CORRECTION

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Author Correction: Predictable and precise template–free CRISPR editing of pathogenic variants

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Correction to: *Nature* https://doi.org/10.1038/s41586-018-0686-x, published online 07 November 2018.

In this Article, a data processing error had a minor effect on Fig. 3e and Extended Data Table 2. The error was caused by a single line of code used to analyse some of the high-throughput DNA sequencing (HTS) data, which failed to re-initialize a temporary memory buffer holding data processing results for each read. This buffer was flushed at each 1% of progress during data processing on sequencing read files. This bug resulted in copying each sequence alignment a uniformly random number of times between 1 and 100 before calculating the average frequencies of each Cas9-induced mutant genotype. This erroneous code was only used in some data analysis, and we have re-analysed all such datasets with the corrected code. Owing to our experimental design choices of maintaining, on average, >2,000 cells per target site, and performing deep sequencing with sufficiently large depth, each unique editing outcome was independently observed many times. As a result, and by the central limit theorem, the total counts of each Cas9-induced mutant genotype clustered tightly around the ratio 50.5:1, in which 50.5 is the mean value of the integer range 1–100. All downstream calculations converted counts to relative frequency (count of each unique event, divided by the total count of all events), eliminating the 50.5× overcounting. As a result, the mean frequency of each Cas9-induced mutant genotype resulting from the erroneous code and corrected code were expected to be consistent given sufficiently large *n* for the central limit theorem. For most datasets analysed with the erroneous code, the median correlation between values reported in the paper and values re-analysed with the corrected code is >0.99, indicating that the error had a negligible effect on the reported data. However, for the experiment that corresponds to Fig. 3e and Extended Data Table 2, in which we tested ten guide RNAs (gRNAs) predicted to induce

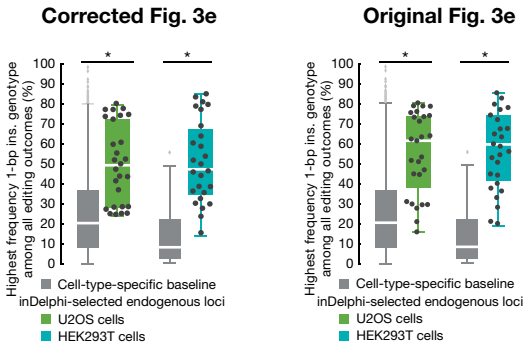

Fig. 1 | This is the corrected Fig. 3e and the incorrect Fig. 3e published in the original Article.

precision-40 1-base-pair (1-bp) insertion repair profiles in the endogenous genome of human HEK293 and U2OS cells, the corrected results differ slightly from those originally reported. Figure 3e and Extended Data Table 2 of the original Article have been corrected, and Fig. 1 of this Amendment shows the original panels, for transparency.

As a result of the re-analysis, the sentence: "We observed that 10 out of 14 predicted precision-40 1-bp insertion gRNAs induced a single 1-bp insertion genotype in ≥40% of edited products with an overall significantly higher precision ($P < 4.2 \times 10^{-8}$) than baseline data in HEK293T (median 55% compared with 25% baseline in VO target sites in HEK293) and U2OS cells (median 57% compared with 14% baseline in lib-A, U2OS, Fig. 3e)." should read "We observed that **9** out of 14 predicted precision-40 1-bp insertion gRNAs induced a single 1-bp insertion genotype in ≥40% of edited products with an overall significantly higher precision ($P < \mathbf{8.0 \times 10^{-4}}$) than baseline data in HEK293T (median **48%** compared with **14%** baseline in VO target sites in HEK293) and U2OS cells (median **50%** compared with **25%** baseline in lib-A, U2OS, Fig. 3e)." (with changes highlighted in bold).

In addition, in the sentence starting "Building on this idea of precision gRNAs,…" the reported median value among edited products should be '49%' rather than '61%'. We apologize for these errors, and the altered analysis does not change any of the conclusions of the manuscript. The original Article has been corrected online.

CORRECTIONS & AMENDMENTS

Corrected Extended Data Table 2

Gene, exon/chr, cutsite (hg19)	Observed frequency among all edited products from deep sequencing at endogenous loci (%)			
	Frameshift, U2OS	Most frequent genotype, U2OS	Frameshift, HEK293T	Most frequent genotype, HEK293T
VEGFA exon1: 458	91, 87	36, 34*	90, 90	43, 40*
VEGFR2 exon5: 2	91, 91	50, 53*	91, 91	50, 24*
PDCD1 exon5: 208	90, 90	20, 21*	91, 90	29, 13*
APOB exon25: 147	83, 83	22, 21*	87, 85	35, 18*
VEGFA exon3: 127	85, 89	27, 29*	93, 91	55, 32*
CCR5 exon1: 1941	82, 81	20, 21*	86, 84	43, 27*
CD274 exon2: 271	85, 86	9, 10*	84, 82	31, 14*
APOB exon26: 5590	91, 89	28, 25*	88	37*
VEGFR2 exon26: 19	82, 82	35, 33*	82, 82	40, 24*
CXCR4 exon1: 825	86, 86	32, 33*	91	54*
PCSK9 exon11: 15	81, 78	28, 25†	78	27†
CCR5 exon1: 885	84, 85	55, 52†	67	46†
CCR5 exon1: 1027	92, 94	61, 60†	91, 92	49, 58†
APOB exon26: 5573	93, 93	75, 74†	93, 95	69, 81†
CCR5 exon1: 61	94, 94	37, 25†	83, 89	29, 38†
CCR5 exon1: 1577	81, 81	28, 29†	80, 83	29, 43†
APOB exon22: 100	89, 89	25, 27†	91, 89	23, 38†
APOBEC3B exon3: 202	83, 84	50, 52†	75, 88	51, 60†
MACCHC chr1: 45973892	97, 95	80, 77†‡	97, 98	78, 85†‡
PROK2 chr3: 71821967	93, 94	44, 41†‡	93, 93	45, 53†‡
IDS chrX: 148564700	95, 95	72, 74†‡	93, 95	64, 80†‡
ECM1 chr1: 150484936	87, 89	44, 47†‡	89, 89	32, 35†‡
KCNH2 chr7: 150644566	40	25†‡	65, 95	35, 14†‡
LDLR chr19: 11222303	90, 91	78, 77†‡	90, 96	77, 83†‡

Original Extended Data Table 2

Gene, exon/chr, cutsite (hg19)	Observed frequency among all edited products from deep sequencing at endogenous loci (%)			
	Frameshift, U2OS	Most frequent genotype, U2OS	Frameshift, HEK293T	Most frequent genotype, HEK293T
VEGFA exon1: 458	72, 72	9, 11*	81, 71	28, 9*
VEGFR2 exon5: 2	91, 91	49, 52*	91, 91	49, 23*
PDCD1 exon5: 208	90, 90	20, 22*	91, 91	29, 13*
APOB exon25: 147	83, 83	22, 21*	87, 85	36, 17*
VEGFA exon3: 127	86, 89	28, 30*	92, 91	56, 32*
CCR5 exon1: 1941	83, 81	20, 21*	86, 84	43, 27*
CD274 exon2: 271	85, 86	9, 10*	84, 82	31, 14*
APOB exon26: 5590	91, 89	30, 27*	89	40*
VEGFR2 exon26: 19	82, 82	35, 33*	83, 82	41, 23*
CXCR4 exon1: 825	86, 86	32, 33*	91	55*
PCSK9 exon11: 15	91, 89	64, 64†	89	60†
CCR5 exon1: 885	90, 91	74, 71†	78	65†
CCR5 exon1: 1027	92, 94	62, 62†	91, 92	50, 60†
APOB exon26: 5573	93, 93	75, 74†	93, 95	69, 82†
CCR5 exon1: 61	94, 92	21, 16†	84, 88	19, 28†
CCR5 exon1: 1577	81, 81	29, 30†	80, 84	29, 46†
APOB exon22: 100	89, 90	28, 31†	90, 89	26, 40†
APOBEC3B exon3: 202	83, 83	52, 54†	74, 87	52, 62†
MACCHC chr1: 45973892	97, 95	81, 77†‡	97, 98	79, 86†‡
PROK2 chr3: 71821967	92, 93	45, 45†‡	92, 93	49, 58†‡
IDS chrX: 148564700	96, 95	73, 76†‡	93, 95	63, 79†‡
ECM1 chr1: 150484936	87, 89	47, 52†‡	88, 89	33, 37†‡
KCNH2 chr7: 150644566	46	30†‡	89, 93	71, 75†‡
LDLR chr19: 11222303	91, 92	79, 78†‡	90, 96	78, 84†‡

Fig. 2 | This is the corrected Extended Data Table 2 and the incorrect Extended Data Table 2 published in the original Article.