragment length distribution, C is a normalization constant to account for limited range of δ, and r is the read length.

Integration of this probability density function arises several times throughout the rest of this document. We compute these integrals using a helper Gaussian distribution X:

$$f_X(x) = \frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{1}{2\sigma^2}(x-\mu)^2} \qquad ; -\infty \leq x \leq \infty \tag{3}$$

and it's cumulative density function (CDF):

$$F_X(x) = \int_{-\infty}^{x} f_X(x)dx \tag{4}$$

1) For $r \leq a, b \leq \infty$:

$$\begin{aligned} \int_a^b f_\Delta(\delta)d\delta &= F_\Delta(b) - F_\Delta(a) \\ &= \frac{1}{C}\{F_X(b) - F_X(a)\} \end{aligned}$$

2) For $r \leq a, b \leq \infty$:

$$\begin{aligned}\int_a^b (\delta-\mu) f_\Delta(\delta) d\delta &= \frac{1}{C\sqrt{2\pi}\sigma}\int_a^b (\delta-\mu) e^{-\frac{1}{2\sigma^2}(\delta-\mu)^2} d(\delta-\mu) \\ &= -\frac{\sigma}{C\sqrt{2\pi}}\{e^{-\frac{1}{2\sigma^2}(b-\mu)^2} - e^{-\frac{1}{2\sigma^2}(a-\mu)^2}\} \\ &= -\frac{\sigma^2}{C}\{f_X(b) - f_X(a)\}\end{aligned}$$

A read pair is classified as spanning if it's two mates are mapped in the flanking region before and after the TR locus.

$$\begin{aligned}P(c_i = S; A) &= P(S_1 < F, S_2 > F + A\cdot m - r) \\ &= \int_{2r}^{2F+A\cdot m} P(S_1 < F, S_2 > F + A\cdot m - r|\Delta = \delta) f_\Delta(\delta) d\delta \\ &= \int_{2r}^{2F+A\cdot m} P(S_1 < F, S_1 + \Delta - r > F + A\cdot m - r|\Delta = \delta) f_\Delta(\delta) d\delta \\ &= \int_{2r}^{2F+A\cdot m} P(F + A\cdot m - \Delta < S_1 < F)|\Delta = \delta) f_\Delta(\delta) d\delta \qquad (5) \\ &= \int_{2r}^{2F+A\cdot m} \frac{(F) - (F + A\cdot m - \delta)}{2F + A\cdot m - 2r} u(\delta - A\cdot m) f_\Delta(\delta) d\delta \qquad (6) \\ &= \int_{max\{2r, A\cdot m\}}^{2F+A\cdot m} \frac{\delta - A\cdot m}{2F + A\cdot m - 2r} f_\Delta(\delta) d\delta\end{aligned}$$

Step function $u(.)$ is introduced in (6) to satisfy the condition in (5), $x + A\cdot m - \Delta < x$, which simplifies to $\Delta > A\cdot m$. This condition is then imposed in the integral limit. We continue the calculation using the helper integrals from Section 1.1.3.

$$\begin{aligned}P(c_i = S; A) &= \int_{max\{2r, A\cdot m\}}^{2F+A\cdot m} \frac{(\delta-\mu) + \mu - A\cdot m}{2F + A\cdot m - 2r} f_\Delta(\delta) d\delta \\ &= \frac{1}{2F + A\cdot m - 2r}\Big\{(\mu - A\cdot m)\int_{max\{2r, A\cdot m\}}^{2F+A\cdot m} f_\Delta(\delta) d\delta \\ &+ \int_{max\{2r, A\cdot m\}}^{2F+A\cdot m} (\delta - \mu) f_\Delta(\delta) d\delta\Big\} \\ &= \frac{\mu - A\cdot m}{C(2F + A\cdot m - 2r)}\Big[F_X\big(2F + A\cdot m\big) - F_X\big(max\{2r, A\cdot m\}\big)\Big] \\ &- \frac{\sigma^2}{C(2F + A\cdot m - 2r)}\Big[f_X\big(2F + A\cdot m\big) - f_X\big(max\{2r, A\cdot m\}\big)\Big] \\ &= \frac{1}{C(2F + A\cdot m - 2r)}\Bigg\{(\mu - A\cdot m)\Big[F_X\big(2F + A\cdot m\big) - F_X\big(max\{2r, A\cdot m\}\big)\Big] \\ &- \sigma^2\Big[f_X\big(2F + A\cdot m\big) - f_X\big(max\{2r, A\cdot m\}\big)\Big]\Bigg\}\end{aligned}$$

1.1.4 Class Probability of Flanking Reads

Without loss of generality, we assume the first mate in the pair is flanking. The calculation is similar for the other mate. Assuming uniform coverage, we use a uniform distribution to find the probability of observing a flanking read.

$$
\begin{aligned}
P(c_i = F; A) &= P\big(S_1 < F, S_1 + r < F + A \cdot m, S_1 + r > F\big) \\
&= P\big(F - r < S_1 < min\{F, F + A \cdot m - r\}\big) \\
&= \frac{min\{F + A \cdot m - r, F\} - (F - r)}{2F + A \cdot m - 2r} \\
&= \frac{F + min\{A \cdot m - r, 0\} - F + r}{2F + A \cdot m - 2r} \\
&= \frac{min\{A \cdot m, r\}}{2F + A \cdot m - 2r}
\end{aligned} \tag{7}
$$

1.1.5 Class Probability of FRRs

$$
\begin{aligned}
P(c_i = FRR; A) &= P(S_1 \leq F, F \leq S_2 \leq F + A \cdot m - r) \\
&= \int_{2r}^{2F + A\cdot m} P(S_1 \leq F, F \leq S_1 + \Delta - r \leq F + A \cdot m - r | \Delta = \delta) f_\Delta(\delta) d\delta \\
&= \int_{2r}^{2F + A\cdot m} P(S_1 \leq x, S_1 \leq F + A \cdot m - \delta, S_1 \geq x + r - \delta) f_\Delta(\delta) d\delta
\end{aligned} \tag{8}
$$

We combine the inequalities describing S_1 in (8) to derive conditions that need to hold for this integral to have non-zero value.

- $\left.\begin{matrix} S_1 \geq F + r - \delta \\ S_1 \leq F + A \cdot m - \delta \end{matrix}\right\} \Rightarrow F + A \cdot m - \delta \geq F + r - \delta \Rightarrow A \cdot m \geq r$

  $\Rightarrow$ This condition is the clear condition underlying presence of FRR reads. Smaller TR lengths have 0 probability of having an FRR read.

- $\left.\begin{matrix} S_1 \geq F + r - \delta \\ S_1 \leq F \end{matrix}\right\} \Rightarrow F \geq F + r - \delta \Rightarrow \delta \geq r$

  $\Rightarrow$ The lower limit of the integral is $\delta \geq 2r$, hence this condition is satisfied for the range of possible δ values.

Since there are two upper bounds for S_1 in (8), we need to consider two different scenarios:

- $x \leq F + A \cdot m - \delta \Rightarrow \delta \leq A \cdot m$
  Therefore, for $2r \leq \delta \leq A \cdot m$; $A \cdot m \geq 2r$, integrand is simplified to:
  $\Rightarrow P(S_1 \leq F, S_1 \leq F + A \cdot m - \delta, S_1 \geq F + r - \delta) = P(F + r - \delta \leq S_1 \leq F)$
  For $A \cdot m < 2r$, this part has no contribution.

- $F > F + A \cdot m - \delta \Rightarrow \delta > A \cdot m$
  Similarly, for $A \cdot m \leq \delta \leq 2F + A \cdot m$, integrand is simplified to:
  $\Rightarrow P(S_1 \leq F, S_1 \leq F + A \cdot m - \delta, S_1 \geq F + r - \delta) = P(F + r - \delta \leq S_1 \leq F + A \cdot m - \delta)$

Continuing integration for $A \cdot m \geq 2r$:

$$\begin{aligned}
P(c_i = FRR; A) &= \int_{2r}^{A\cdot m} P(F + r - \delta \leq S_1 \leq F) f_\Delta(\delta) d\delta \\
&+ \int_{A\cdot m}^{2F+A\cdot m} P(F + r - \delta \leq S_1 \leq F + A\cdot m - \delta) f_\Delta(\delta) d\delta \\
&= \int_{2r}^{A\cdot m} \frac{(F) - (F + r - \delta)}{2F + A\cdot m - 2r} f_\Delta(\delta) d\delta \\
&+ \int_{A\cdot m}^{2F+A\cdot m} \frac{(F + A\cdot m - \delta) - (F + r - \delta)}{2F + A\cdot m - 2r} f_\Delta(\delta) d\delta \\
&= \int_{2r}^{A\cdot m} \frac{(\delta - \mu) + (\mu - r)}{2F + A\cdot m - 2r} f_\Delta(\delta) d\delta \\
&+ \int_{A\cdot m}^{2F+A\cdot m} \frac{A\cdot m - r}{2F + A\cdot m - 2r} f_\Delta(\delta) d\delta \\
&= \frac{1}{C(2F + A\cdot m - 2r)} \Big\{ -\sigma^2 \big[f_X(A\cdot m) - f_X(2r)\big] \\
&+ (\mu - r)\big[F_X(A\cdot m) - F_X(2r)\big] \\
&+ (A\cdot m - r)\big[F_X(2F + A\cdot m) - F_X(A\cdot m)\big] \Big\} \qquad ; A\cdot m \geq 2r
\end{aligned}$$

The result is similar for $A \cdot m < 2r$, except the first two terms are zero in this case:

$$P(c_i = FRR; A) = \frac{A\cdot m - r}{C(2F + A\cdot m - 2r)} \Big\{ F_X(2F + A\cdot m) - F_X(A\cdot m) \Big\} \quad ; A\cdot m < 2r \tag{9}$$

1.2 Read probabilities

For each class of informative reads, the read probability describes the distribution of the informative characteristic of the class, given an underlying allele A **(Figure 2)**. The details of read probability for each class of informative reads is presented in the following sections.

1.2.1 Enclosing Reads

Enclosing reads contain the whole repeating region, as well as flanking regions before and after. Therefore, the number of copies can be directly extracted after performing the local realignment step..

The HipSTR stutter model [1] explains the distribution of the number of repeat copies in enclosing reads. Equation (10) shows the probability of a read with r_i copies having an error of length δ copies compared to the underlying true number of copies A. In this model, u and d correspond to the probability of stutter adding or removing copies of the motif, and ρ_s is the parameter of the geometric distribution that governs the number of stutter deviations from true number of copies A.

$$P(r_i - A = \delta | c_i = E; A) = \begin{cases} 1 - u - d & \delta = 0 \\ u\rho_s (1 - \rho_s)^{\delta - 1} & \delta > 0 \\ d\rho_s (1 - \rho_s)^{-\delta - 1} & \delta < 0 \end{cases} \tag{10}$$

1.2.2 Flanking Reads

Flanking reads with n copies of the motif imply that one of the alleles has at least n copies of the motif. We use a uniform distribution (similar to [2]) to model the distribution of reads in the flanking class:

$$P(r_i = n | c_i = F; A) = \begin{cases} \frac{1}{A} & n \leq A \\ 0 & n > A \end{cases} \tag{11}$$

1.2.3 Spanning Reads

Fragments that completely span the TR region can create spanning read pairs. Spanning read pairs consist of two mates that are mapped to the flanking region before and after the TR. During alignment, spanning reads originating from an expanded TR allele experience a decrease in the observed fragment length (**Figure 2C-D**). Therefore, the distribution of fragment lengths for spanning reads is similar to the fragment length distribution in section 1.1.3, with a decrease in average fragment length by an amount equal to the size of expansion. If the reference has R copies of an m base pair motif, we can describe the class probability of spanning reads with the following Gaussian distribution:

$$P(r_i | c_i = S) \sim N(\mu - (A - R) \cdot m, \sigma) \tag{12}$$

1.2.4 Fully Repetitive Reads (FRRs)

FRR reads are extracted from both on and off target regions to create the repetitive read count term in the likelihood model. Here we discuss another informative aspect of FRR reads, the distance of an anchored mate to the repeat region (**Figure 2**).

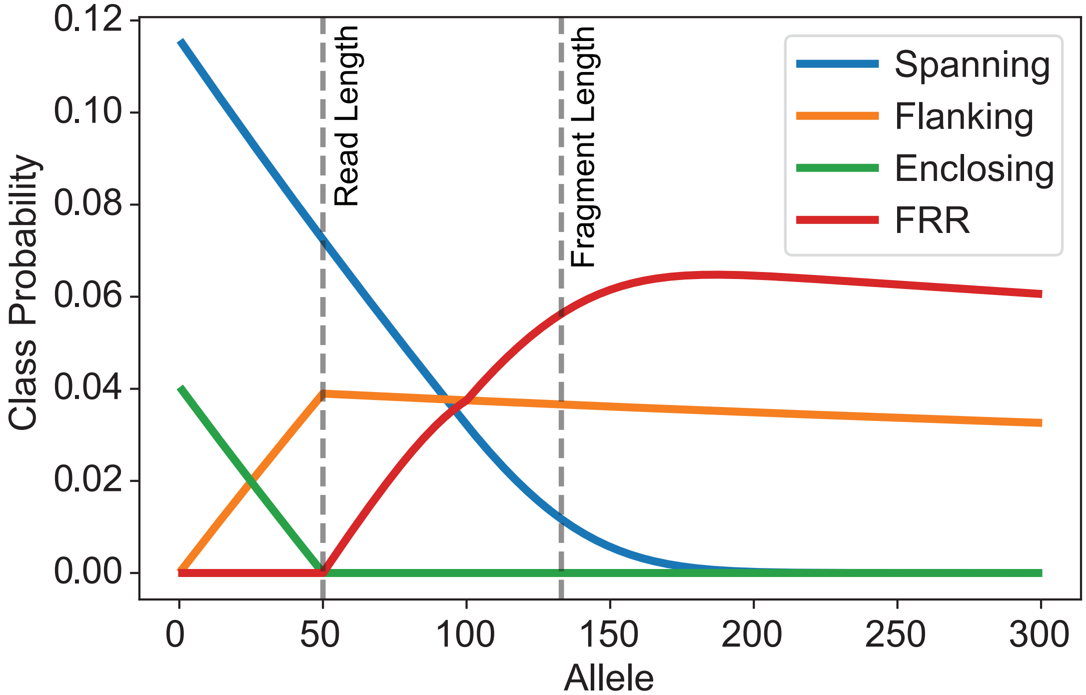
Anchored FRRs are read pairs that contain one read completely consisting of repeats, while the other mate pair is mapped to the flanking region before or after the TR. Using the fragment length distribution (see 1.1.3), we model the distance of the anchor read from the repeat region (shown by Ω) to obtain read probability of this class of reads. We use the notation from section 1.1.3 to derive the read probability of anchored FRR reads.

$$\begin{aligned} P(r_i | c_i = FRR; A) &= P(\Omega + 2r < \Delta < \Omega + r + L) && (13) \\ &= F_\Delta(\Omega + r + L) - F_\Delta(\Omega + 2r) && (14) \\ &= \frac{1}{C}[F_X(\Omega + r + L) - F_X(\Omega + 2r)] && (15) \end{aligned}$$

On the other hand, fragments that originate from within the repeating region generate FRR read pairs (both mates repetitive). These read pairs do not have an anchor, and are most likely aligned to one of the off-target regions associated with the TR. These read pairs contribute to both FRR count term (adding two FRR reads) and read pair term (FRR class probability computed for $\Omega = -r$).

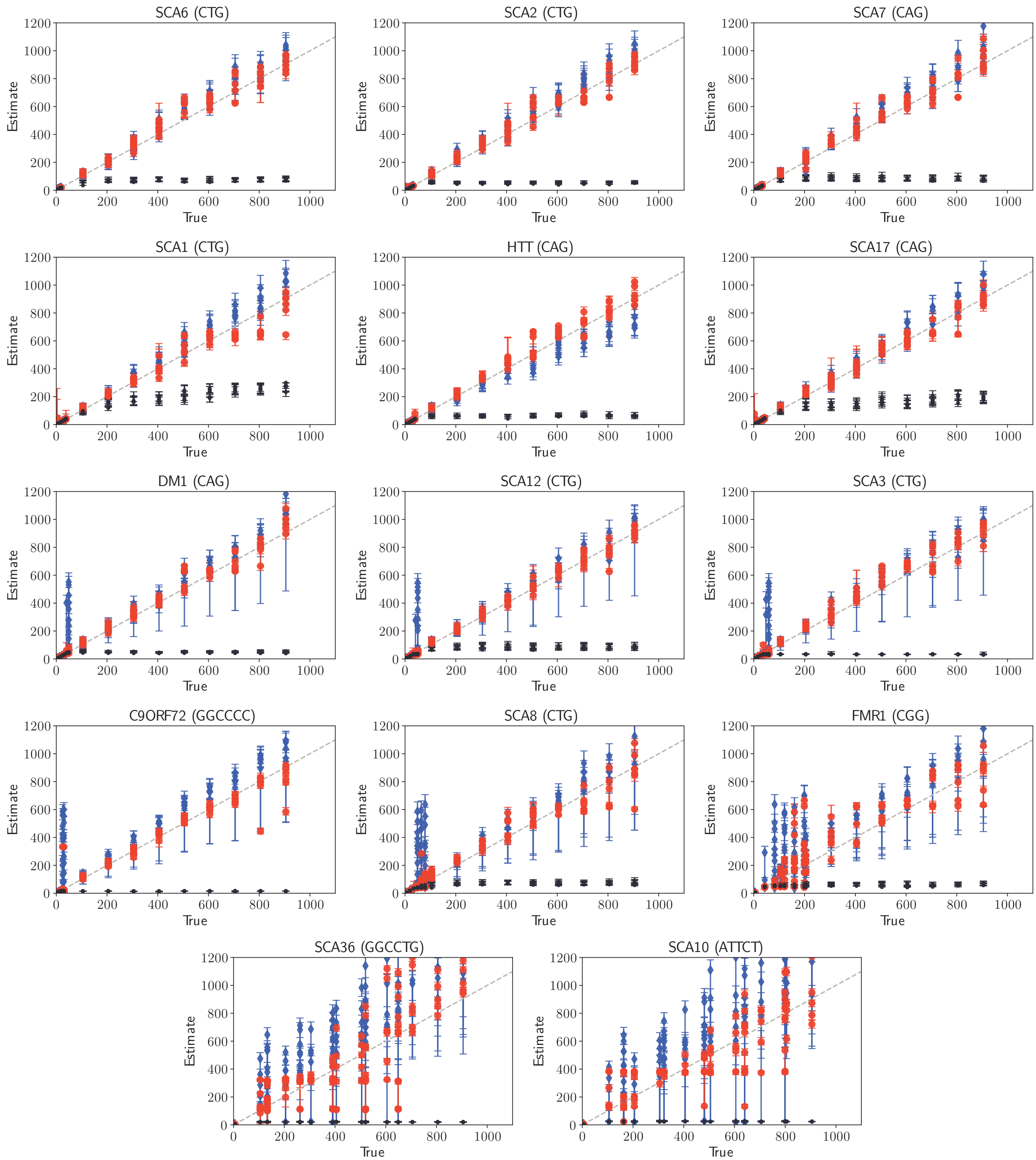
2 Supplementary Figures

Supplementary Figure 1



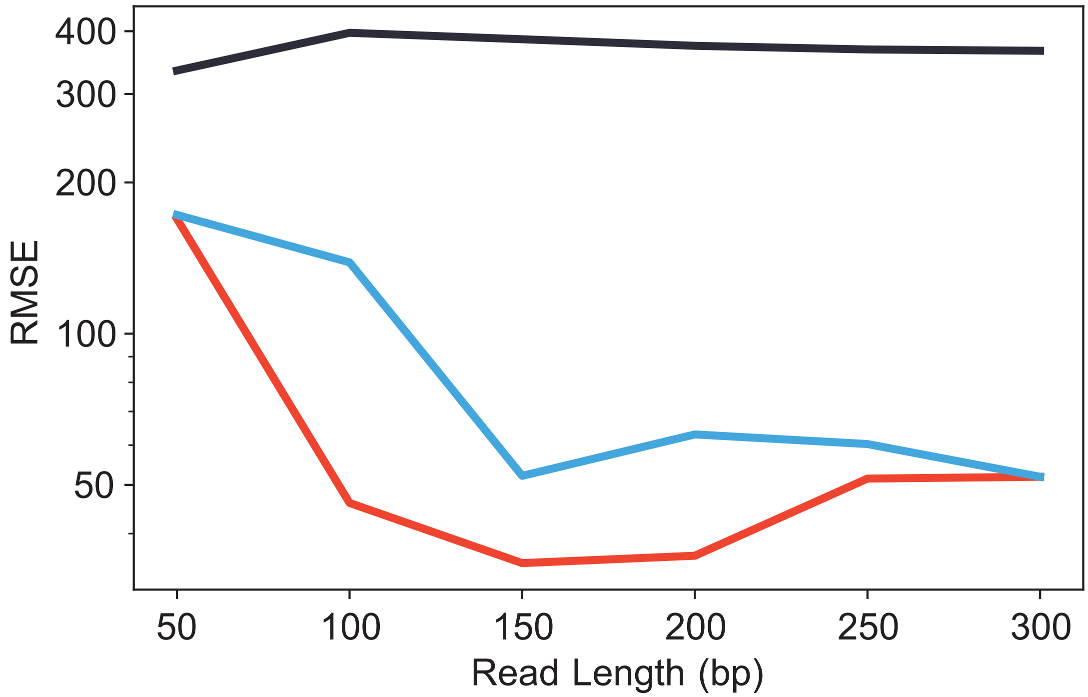
Class probabilities as a function of TR length. The x-axis shows the allele length in number of repeats. The y-axis shows the probability that a read mapped to the TR region would be from each class. Results were calculated using a 3bp long repeat unit, read length=100bp, and fragment length=400bp. Blue=spanning reads, green=flanking reads, red=enclosing reads, and purple=FRR reads.

Supplementary Figure 2



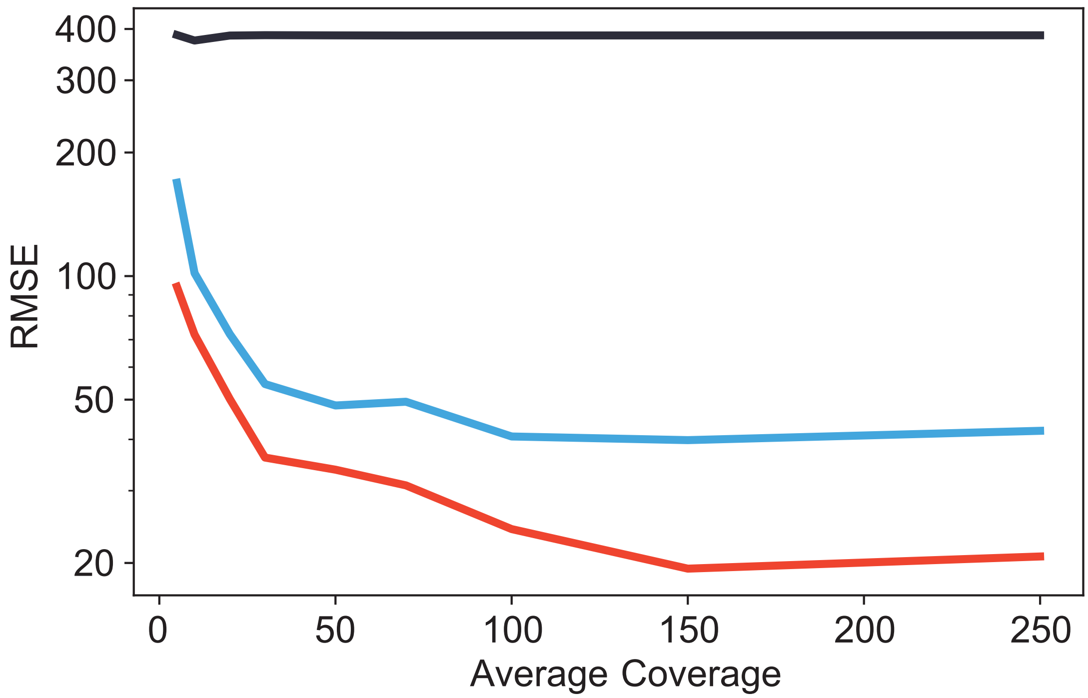
Comparison of true vs. estimated repeat number on simulated data for different loci The x-axis shows the simulated allele length in number of repeats. The y-axis shows the estimated allele length in number of repeats. The accuracy (root mean square error) for each panel is plotted in Figure 3A. The motif for each locus is specified in parentheses in plot title. In all panels, red=GangSTR; blue=ExpansionHunter; black=Tredparse.

Supplementary Figure 3



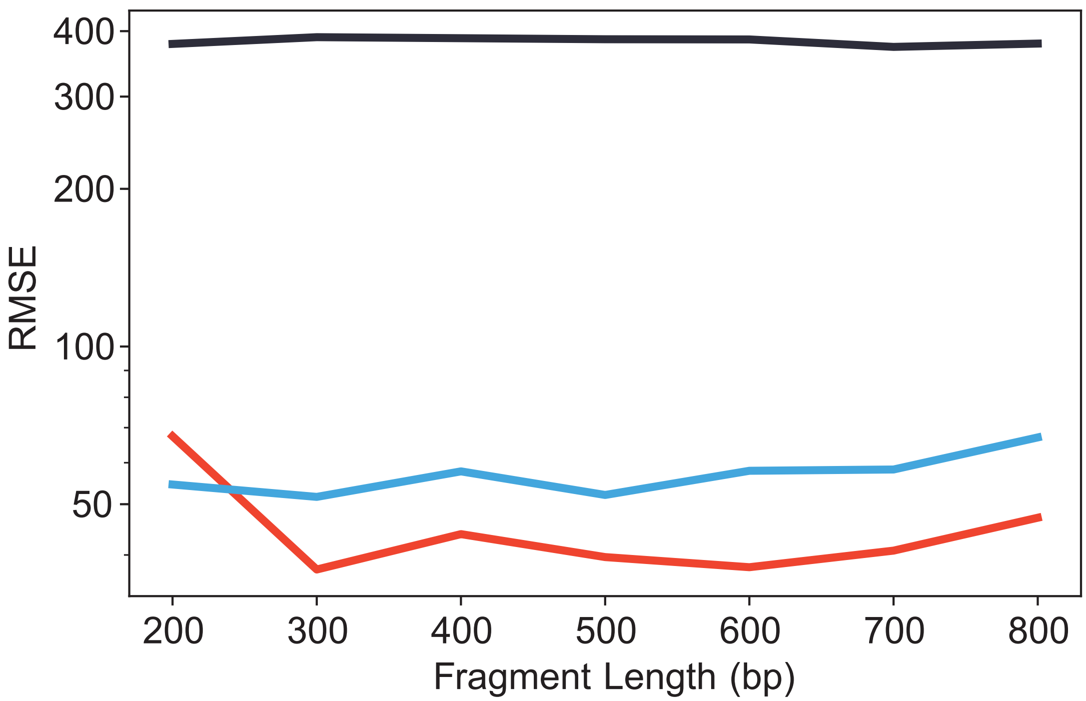
Estimation accuracy for simulated samples of HTT vs. read length Root Mean Square Error (RMSE) for estimation of simulated samples of the HTT locus with different read lengths. Red=GangSTR; blue=ExpansionHunter; black=Tredparse.

Supplementary Figure 4



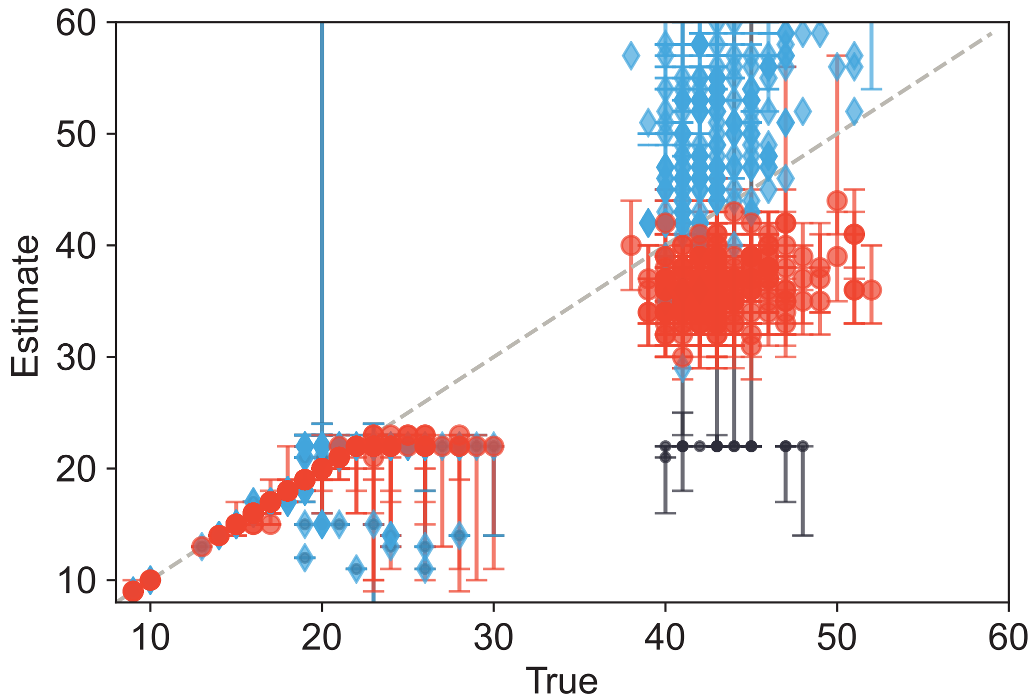
Estimation accuracy for simulated samples of HTT vs. average coverage Root Mean Square (RMSE) for estimation of simulated samples of the HTT locus with different coverages. Red=GangSTR; blue=ExpansionHunter; black=Tredparse.

Supplementary Figure 5



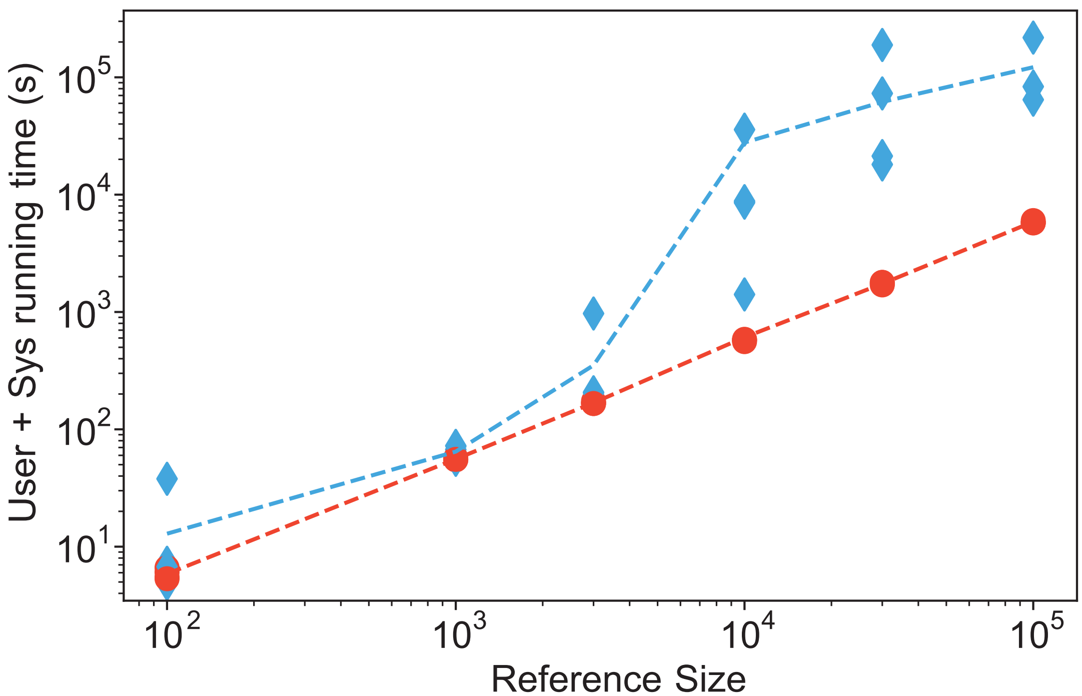
Estimation accuracy for simulated samples of HTT vs. fragment length Root Mean Square (RMSE) for estimation of simulated samples of HTT locus with different fragment lengths. Red=GangSTR; blue=ExpansionHunter; black=Tredparse.

Supplementary Figure 6



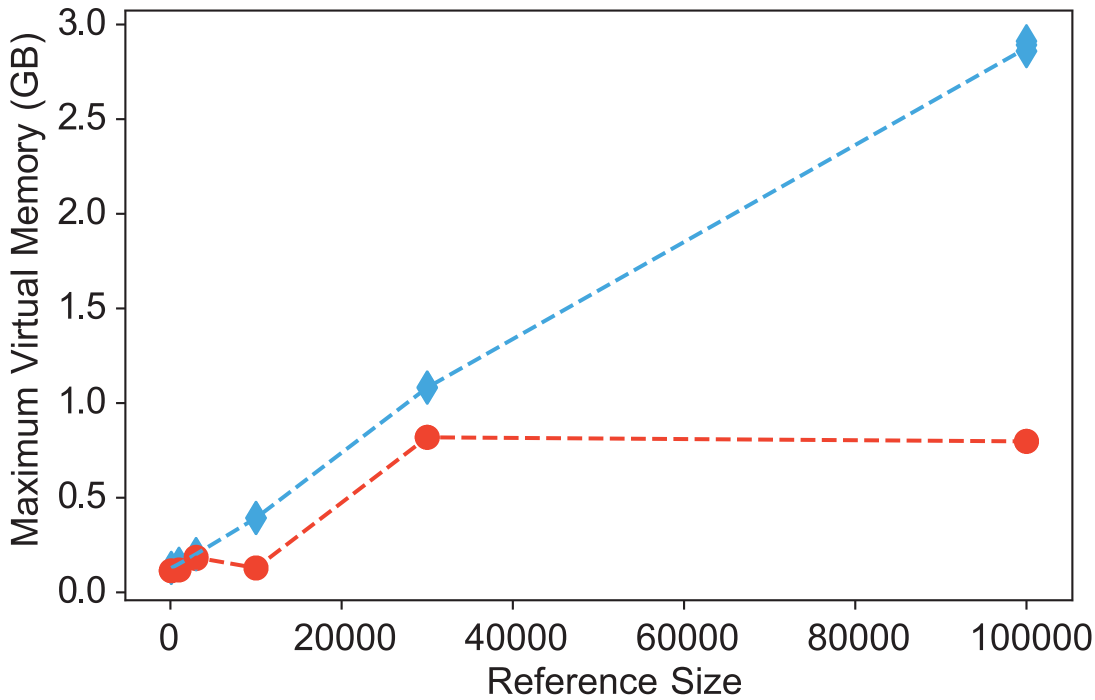
Comparison of true vs. estimated repeat number using real HTT exome data The x-axis shows the experimentally validated allele length in number of repeats. The y-axis shows the estimated allele length in number of repeats. Gray dashed line gives the diagonal. red=GangSTR; blue=ExpansionHunter; black=Tredparse.

Supplementary Figure 7



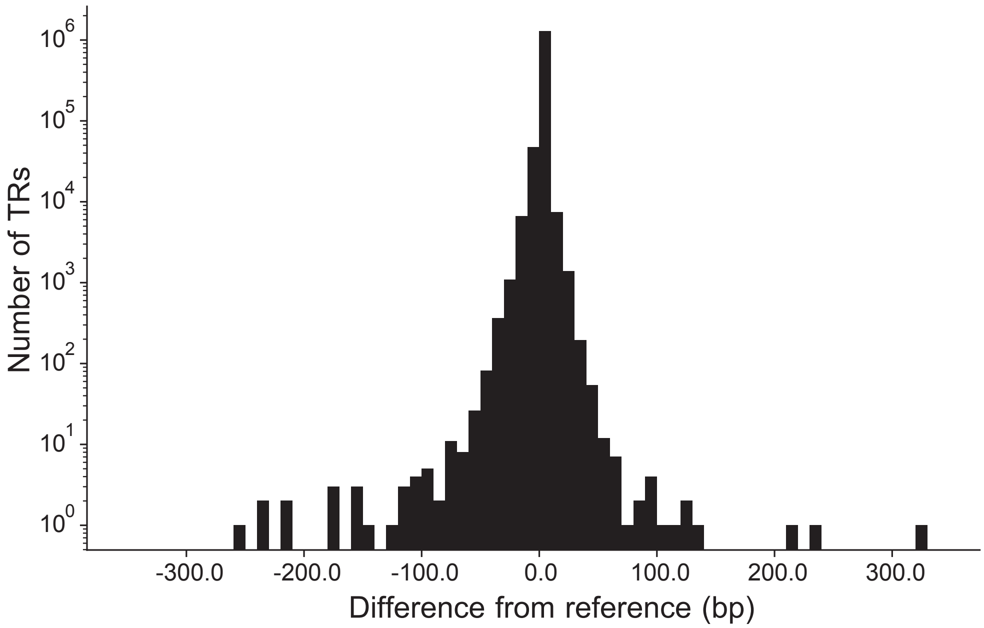
Running time of GangSTR and ExpansionHunter vs. reference size The x-axis shows the number of TRs in the reference set used. The y-axis shows running time (User + Sys) in seconds. Lines give mean value across 5 runs. Points ("x") give raw data values for each of 5 runs. For two runs with 10^5 TRs ExpansionHunter did not run to completion. Red=GangSTR, blue=ExpansionHunter.

Supplementary Figure 8



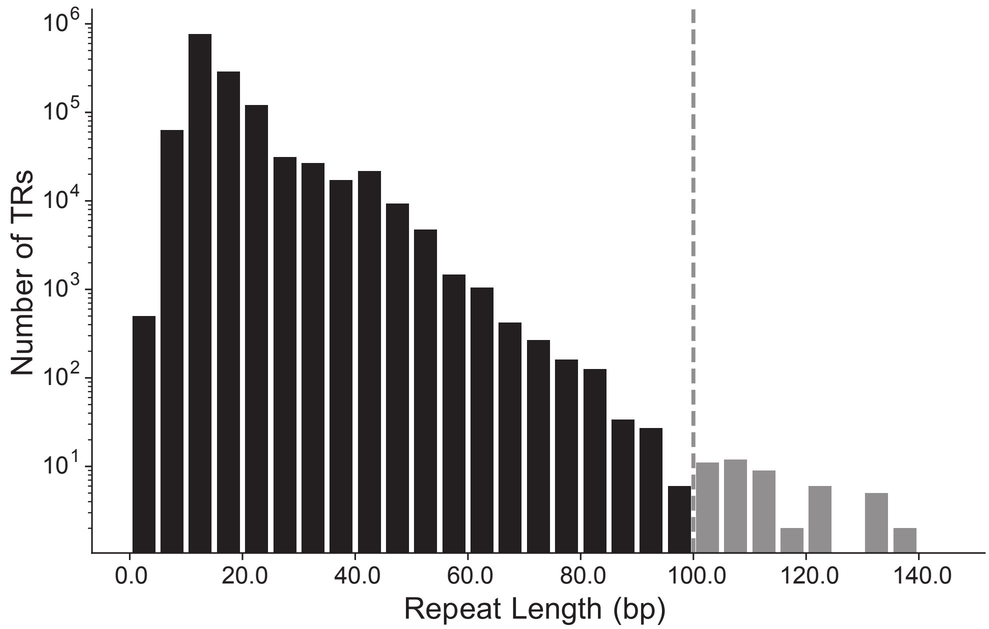
Peak memory usage by GangSTR and ExpansionHunter vs. reference size The x-axis shows the number of TRs in the reference set used. The y-axis shows maximum virtual memory usage in gigabytes. Lines give mean value across 5 runs. Points ("x") give raw data values for each of 5 runs. Red=GangSTR, blue=ExpansionHunter.

Supplementary Figure 9



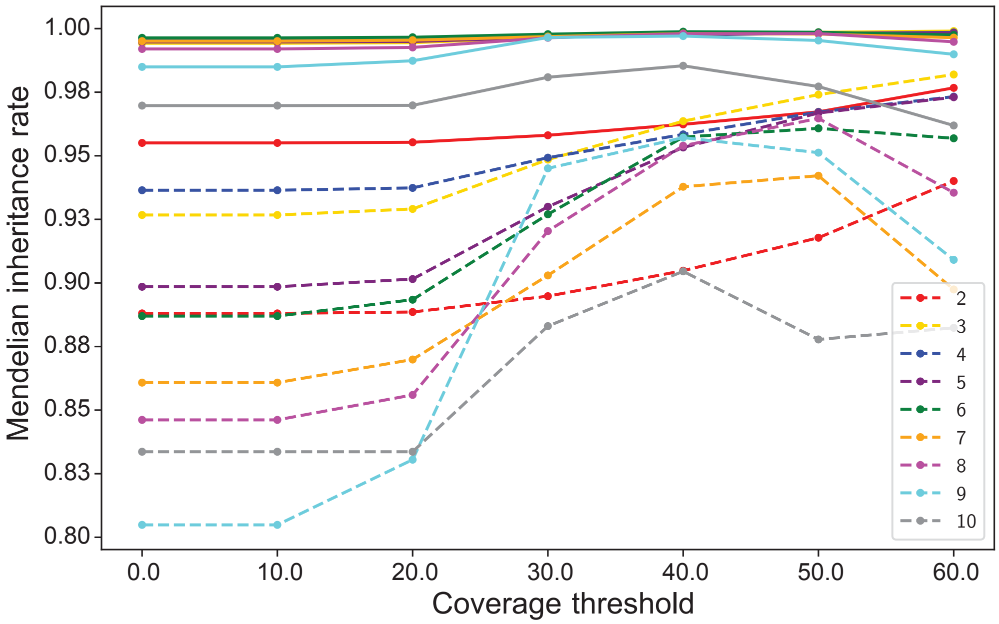
Distribution of repeat lengths in NA12878 compared to the hg19 reference. Y-axis is on a log10 scale.

Supplementary Figure 10



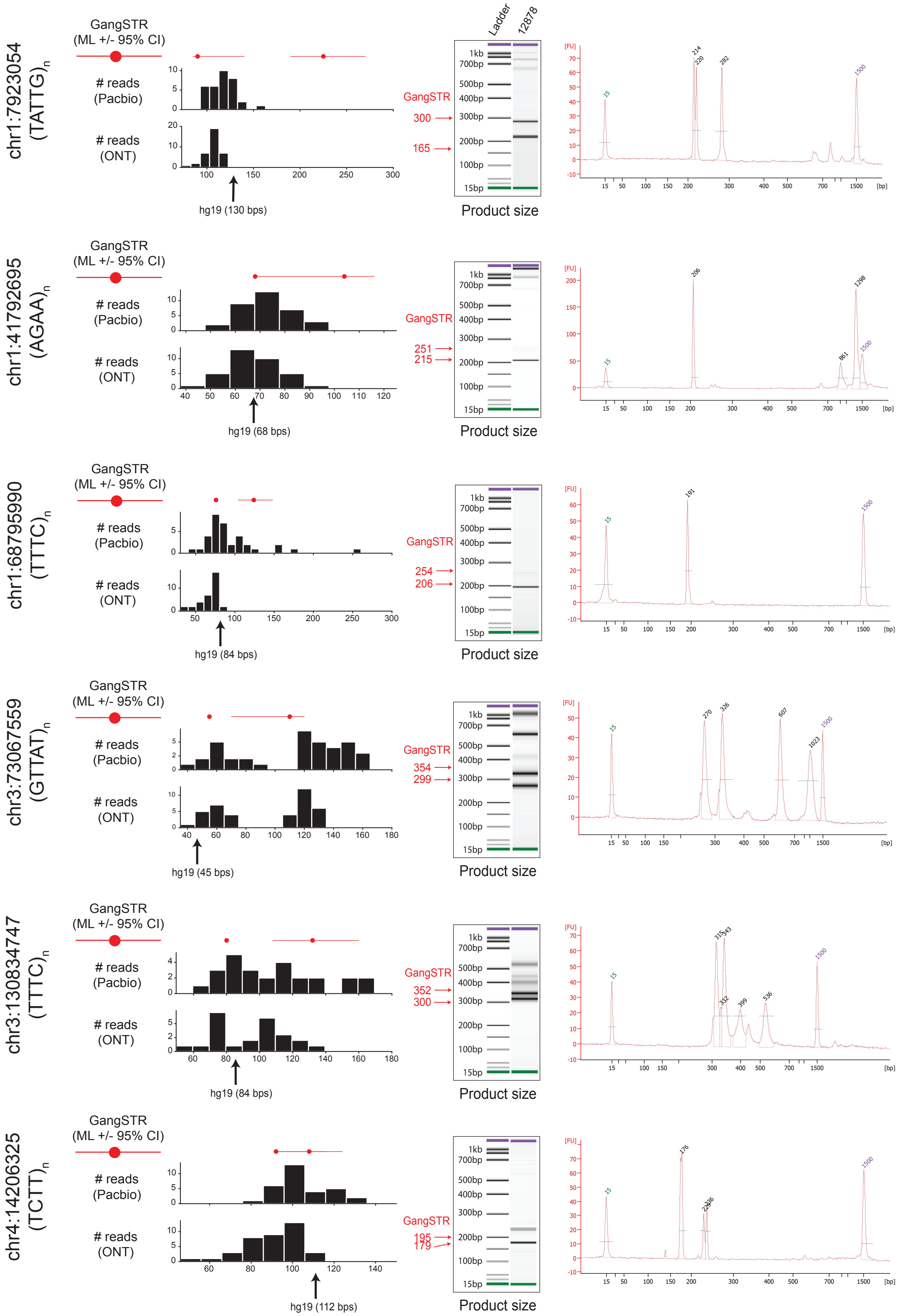
Distribution of total repeat lengths in NA12878. Y-axis is on a log10 scale. Gray bars to the right of the dashed line indicate alleles longer than the read length of 101bp.

Supplementary Figure 11



Mendelian inheritance of GangSTR genotypes in a CEU trio as a function of the number of informative read pairs Mendelian inheritance of GangSTR genotypes in a CEU trio as a function of the number of informative read pairs. Colors denote repeat lengths. Solid lines give mean Mendelian inheritance rate across all TRs, computed using maximum likelihood GangSTR genotypes as described in Methods. Dashed lines are computed after excluding loci where all three samples were homozygous for the reference allele.

Supplementary Figure 12



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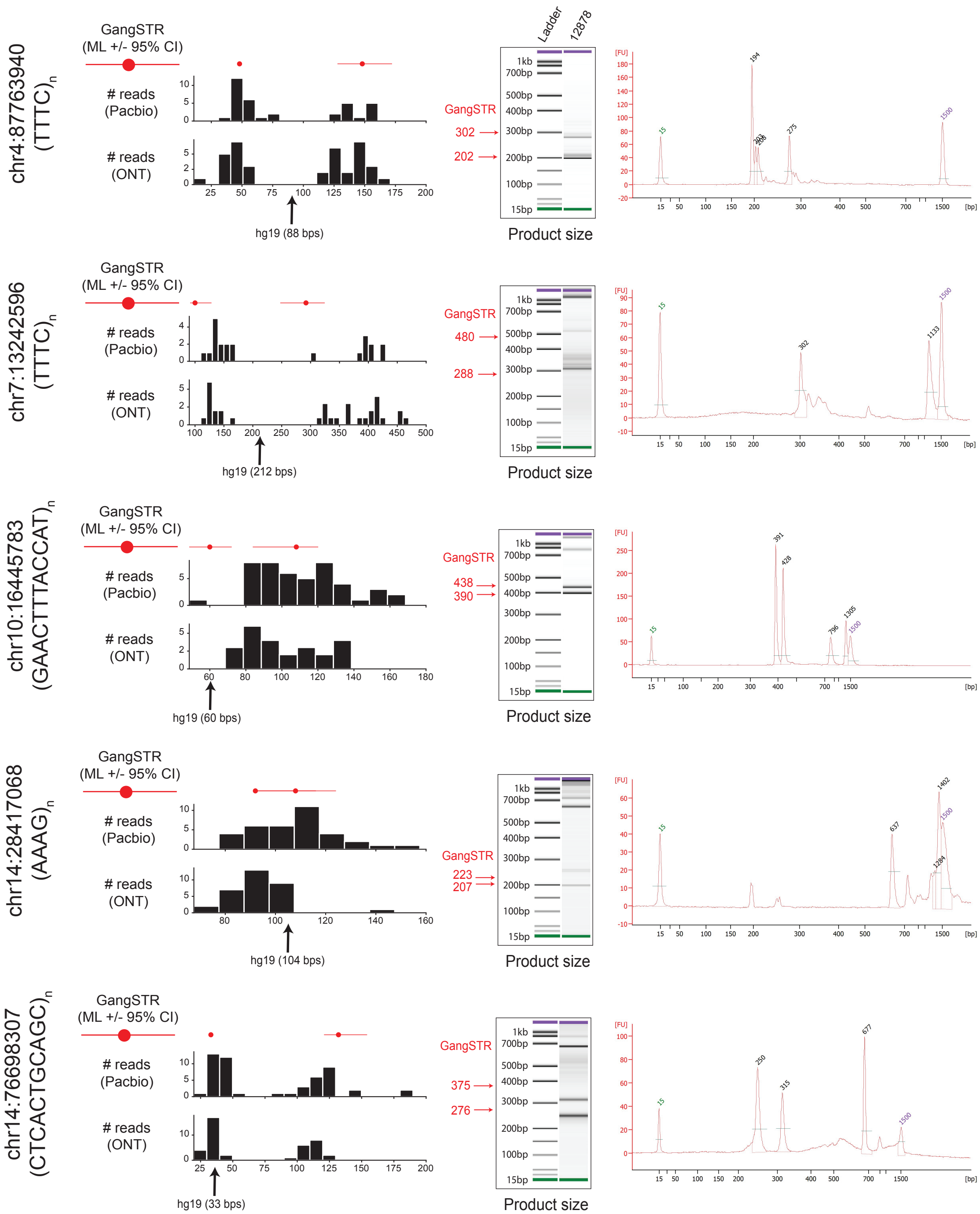

Discovery and validation of genome-wide TR expansions. For each of the 9 TRs shown, left plots compare GangSTR genotypes to those predicted by long reads. Red dots give the maximum likelihood repeat lengths predicted by GangSTR and red lines give the 95% confidence intervals for each allele. Black histograms give the distribution of repeat lengths supported by PacBio (top) and ONT (bottom) reads. The black arrow denotes the length in hg19. The middle plots show PCR product sizes for each TR as estimated using capillary electrophoresis. Left bands show the ladder and right bands show product sizes in NA12878. Green and purple bands show the lower and upper limits of the ladder, respectively. Red arrows and numbers give product sizes expected for the two alleles called by GangSTR. Right plots give the capillary electrophoresis traces produced by the Agilent Bioanalyzer.

3 Supplementary Tables

Supplementary Table 1: Target pathogenic repeats used in benchmarking experiments.

Abbreviation	Disease	Gene	Motif	Repeat location	Pathogenic cutoff	Simulation repeat range[a]
SCA6	Spinocerebellar ataxia 6	*CACNA1A*	CTG	chr19:13207859-13207897 (hg38) chr19:13318673-13318711 (hg19)	20 (60 bps)	[4, 7, 10, 13, 16, 19]
SCA2	Spinocerebellar ataxia 2	*ATXN2*	CTG	chr12:111598951-111599019 (hg38) chr12:112036755-112036823 (hg19)	33 (99 bps)	[2, 8, 14, 20, 26, 32]
SCA7	Spinocerebellar ataxia 7	*ATXN7*	CAG	chr3:63912686-63912715 (hg38) chr3:63898362-63898391 (hg19)	34 (102 bps)	[3, 9, 15, 21, 27, 33]
SCA1	Spinocerebellar ataxia 1	*ATXN1*	CTG	chr6:16327636-16327722 (hg38) chr6:16327867-16327953 (hg19)	39 (117 bps)	[3, 10, 17, 24, 31, 38]
HTT	Huntingtons Disease	*HTT*	CAG	chr4:3074877-3074933 (hg38) chr4:3076604-3076660 (hg19)	40 (120bps)	[4, 11, 18, 25, 32, 39]
SCA17	Spinocerebellar ataxia 17	*TBP*	CAG	chr6:170561908-170562021 (hg38) chr6:170870996-170871109 (hg19)	43 (123 bps)	[2, 10, 18, 26, 34, 42]
DM1	Myotonic Dystrophy 1	*DMPK*	CAG	chr19:45770205-45770264 (hg38) chr19:46273463-46273522 (hg19)	50 (150 bps)	[4, 13, 22, 31, 40, 49]
SCA12	Spinocerebellar ataxia 12	*PPP2R2B*	CTG	chr5:146878729-146878758 (hg38) chr5:146258292-146258321 (hg19)	51 (153 bps)	[5, 14, 23, 32, 41, 50]
SCA3	Spinocerebellar ataxia 3	*ATXN3*	CTG	chr14:92071011-92071034 (hg38) chr14:92537355-92537378 (hg19)	60 (120bps)	[4, 15, 26, 37, 48, 59]
C9ORF72	ALS	*C9ORF72*	GGCCCC	chr9:27573529-27573546 (hg38) chr9:27573527-27573544 (hg19)	31 (186 bps)	[5, 10, 15, 20, 25, 30]
SCA8	Spinocerebellar ataxia 8	*ATXN8OS*	CTG	chr13:70139384-70139428 (hg38) chr13:70713516-70713560 (hg19)	80 (240 bps)	[4, 19, 34, 49, 64, 79]
FMR1	Fragile X syndrome	*FMR1*	CGG	chrX:147912051-147912110 (hg38) chrX:146993569-146993628 (hg19)	200 (600 bps)	[4, 43, 82, 121, 160, 199]
SCA36	Spinocerebellar ataxia 36	*NOP56*	GGCCTG	chr20:2652734-2652757 (hg38) chr20:2633380-2633403 (hg19)	650 (3900 bps)	[4, 133, 262, 391, 520, 649]
SCA10	Spinocerebellar ataxia 10	*ATXN10*	ATTCT	chr22:45795355-45795424 (hg38) chr22:46191235-46191304 (hg19)	800 (4000 bps)	[4, 163, 322, 481, 640, 799]

[a]The other allele for all TRs covers the range (5, 1005) with step size 100. Simulation repeat range is given in terms of repeat copy number.

Repeat locations are given for both hg19 and hg38 genomic coordinates.

Supplementary Table 2: Candidate TRs long alleles (>101bp) in NA12878.

Coord (hg19)	Refcopy[a]	Motif	GangSTR[b]	P(het)[c]	P(hom)[d]	MI[e]	Parent[f]	PacBio[g]	ONT[h]	Assembly[i]
chr1:2897558	4	AACAGGAGGTCTGGT	1,7	1.00	0.00	True	NA	147	108	2.9,6.0
chr1:7923054	26	AATAC	18,45	0.93	0.07	True	NA12891,NA12892	154	123	22.4,22.4
chr1:22720748	13	AAAG	16,30	1.00	0.00	True	NA12891,NA12892	163	87	21.5,15.8
chr1:35267829	44	AAACC	20,90	0.28	0.72	True	NA12891,NA12892	377	275	44.8,46.0
chr1:41792695	17	AAAG	17,26	1.00	0.00	True	NA12891	225	93	16.5,18.8
chr1:61347419	3	AAAG	3,33	1.00	0.00	True	NA12891,NA12892	64	23	2.8,2.8
chr1:64329379	19	AATAC	17,22	1.00	0.00	True	NA12892	231	109	19.8,17.8
chr1:68795990	21	AAAG	19,31	1.00	0.00	True	NA12892	363	85	19.0,18.8
chr1:154098099	29	AAGG	26,26	0.74	0.26	NA	NA12891	241	217	NA,NA
chr1:208680308	6	AATGTGGTATATATACAT	4,5	0.67	0.29	NA	NA	168	141	4.9,5.9
chr10:16445783	5	AAAGTTCATGGT	5,9	1.00	0.00	True	NA12891,NA12892	169	135	6.9,9.8
chr10:99438638	60	AC	46,59	0.73	0.27	True	NA12891,NA12892	147	168	51.5,NA
chr10:125413213	15	AAAGG	14,21	1.00	0.00	True	NA	192	134	13.8,21.4
chr11:17574076	3	ACACAGGACAGGTGGGGG	6,6	0.13	0.87	NA	NA	557	495	23.9,24.0
chr11:31932832	26	AAAGG	20,49	0.58	0.42	True	NA12891,NA12892	280	199	35.2,26.8
chr11:107461059	53	AG	47,62	0.77	0.23	True	NA12891,NA12892	223	89	NA,46.5
chr12:15314073	22	AAAG	22,28	0.98	0.02	True	NA12891,NA12892	211	127	27.8,22.8
chr12:117836405	20	AAAAT	9,21	1.00	0.00	True	NA12891	138	111	9.0,19.6
chr13:29027163	23	AAAGG	16,23	0.88	0.12	True	NA12891,NA12892	205	105	19.6,20.8
chr13:44716269	35	AGCCG	14,22	1.00	0.00	True	NA12891	182	133	16.2,21.8
chr13:87882390	3	AAAG	3,33	1.00	0.00	True	NA12891,NA12892	92	60	5.0,2.8
chr13:96047512	16	AAAGG	17,24	1.00	0.00	True	NA12891	155	113	NA,21.6
chr14:28417068	26	AAAG	23,27	0.80	0.20	True	NA12891,NA12892	216	143	24.8,24.8
chr14:76698307	3	ACTGCAGCCTC	3,12	1.00	0.00	True	NA12891,NA12892	535	125	9.9,2.9
chr15:54367612	5	AAGCTCCGGCTCACTGC	4,5	0.88	0.11	True	NA	189	94	5.1,5.0
chr15:61429219	20	AAAG	21,26	1.00	0.00	True	NA12892	143	112	20.8,NA
chr15:90651456	13	AAAAT	8,21	1.00	0.00	NA	NA	114	119	7.8,NA
chr16:3899380	55	AC	36,55	0.97	0.03	True	NA12891,NA12892	584	124	46.0,46.0
chr16:50509578	53	AAAG	17,39	1.00	0.00	True	NA12891,NA12892	169	90	20.8,18.2
chr16:58865692	10	AAGGAGGG	7,14	1.00	0.00	True	NA12891,NA12892	140	110	13.8,12.9
chr17:32835083	21	AAAGG	18,27	0.92	0.08	True	NA12891,NA12892	146	146	22.8,16.0
chr19:39720793	15	AAAGG	20,26	0.55	0.45	True	NA12891,NA12892	218	275	NA,NA
chr2:54425083	18	AATAC	17,24	1.00	0.00	True	NA12892	156	140	16.8,16.8
chr2:163609414	25	AAAAG	67,89	0.00	1.00	True	NA12891,NA12892	426	287	51.0,51.6
chr21:36720944	18	AATAG	19,37	0.78	0.22	True	NA12891,NA12892	182	156	28.8,23.8
chr22:47769363	3	AAGGGAGGCCAGGAGGAG	3,6	1.00	0.00	True	NA12891	117	113	2.9,5.9
chr3:5830605	11	AAATGCACAGGAAT	6,16	0.61	0.39	True	NA12891,NA12892	230	180	11.9,10.9
chr3:73067559	9	AACAT	11,22	1.00	0.00	True	NA12892	165	135	23.8,NA
chr3:86384908	19	AAAAT	18,22	0.70	0.30	NA	NA	162	120	19.0,19.0
chr3:130834747	21	AAAG	20,33	1.00	0.00	True	NA12892	167	135	20.8,20.2
chr4:14206325	28	AAAG	23,27	0.90	0.10	True	NA12891,NA12892	203	115	24.8,24.0
chr4:21716410	61	AAAAT	18,48	0.71	0.29	True	NA12891,NA12892	293	287	42.8,52.8
chr4:87763940	22	AAAG	12,37	1.00	0.00	True	NA12892	303	168	12.8,12.2
chr4:90302001	3	AAAG	3,26	1.00	0.00	True	NA	129	48	6.5,5.5
chr5:75792512	3	AAAG	3,28	1.00	0.00	True	NA12891,NA12892	67	18	4.8,2.8
chr5:157994659	20	AAAG	17,26	1.00	0.00	True	NA12891	143	107	20.8,19.8
chr6:128925487	18	AGAGCGGG	5,17	1.00	0.00	True	NA12891,NA12892	515	161	15.9,17.9
chr7:2852271	12	ACATC	18,39	0.78	0.22	True	NA12891,NA12892	188	181	27.8,25.8
chr7:6460939	18	AGCGCGGGAGGCGCAGGC	4,6	0.99	0.00	True	NA12892	652	431	24.7,NA
chr7:13242596	53	AAAG	25,73	0.60	0.40	True	NA12891,NA12892	428	469	NA,35.8
chr7:105084942	6	AACACCTATAGC	3,8	0.88	0.00	True	NA	544	318	NA,NA
chr7:127898719	17	AAAG	22,26	0.89	0.11	NA	NA12892	184	126	29.0,29.8
chr7:134201476	15	AAAAG	15,22	1.00	0.00	True	NA12891	156	115	15.4,15.0
chr8:119927182	13	AGAGAGCG	11,20	0.90	0.10	True	NA12891,NA12892	263	136	13.9,13.9
chr8:130361920	15	AAAAT	16,21	0.88	0.12	NA	NA12892	141	116	20.8,19.8
chr8:140126207	5	AAGACGACTCCACCCCACAG	3,6	1.00	0.00	NA	NA	133	121	3.0,5.0

[a]Number of copies of the motif in hg19

[b]Maximum likelihood diploid repeat copy number returned by GangSTR.

[c]Posterior probability that the genotype is heterozygous for one allele greater than 101bp.

[d]Posterior probability that the genotype is homozygous for both alleles greater than 101bp.

[e]Indicates whether confidence intervals in the trio are consistent with Mendelian inheritance. NA indicates one or more parents failed filtering steps so Mendelian inheritance couldn't be determined.

[f]Lists which parents show evidence (>80% posterior probability) of an expansion

[g]Maximum allele length supported by PacBio reads for NA12878. "-" indicates no PacBio reads were found in the region.

[h]Maximum allele length supported by ONT reads for NA12878. "-" indicates no ONT reads were found in the region.

[i]Diploid repeat copy number from maternal and paternal TrioCanu assembly (in that order)

Supplementary Table 3: Enrichment of motifs with long alleles in NA12878.

Motif	Num. TRs	P-val
AAAG	17	1.23e-10
AAAGG	6	6.15e-08
AATAC	3	1.51e-05
AAAAT	5	9.15e-02
AAAAG	2	4.10e-01
AC	2	9.41e-01

All motifs found at least twice in long alleles (>101bp) in NA12878 are shown. P-values were computed using a one-sided Fisher's exact test.

Supplementary Table 4: Comparison of STRetch and GangSTR output.

Chrom	STR Pos (hg19)	Motif	hg19 copy num	STRetch copy num [a]	GangSTR gt [b]	GangSTR filter [c]	QEXP [d]
chr20	49282720	AAAAG	7	23.90	.	NOCALL	.
chr3	121505017	AAAAG	8	24.90	13,13	PASS	1.00,0.00,0.00
chr4	36460354	ACACAT	7	17.70	12,12	PASS	0.98,0.02,0.00
chr7	2852270	ACATC	11	23.80	18,39	PASS	0.00,0.78,0.22
chr6	72287642	AGAGAT	3	12.80	.	SpanBoundOnly	.
chr3	47788930	AAATAT	6	12.40	10,13	PASS	1.00,0.00,0.00
chr3	123773204	AAAAAT	3	7.80	8,9	PASS	1.00,0.00,0.00
chr4	30718515	AGC	11	20.60	12,28	PASS	1.00,0.00,0.00
chr1	208440810	AGC	8	14.30	9,22	PASS	1.00,0.00,0.00
chr16	57893926	AAAAT	13	16.80	15,15	PASS	1.00,0.00,0.00
chr16	65292358	ACATAT	3	6.10	4,12	PASS	1.00,0.00,0.00
chr2	112925446	AACAT	9	12.80	.	SpanBoundOnly	.
chr4	10768264	AAAAG	14	17.80	.	SpanBoundOnly	.
chr10	49500011	AAAG	5	8.50	7,22	PASS	0.87,0.13,0.00
chr16	17564764	CCG	4	8.70	.	LowCallDepth, SpanBoundOnly	.
chr17	15378610	AAAAG	9	11.80	13,16	PASS	1.00,0.00,0.00
chr2	17512498	ACACAT	3	5.30	5,10	PASS	1.00,0.00,0.00
chr3	188449305	AAAAC	3	5.80	4,12	PASS	1.00,0.00,0.00
chr5	11846	ACCCCG	3	5.30	.	LowCallDepth	.
chr5	176523778	AGG	3	7.70	4,4	PASS	1.00,0.00,0.00
chr6	65241442	AAAAT	9	11.80	9,15	PASS	1.00,0.00,0.00
chr7	134201475	AAAAG	14	16.80	15,22	PASS	0.00,1.00,0.00
chr8	87100322	AAAAT	6	8.80	9,14	PASS	1.00,0.00,0.00
chr1	234275697	AAAAT	9	10.80	14,17	PASS	0.89,0.11,0.00
chr1	41410562	AAAGC	10	11.80	.	SpanBoundOnly	.
chr1	59446780	AAAG	41	43.30	15,17	PASS	1.00,0.00,0.00
chr1	85576133	AAAT	7	9.30	11,13	PASS	1.00,0.00,0.00
chr10	106199462	AAC	8	11.10	14,15	PASS	1.00,0.00,0.00
chr10	99438637	AC	59	63.60	46,59	PASS	0.00,0.73,0.27
chr11	62855843	AACATC	3	4.50	8,8	PASS	1.00,0.00,0.00
chr12	79152282	AATGT	11	12.80	11,12	PASS	1.00,0.00,0.00
chr13	113588869	AGC	7	10.10	9,17	PASS	1.00,0.00,0.00
chr15	75186380	AC	33	37.60	.	LowCallDepth, SpanBoundOnly	.
chr18	4057004	AC	27	31.60	24,28	PASS	1.00,0.00,0.00
chr19	53608032	AACAT	4	5.80	5,10	PASS	1.00,0.00,0.00
chr2	163609413	AAAAG	24	25.80	67,89	PASS	0.00,0.00,1.00
chr2	206247807	AGAT	13	15.30	14,22	PASS	0.89,0.11,0.00
chr21	34315567	AAAAG	7	8.80	9,14	PASS	1.00,0.00,0.00
chr22	22928364	AAAG	27	29.30	23,31	PASS	0.00,0.75,0.25
chr3	139970426	AAAGG	10	11.80	13,17	PASS	0.92,0.08,0.00
chr5	168182394	AAAG	13	15.30	13,13	PASS	1.00,0.00,0.00
chr6	43120472	AACAT	11	12.80	11,16	PASS	1.00,0.00,0.00
chr7	105372194	AAAAG	10	11.80	11,17	PASS	0.94,0.06,0.00
chr7	55955293	CCG	12	15.10	9,20	PASS	1.00,0.00,0.00
chr8	136094609	ATCCC	5	6.80	6,12	PASS	1.00,0.00,0.00

[a] Estimated repeat copy number returned by STRetch

[b] Maximum likelihood genotype (in terms of repeat copy number) returned by GangSTR.

[c] Locus-level GangSTR filters

[d] Expansion probability returned by GangSTR, which gives the probability of no expansion, a heterozygous expansion, or a homozygous expansion based on comparison to a predefined threshold. In this case the threshold was set to the read length of 101bp.

Supplementary Table 5: Primers for capillary electrophoresis validation.

Chrom	STR Pos (hg19)	Forward Primer	Reverse Primer
chr1	7923054	CAATAAGGCCTACCCTGACG	GGGCAACAAGAGCAAAACTT
chr1	41792695	AGCTGCTTGAGAAGCTGAGG	CCCCATGGCTTTAACTCACT
chr1	68795990	TTCCTCTCCCCAACACTTTTT	TGAGCCTCAGGAGATTGTTG
chr3	73067559	GGTTGACAGCGGGATTTAAG	GAGCCATGGACACATCACTG
chr3	130834747	TGGCGAGGTATTGTGGTAGA	TGACGAGTTAATGGGTGCAG
chr4	14206325	ACAAACTTCTATGGGCTCGAT	CCTGGGCAAAGAGAGTGAAA
chr4	87763940	AGCTGTCCTGAGTTGCATCA	GACTGAGGCAGGAGAAATGC
chr7	13242596	GCATTTTCCTGATGGCTAAA	TTAGCCGGGTGTGGTAGC
chr10	16445783	TGCCCAATAAGTATGAGAAGAACA	AAGTTCAAAAGGCCAGACCA
chr14	28417068	CTGGGCGATAGAGCAAGACT	CCCTCATACCAAAGTGAACAAA
chr14	76698307	ATAGAGTGCAGTGGGGCAAA	GAGCCCAAGAGTTCAACACC

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