

# Supporting Information

## CRISPR-Based Assay for Point-of-Care Pharmacogenetic

### CYP2C19 Genotyping

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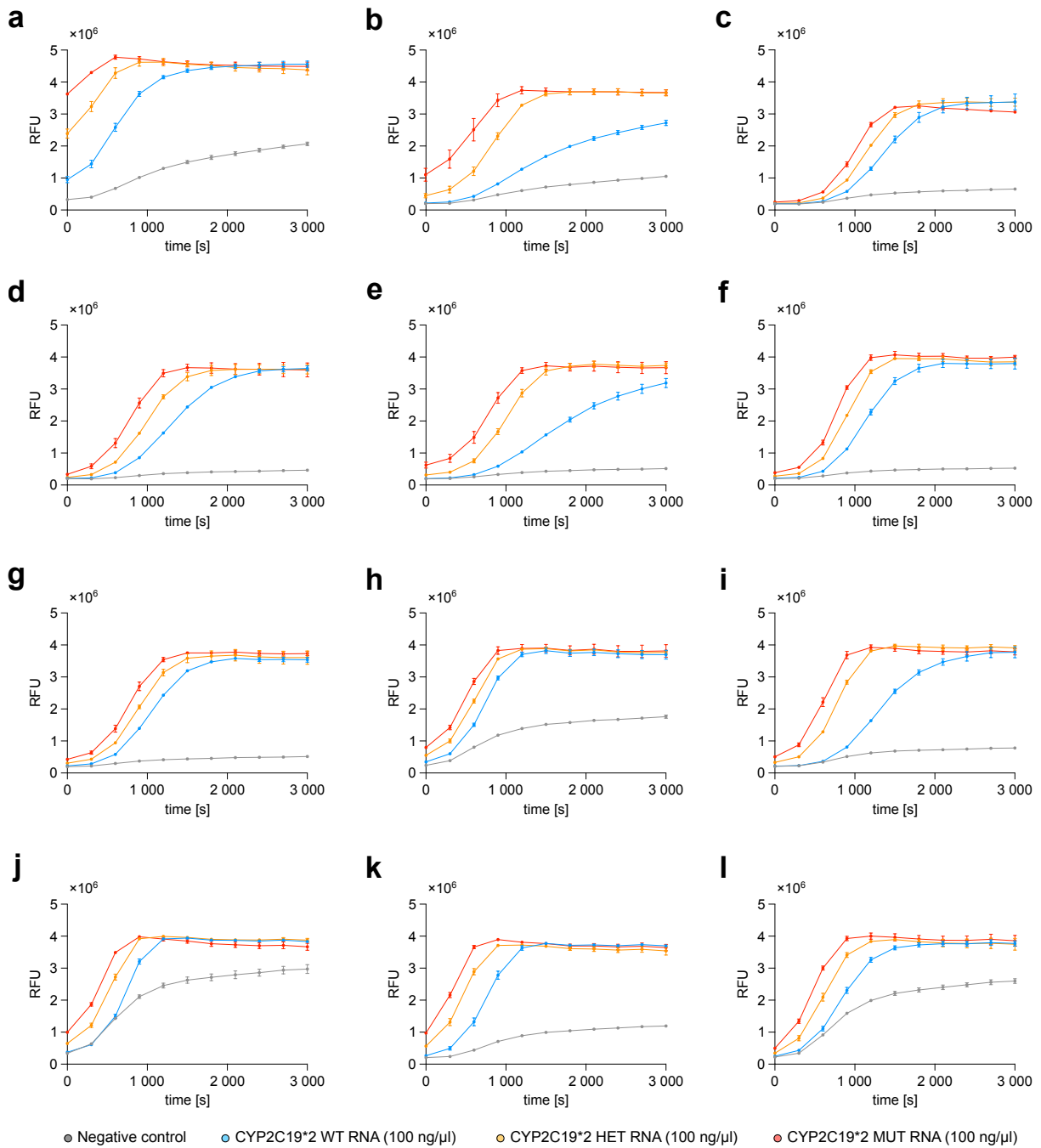
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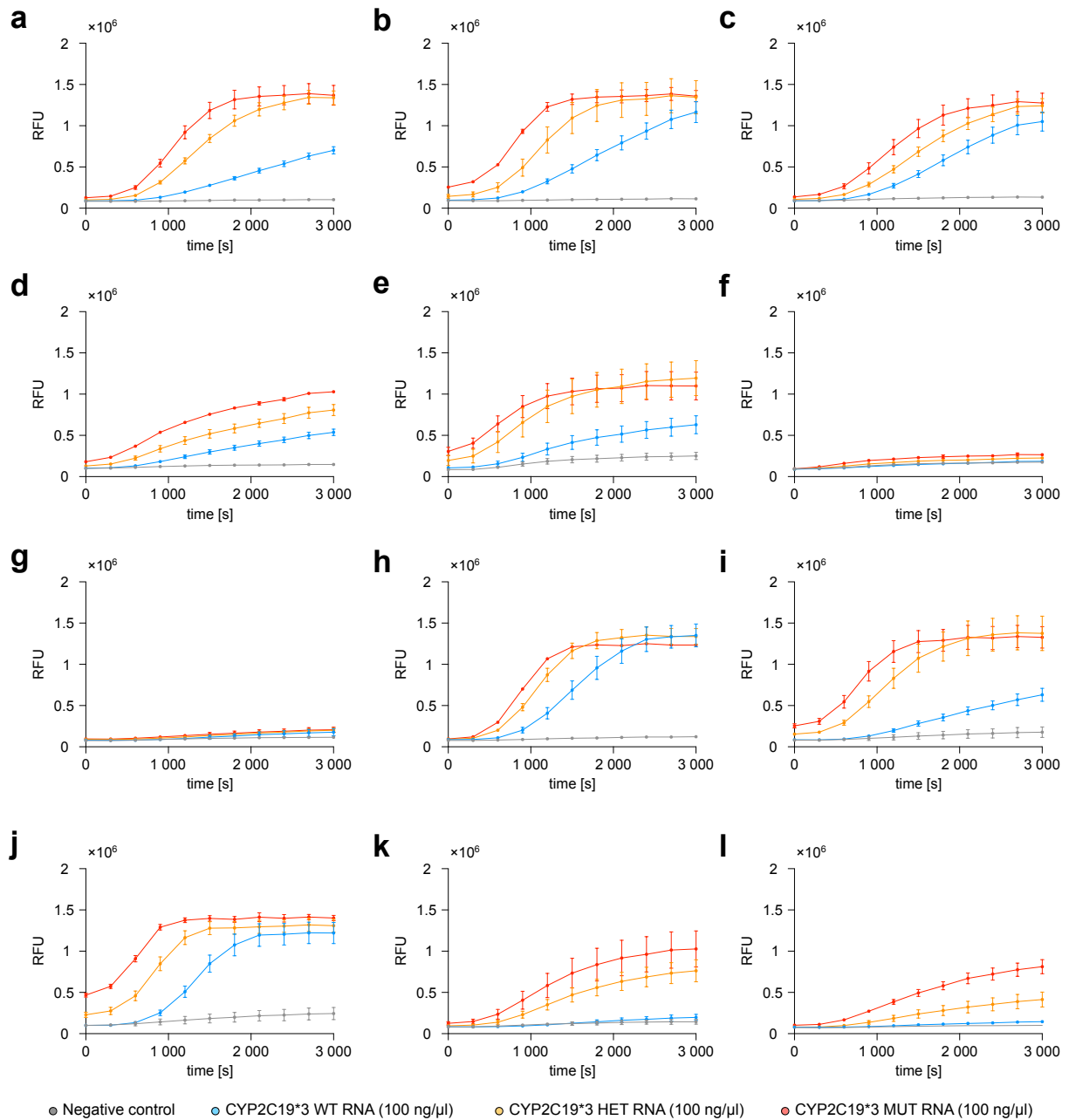
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**Supplementary figure 1**



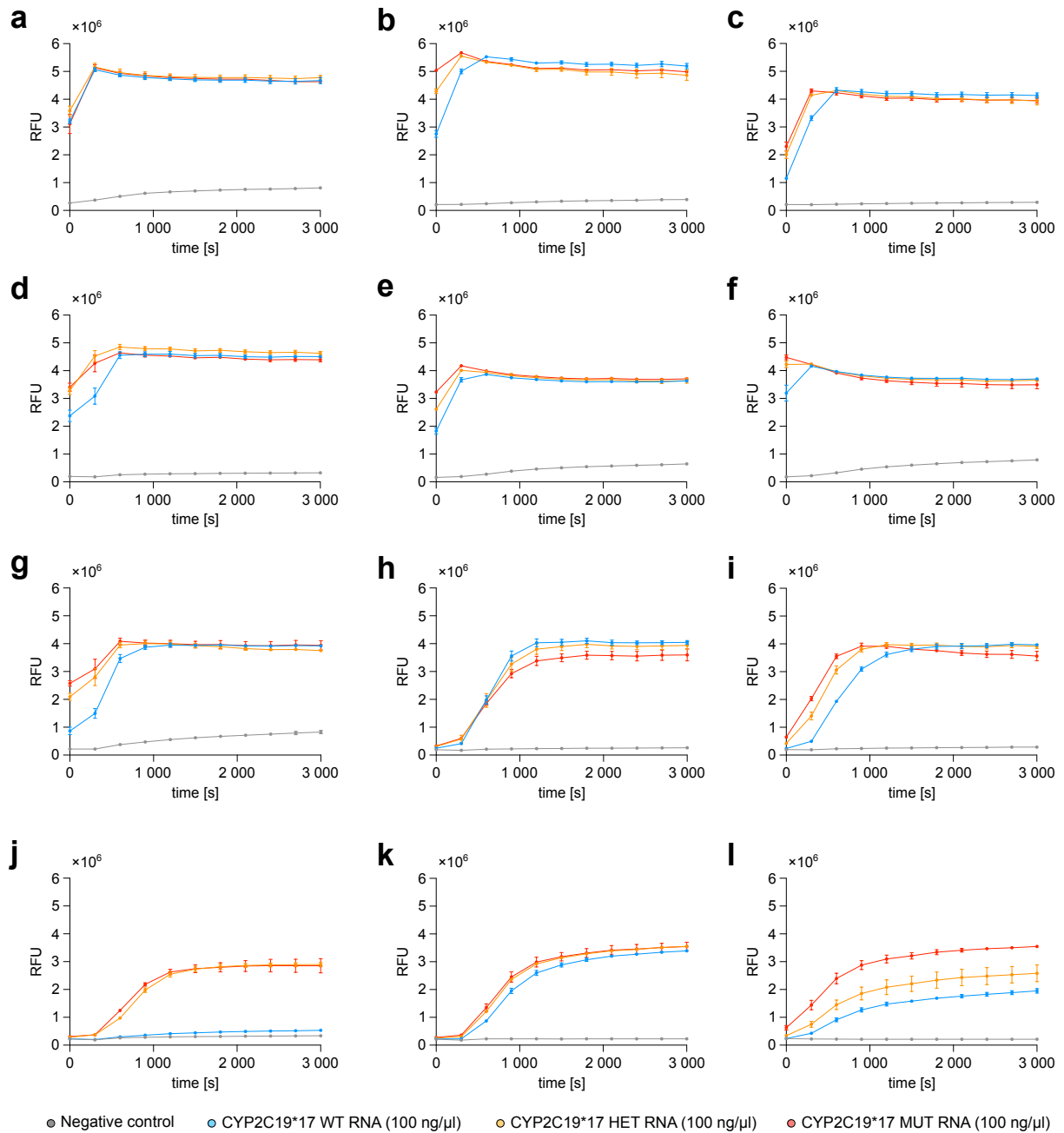
**Supplementary figure 1 | Raw fluorescence data for systematic LwaCas13a gRNA screen for CYP2C19\*2 on synthetic RNA targets.** Line graphs showing the fluorescence signal of the tested gRNAs for CYP2C19\*2. (a) for gRNA 2-1, (b) for gRNA 2-2, (c) for gRNA 2-3, (d) for gRNA 2-4, (e) for gRNA 2-5, (f) for gRNA 2-6, (g) for gRNA 2-7, (h) for gRNA 2-8, (i) for gRNA 2-9, (j) for gRNA 2-10, (k) for gRNA 2-11, and (l) for gRNA 2-12. x-axis indicates time in seconds, y-axis indicates relative fluorescence signal units (RFU), and error bars indicate mean  $\pm$  SD. n = 3 technical replicates. Synthetic RNA targets at 100 ng/ $\mu$ l.

## Supplementary figure 2



**Supplementary figure 2 | Raw fluorescence data for systematic LwaCas13a gRNA screen for CYP2C19\*3 on synthetic RNA targets.** Line graphs showing the fluorescence signal of the tested gRNAs for CYP2C19\*3. (a) for gRNA 3-1, (b) for gRNA 3-2, (c) for gRNA 3-3, (d) for gRNA 3-4, (e) for gRNA 3-5, (f) for gRNA 3-6, (g) for gRNA 3-7, (h) for gRNA 3-8, (i) for gRNA 3-9, (j) for gRNA 3-10, (k) for gRNA 3-11, and (l) for gRNA 3-12. x-axis indicates time in seconds, y-axis indicates RFU, and error bars indicate mean  $\pm$  SD. n = 3 technical replicates. Synthetic RNA targets at 100 ng/μl.

### Supplementary figure 3



**Supplementary figure 3 | Raw fluorescence data for systematic LwaCas13a gRNA screen for CYP2C19\*17 on synthetic RNA targets.** Line graphs showing the fluorescence signal of the tested gRNAs for CYP2C19\*17. (a) for gRNA 17-1, (b) for gRNA 17-2, (c) for gRNA 17-3, (d) for gRNA 17-4, (e) for gRNA 17-5, (f) for gRNA 17-6, (g) for gRNA 17-7, (h) for gRNA 17-8, (i) for gRNA 17-9, (j) for gRNA 17-10, (k) for gRNA 17-11, and (l) for gRNA 17-12. x-axis indicates time in seconds, y-axis indicates RFU, and error bars indicate mean  $\pm$  SD. n = 3 technical replicates. Synthetic RNA targets at 100 ng/μl.

## Supplementary figure 4

**a**

WT 5'...CTATCATTGATTATTCCCGGAACCCATAACAATTAC...3'  
3'...GATAGTAACATAAAGGCCCTTGGGTATTGTTTAATG...5'

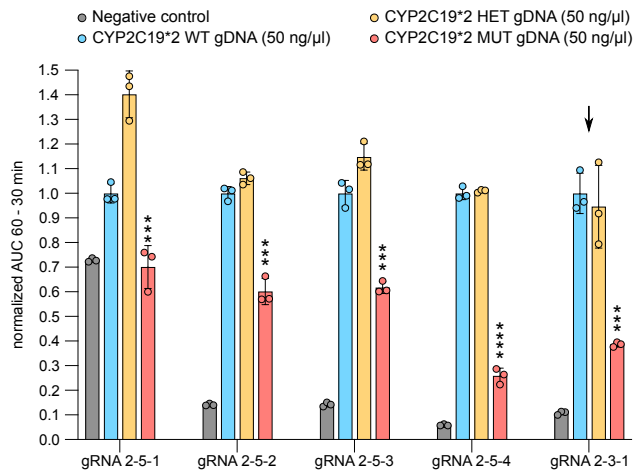
PAM 1 5'...CTATCATTGATTATTCCCGGAACCCATAACAATTAC...3'  
2-5-1 3'...AAGGGCCCTTGGGTATTGTT...5'

PAM 2 5'...CTATCATTGATTATTCCCGGAACCCATAACAATTAC...3'  
2-5-2 3'...GGCCCTTGGGTATTGTTAA...5'

PAM 3 5'...CTATCATTGATTATTCCCGGAACCCATAACAATTAC...3'  
2-5-3 3'...GCCCTTGGGTATTGTTTAAT...5'

PAM 4 5'...CTATCATTGATTATTCCCGGAACCCATAACAATTAC...3'  
2-5-4 3'...CCCTTGGGTATTGTTTAATG...5'

PAM 5 3'...GATAGTAACATAAAGGCCCTTGGGTATTGTTTAATG...5'  
2-3-1 5'...CTATCATTGATTATTCCCG...3'



**b**

WT 5'...GGATTGTAAGCACCCCTGGATCCAGGTAAGGCCAAGTT...3'  
3'...CCTAACATTCGTGGGGACCTAGGTCCATTCCGGTTCAA...5'

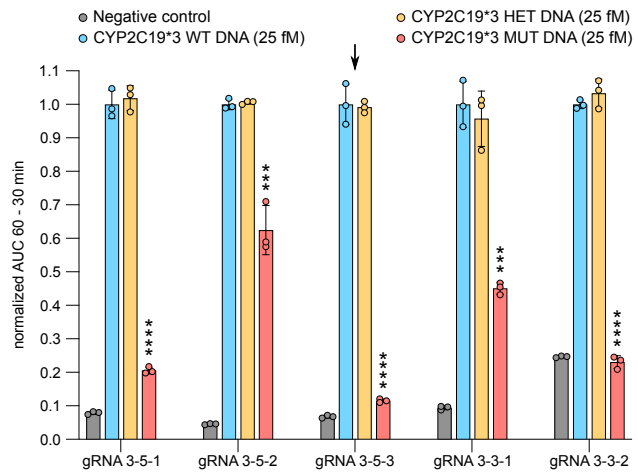
PAM 1 5'...GGATTGTAAGCACCCCTGGATCCAGGTAAGGCCAAGTT...3'  
3-5-1 3'...GGGACCTAGGTCCATTCCGG...5'

PAM 2 5'...GGATTGTAAGCACCCCTGGATCCAGGTAAGGCCAAGTT...3'  
3-5-2 3'...ACCTAGGTCCATTCCGGTTC...5'

PAM 3 5'...GGATTGTAAGCACCCCTGGATCCAGGTAAGGCCAAGTT...3'  
3-5-3 3'...CCTAGGTCCATTCCGGTTCA...5'

PAM 4 3'...CCTAACATTCGTGGGGACCTAGGTCCATTCCGGTTCAA...5'  
3-3-1 5'...AAGCACCCCTGGATCCAGG...3'

PAM 5 3'...CCTAACATTCGTGGGGACCTAGGTCCATTCCGGTTCAA...5'  
3-3-2 5'...TTGTAAGCACCCCTGGATC...3'



**c**

WT 5'...GTGCTTCTGTCTCAAAGCATCTCTGATGTAAGAGATA...3'  
3'...CACAGAAGACAAGAGTTTCGTAGAGACTACATTCTCTAT...5'

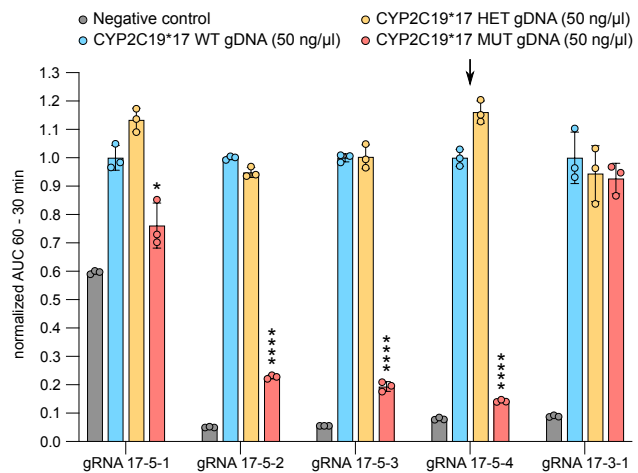
PAM 1 5'...GTGCTTCTGTCTCAAAGCATCTCTGATGTAAGAGATA...3'  
17-5-1 3'...AGAGTTTCGTAGAGACTACA...5'

PAM 2 5'...GTGCTTCTGTCTCAAAGCATCTCTGATGTAAGAGATA...3'  
17-5-2 3'...GTTTCGTAGAGACTACATTC...5'

PAM 3 5'...GTGCTTCTGTCTCAAAGCATCTCTGATGTAAGAGATA...3'  
17-5-3 3'...TTTCGTAGAGACTACATTCT...5'

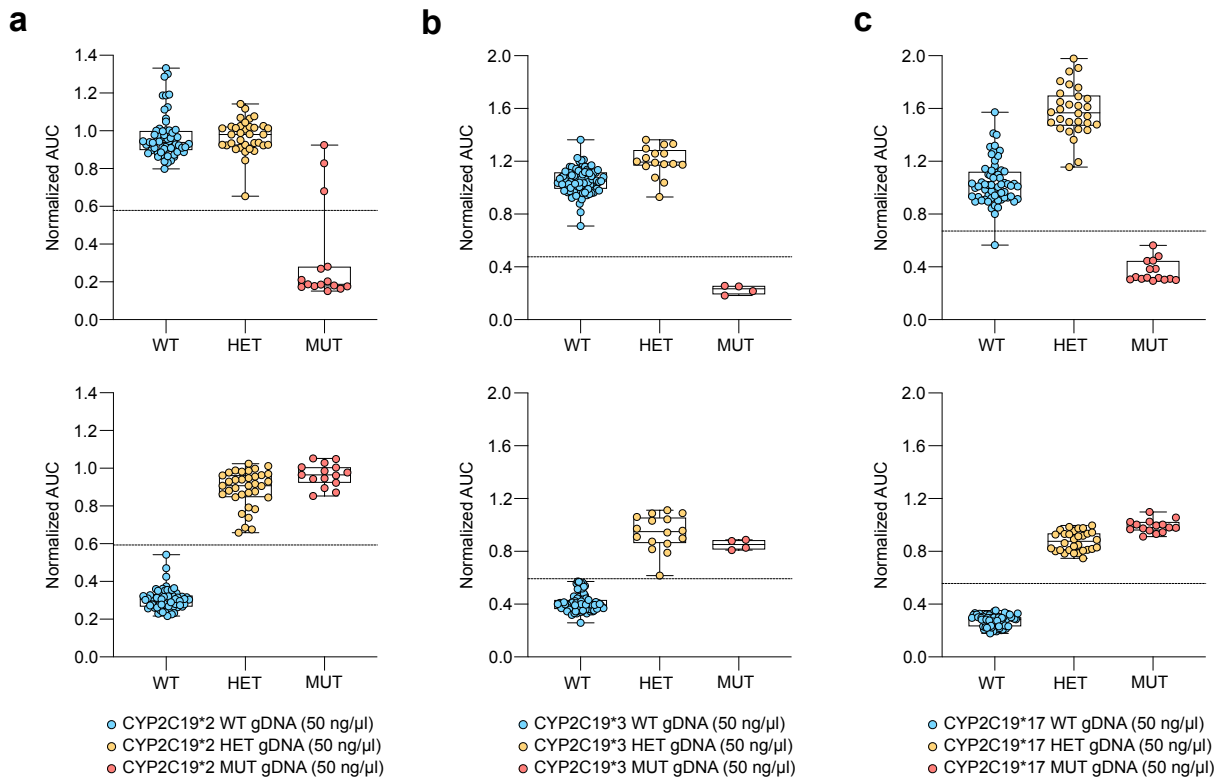
PAM 4 5'...GTGCTTCTGTCTCAAAGCATCTCTGATGTAAGAGATA...3'  
17-5-4 3'...TTTCGTAGAGACTACATTCT...5'

PAM 5 3'...CACAGAAGACAAGAGTTTCGTAGAGACTACATTCTCTAT...5'  
17-3-1 5'...GTTCTCAAAGCATCTCTGAT...3'



**Supplementary figure 4 | Systematic LbaCas12a gRNA screen for CYP2C19 genotyping. a, b, c, Left:** Alignment of target sequences and design of 5 different LbaCas12a WT-sensing gRNAs for CYP2C19\*2 (a), \*3 (b), and \*17 (c). The WT sequence is highlighted in blue, and the position of the PAM-sequence in grey. **Right:** Bar graphs showing the fluorescence signal of the tested gRNAs for CYP2C19\*2 (a), \*3 (b), and \*17 (c). n = 3 independent replicates. gDNA samples at 50 ng/μl for CYP2C19\*2 and \*17, and synthetic DNA targets at 25 fM for \*3. Bar graphs indicate mean ± SD. P < 0.05 (\*), P < 0.01 (\*\*), P < 0.001 (\*\*\*), and P < 0.0001 (\*\*\*\*). Among those, we selected the gRNAs with the highest WT/MUT fluorescence ratios. Selected gRNAs are marked by arrows.

## Supplementary figure 5



**Supplementary figure 5 | CRISPR-based CYP2C19 genotyping in a patient cohort using the dual-guide system.** **a-c**, Box plots showing CRISPR-based genotyping for 110 samples from study participants collected from the USA, Germany, and Taiwan. gDNA samples at 50 ng/μl were genotyped with the CRISPR-based assay for CYP2C19\*2 (**a**), \*3 (**b**), and \*17 (**c**) using the dual-guide system. LbaCas12a is illustrated on the top and LwaCas13a at the bottom. Data points represent the mean of 3 independent replicates, with each point corresponding to a different patient. Box plots indicate the median and interquartile range. Whiskers indicate the minimum and maximum values. Normalized AUC values were calculated by normalizing the AUC of each patient sample to the AUC of the corresponding synthetic positive control between 30 and 60 min. MUT synthetic standard was used for LwaCas13a, and WT synthetic standard for LbaCas12a.

**Supplementary table 1**

Name	MUT/HET ratio	MUT/WT ratio	Figure
gRNA 2-1	1.06	1.22	Fig. 1a
<b>gRNA 2-2</b>	<b>1.15</b>	<b>2.12</b>	<b>Fig. 1a</b>
gRNA 2-3	1.04	1.18	Fig. 1a
gRNA 2-4	1.12	1.33	Fig. 1a
gRNA 2-5	1.11	1.86	Fig. 1a
gRNA 2-6	1.09	1.28	Fig. 1a
gRNA 2-7	1.09	1.22	Fig. 1a
gRNA 2-8	1.05	1.13	Fig. 1a
gRNA 2-9	1.06	1.48	Fig. 1a
gRNA 2-10	1.02	1.12	Fig. 1a
gRNA 2-11	1.08	1.19	Fig. 1a
gRNA 2-12	1.09	1.22	Fig. 1a
gRNA 3-1	1.21	2.90	Fig. 1b
gRNA 3-2	1.20	2.00	Fig. 1b
gRNA 3-3	1.23	1.70	Fig. 1b
gRNA 3-4	1.41	2.29	Fig. 1b
gRNA 3-5	1.08	2.37	Fig. 1b
gRNA 3-6	1.21	1.48	Fig. 1b

gRNA 3-7	1.08	1.24	Fig. 1b
gRNA 3-8	1.02	1.29	Fig. 1b
gRNA 3-9	1.15	3.41	Fig. 1b
gRNA 3-10	1.21	1.68	Fig. 1b
gRNA 3-11	1.48	4.91	Fig. 1b
<b>gRNA 3-12</b>	<b>1.98</b>	<b>4.33</b>	<b>Fig. 1b</b>
gRNA 17-1	0.98	1.01	Fig. 1c
gRNA 17-2	1.02	1.00	Fig. 1c
gRNA 17-3	1.00	1.00	Fig. 1c
gRNA 17-4	0.95	1.03	Fig. 1c
gRNA 17-5	1.02	1.06	Fig. 1c
gRNA 17-6	0.98	0.98	Fig. 1c
<b>gRNA 17-7</b>	<b>1.04</b>	<b>1.10</b>	<b>Fig. 1c</b>
gRNA 17-8	0.91	0.88	Fig. 1c
<b>gRNA 17-9</b>	<b>1.00</b>	<b>1.10</b>	<b>Fig. 1c</b>
gRNA 17-10	1.02	5.41	Fig. 1c
gRNA 17-11	1.02	1.12	Fig. 1c
<b>gRNA 17-12</b>	<b>1.47</b>	<b>2.07</b>	<b>Fig. 1c</b>

**Supplementary table 2**

Name	Groups Compared	P-Value	Analysis	Figure
gRNA 2-1	HET vs WT	0.00196	Multiple t-tests	Fig. 1a
gRNA 2-1	HET vs MUT	0.03341	Multiple t-tests	Fig. 1a
<b>gRNA 2-2</b>	<b>HET vs WT</b>	<b>0.00001</b>	<b>Multiple t-tests</b>	<b>Fig. 1a</b>
<b>gRNA 2-2</b>	<b>HET vs MUT</b>	<b>0.00706</b>	<b>Multiple t-tests</b>	<b>Fig. 1a</b>
gRNA 2-3	HET vs WT	0.02064	Multiple t-tests	Fig. 1a
gRNA 2-3	HET vs MUT	0.11808	Multiple t-tests	Fig. 1a
gRNA 2-4	HET vs WT	0.00119	Multiple t-tests	Fig. 1a
gRNA 2-4	HET vs MUT	0.02689	Multiple t-tests	Fig. 1a
gRNA 2-5	HET vs WT	0.00006	Multiple t-tests	Fig. 1a
gRNA 2-5	HET vs MUT	0.01959	Multiple t-tests	Fig. 1a
gRNA 2-6	HET vs WT	0.00242	Multiple t-tests	Fig. 1a
gRNA 2-6	HET vs MUT	0.00340	Multiple t-tests	Fig. 1a
gRNA 2-7	HET vs WT	0.01853	Multiple t-tests	Fig. 1a
gRNA 2-7	HET vs MUT	0.03484	Multiple t-tests	Fig. 1a
gRNA 2-8	HET vs WT	0.01036	Multiple t-tests	Fig. 1a
gRNA 2-8	HET vs MUT	0.11245	Multiple t-tests	Fig. 1a
gRNA 2-9	HET vs WT	0.00007	Multiple t-tests	Fig. 1a
gRNA 2-9	HET vs MUT	0.03488	Multiple t-tests	Fig. 1a
gRNA 2-10	HET vs WT	0.00025	Multiple t-tests	Fig. 1a
gRNA 2-10	HET vs MUT	0.11922	Multiple t-tests	Fig. 1a
gRNA 2-11	HET vs WT	0.00221	Multiple t-tests	Fig. 1a

gRNA 2-11	HET vs MUT	0.00466	Multiple t-tests	Fig. 1a
gRNA 2-12	HET vs WT	0.00648	Multiple t-tests	Fig. 1a
gRNA 2-12	HET vs MUT	0.02042	Multiple t-tests	Fig. 1a
gRNA 3-1	HET vs WT	0.00012	Multiple t-tests	Fig. 1b
gRNA 3-1	HET vs MUT	0.03851	Multiple t-tests	Fig. 1b
gRNA 3-2	HET vs WT	0.01678	Multiple t-tests	Fig. 1b
gRNA 3-2	HET vs MUT	0.11537	Multiple t-tests	Fig. 1b
gRNA 3-3	HET vs WT	0.01208	Multiple t-tests	Fig. 1b
gRNA 3-3	HET vs MUT	0.05783	Multiple t-tests	Fig. 1b
gRNA 3-4	HET vs WT	0.00308	Multiple t-tests	Fig. 1b
gRNA 3-4	HET vs MUT	0.00185	Multiple t-tests	Fig. 1b
gRNA 3-5	HET vs WT	0.01477	Multiple t-tests	Fig. 1b
gRNA 3-5	HET vs MUT	0.65473	Multiple t-tests	Fig. 1b
gRNA 3-6	HET vs WT	0.02249	Multiple t-tests	Fig. 1b
gRNA 3-6	HET vs MUT	0.03663	Multiple t-tests	Fig. 1b
gRNA 3-7	HET vs WT	0.33858	Multiple t-tests	Fig. 1b
gRNA 3-7	HET vs MUT	0.48670	Multiple t-tests	Fig. 1b
gRNA 3-8	HET vs WT	0.04373	Multiple t-tests	Fig. 1b
gRNA 3-8	HET vs MUT	0.68624	Multiple t-tests	Fig. 1b
gRNA 3-9	HET vs WT	0.00159	Multiple t-tests	Fig. 1b
gRNA 3-9	HET vs MUT	0.25927	Multiple t-tests	Fig. 1b
gRNA 3-10	HET vs WT	0.01170	Multiple t-tests	Fig. 1b
gRNA 3-10	HET vs MUT	0.01005	Multiple t-tests	Fig. 1b

gRNA 3-11	HET vs WT	0.00262	Multiple t-tests	Fig. 1b
gRNA 3-11	HET vs MUT	0.09835	Multiple t-tests	Fig. 1b
<b>gRNA 3-12</b>	<b>HET vs WT</b>	<b>0.00946</b>	<b>Multiple t-tests</b>	<b>Fig. 1b</b>
<b>gRNA 3-12</b>	<b>HET vs MUT</b>	<b>0.00312</b>	<b>Multiple t-tests</b>	<b>Fig. 1b</b>
gRNA 17-1	HET vs WT	0.19052	Multiple t-tests	Fig. 1c
gRNA 17-1	HET vs MUT	0.34301	Multiple t-tests	Fig. 1c
gRNA 17-2	HET vs WT	0.22851	Multiple t-tests	Fig. 1c
gRNA 17-2	HET vs MUT	0.14392	Multiple t-tests	Fig. 1c
gRNA 17-3	HET vs WT	0.72995	Multiple t-tests	Fig. 1c
gRNA 17-3	HET vs MUT	0.96058	Multiple t-tests	Fig. 1c
gRNA 17-4	HET vs WT	0.01047	Multiple t-tests	Fig. 1c
gRNA 17-4	HET vs MUT	0.02138	Multiple t-tests	Fig. 1c
gRNA 17-5	HET vs WT	0.03705	Multiple t-tests	Fig. 1c
gRNA 17-5	HET vs MUT	0.09879	Multiple t-tests	Fig. 1c
gRNA 17-6	HET vs WT	0.33772	Multiple t-tests	Fig. 1c
gRNA 17-6	HET vs MUT	0.16889	Multiple t-tests	Fig. 1c
<b>gRNA 17-7</b>	<b>HET vs WT</b>	<b>0.01462</b>	<b>Multiple t-tests</b>	<b>Fig. 1c</b>
<b>gRNA 17-7</b>	<b>HET vs MUT</b>	<b>0.15702</b>	<b>Multiple t-tests</b>	<b>Fig. 1c</b>
gRNA 17-8	HET vs WT	0.36726	Multiple t-tests	Fig. 1c
gRNA 17-8	HET vs MUT	0.06127	Multiple t-tests	Fig. 1c
<b>gRNA 17-9</b>	<b>HET vs WT</b>	<b>0.00651</b>	<b>Multiple t-tests</b>	<b>Fig. 1c</b>
<b>gRNA 17-9</b>	<b>HET vs MUT</b>	<b>0.91927</b>	<b>Multiple t-tests</b>	<b>Fig. 1c</b>
gRNA 17-10	HET vs WT	0.00001	Multiple t-tests	Fig. 1c

gRNA 17-10	HET vs MUT	0.60030	Multiple t-tests	Fig. 1c
gRNA 17-11	HET vs WT	0.00430	Multiple t-tests	Fig. 1c
gRNA 17-11	HET vs MUT	0.60809	Multiple t-tests	Fig. 1c
<b>gRNA 17-12</b>	<b>HET vs WT</b>	<b>0.01637</b>	<b>Multiple t-tests</b>	<b>Fig. 1c</b>
<b>gRNA 17-12</b>	<b>HET vs MUT</b>	<b>0.00373</b>	<b>Multiple t-tests</b>	<b>Fig. 1c</b>

**Supplementary table 3**

Name	MUT/HET ratio	MUT/WT ratio	Figure
gRNA 2-2	1.09	2.24	Fig. 2a
<b>gRNA 3-12</b>	<b>1.30</b>	<b>3.50</b>	<b>Fig. 2a</b>
gRNA 17-7	1.02	1.48	Fig. 2a
gRNA 17-9	0.99	1.27	Fig. 2a
gRNA 17-12	1.01	1.51	Fig. 2a
gRNA 2-2-R	1.04	1.97	Fig. 2c
<b>gRNA 2-2-L</b>	<b>1.14</b>	<b>3.17</b>	<b>Fig. 2c</b>
gRNA 2-2-LR	1.08	2.93	Fig. 2c
gRNA 17-7-R	1.03	1.21	Fig. 2c
gRNA 17-7-L	0.98	1.19	Fig. 2c
gRNA 17-7-LR	1.09	1.85	Fig. 2c
gRNA 17-9-R	1.11	1.67	Fig. 2c
gRNA 17-9-L	1.05	1.78	Fig. 2c
<b>gRNA 17-9-LR</b>	<b>1.20</b>	<b>4.93</b>	<b>Fig. 2c</b>

gRNA 17-12-R	1.05	1.19	Fig. 2c
gRNA 17-12-L	0.95	0.90	Fig. 2c
gRNA 17-12-LR	1.07	1.28	Fig. 2c

**Supplementary table 4**

Name	Groups Compared	P-Value	Analysis	Figure
gRNA 2-2	HET vs WT	0.00001	Multiple t-tests	Fig. 2a
gRNA 2-2	HET vs MUT	0.00783	Multiple t-tests	Fig. 2a
<b>gRNA 3-12</b>	<b>HET vs WT</b>	<b>0.00060</b>	<b>Multiple t-tests</b>	Fig. 2a
<b>gRNA 3-12</b>	<b>HET vs MUT</b>	<b>0.01420</b>	<b>Multiple t-tests</b>	Fig. 2a
gRNA 17-7	HET vs WT	0.00001	Multiple t-tests	Fig. 2a
gRNA 17-7	HET vs MUT	0.42576	Multiple t-tests	Fig. 2a
gRNA 17-9	HET vs WT	0.00001	Multiple t-tests	Fig. 2a
gRNA 17-9	HET vs MUT	0.56425	Multiple t-tests	Fig. 2a
gRNA 17-12	HET vs WT	0.00096	Multiple t-tests	Fig. 2a
gRNA 17-12	HET vs MUT	0.90686	Multiple t-tests	Fig. 2a
gRNA 2-2-R	HET vs WT	0.00001	Multiple t-tests	Fig. 2c
gRNA 2-2-R	HET vs MUT	0.13711	Multiple t-tests	Fig. 2c
<b>gRNA 2-2-L</b>	<b>HET vs WT</b>	<b>0.00001</b>	<b>Multiple t-tests</b>	<b>Fig. 2c</b>
<b>gRNA 2-2-L</b>	<b>HET vs MUT</b>	<b>0.00055</b>	<b>Multiple t-tests</b>	<b>Fig. 2c</b>
gRNA 2-2-LR	HET vs WT	0.00001	Multiple t-tests	Fig. 2c
gRNA 2-2-LR	HET vs MUT	0.03903	Multiple t-tests	Fig. 2c
gRNA 17-7-R	HET vs WT	0.00001	Multiple t-tests	Fig. 2c

gRNA 17-7-R	HET vs MUT	0.03947	Multiple t-tests	Fig. 2c
gRNA 17-7-L	HET vs WT	0.00001	Multiple t-tests	Fig. 2c
gRNA 17-7-L	HET vs MUT	0.24356	Multiple t-tests	Fig. 2c
gRNA 17-7-LR	HET vs WT	0.00001	Multiple t-tests	Fig. 2c
gRNA 17-7-LR	HET vs MUT	0.00328	Multiple t-tests	Fig. 2c
gRNA 17-9-R	HET vs WT	0.00000	Multiple t-tests	Fig. 2c
gRNA 17-9-R	HET vs MUT	0.00311	Multiple t-tests	Fig. 2c
gRNA 17-9-L	HET vs WT	0.00000	Multiple t-tests	Fig. 2c
gRNA 17-9-L	HET vs MUT	0.31088	Multiple t-tests	Fig. 2c
<b>gRNA 17-9-LR</b>	<b>HET vs WT</b>	<b>0.00001</b>	<b>Multiple t-tests</b>	<b>Fig. 2c</b>
<b>gRNA 17-9-LR</b>	<b>HET vs MUT</b>	<b>0.00504</b>	<b>Multiple t-tests</b>	<b>Fig. 2c</b>
gRNA 17-12-R	HET vs WT	0.00000	Multiple t-tests	Fig. 2c
gRNA 17-12-R	HET vs MUT	0.01085	Multiple t-tests	Fig. 2c
gRNA 17-12-L	HET vs WT	0.02737	Multiple t-tests	Fig. 2c
gRNA 17-12-L	HET vs MUT	0.00751	Multiple t-tests	Fig. 2c
gRNA 17-12-LR	HET vs WT	0.00001	Multiple t-tests	Fig. 2c
gRNA 17-12-LR	HET vs MUT	0.00508	Multiple t-tests	Fig. 2c

**Supplementary table 5**

Name	WT/MUT ratio	Figure
gRNA 2-5-1	1,43	S1a
gRNA 2-5-2	1,66	S1a
gRNA 2-5-3	1,62	S1a

gRNA 2-5-4	3,87	S1a
<b>gRNA 2-3-1</b>	<b>2,59</b>	<b>S1a</b>
gRNA 3-5-1	4,86	S1b
gRNA 3-5-2	1,60	S1b
<b>gRNA 3-5-3</b>	<b>8,69</b>	<b>S1b</b>
gRNA 3-3-1	2,22	S1b
gRNA 3-3-2	4,34	S1b
gRNA 17-5-1	1,31	S1c
gRNA 17-5-2	4,39	S1c
gRNA 17-5-3	5,16	S1c
<b>gRNA 17-5-4</b>	<b>7,00</b>	<b>S1c</b>
gRNA 17-3-1	1,08	S1c

**Supplementary table 6**

Name	Groups Compared	P-Value	Analysis	Figure
gRNA 2-5-1	WT vs MUT	0.00564	Multiple t-tests	S1a
gRNA 2-5-2	WT vs MUT	0.00033	Multiple t-tests	S1a
gRNA 2-5-3	WT vs MUT	0.00033	Multiple t-tests	S1a
gRNA 2-5-4	WT vs MUT	0.00001	Multiple t-tests	S1a
<b>gRNA 2-3-1</b>	<b>WT vs MUT</b>	<b>0.00021</b>	<b>Multiple t-tests</b>	<b>S1a</b>
gRNA 3-5-1	WT vs MUT	0.00001	Multiple t-tests	S1b
gRNA 3-5-2	WT vs MUT	0.00100	Multiple t-tests	S1b

<b>gRNA 3-5-3</b>	<b>WT vs MUT</b>	<b>0.00002</b>	<b>Multiple t-tests</b>	<b>S1b</b>
gRNA 3-3-1	WT vs MUT	0.00019	Multiple t-tests	S1b
gRNA 3-3-2	WT vs MUT	0.00001	Multiple t-tests	S1b
gRNA 17-5-1	WT vs MUT	0.01037	Multiple t-tests	S1c
gRNA 17-5-2	WT vs MUT	0.00001	Multiple t-tests	S1c
gRNA 17-5-3	WT vs MUT	0.00001	Multiple t-tests	S1c
<b>gRNA 17-5-4</b>	<b>WT vs MUT</b>	<b>0.00001</b>	<b>Multiple t-tests</b>	<b>S1c</b>
gRNA 17-3-1	WT vs MUT	0.29729	Multiple t-tests	S1c

**Supplementary table 7**

Name	Cas-Enzyme	Genotype	Genotyping score	Figure
Simplified crude extraction	LbaCas12a	WT	1.00	Fig. 5d
Simplified crude extraction	LbaCas12a	HET	1.24	Fig. 5d
Simplified crude extraction	LbaCas12a	MUT	0.45	Fig. 5d
Simplified crude extraction	LwaCas13a	WT	0.28	Fig. 5d
Simplified crude extraction	LwaCas13a	HET	1.20	Fig. 5d
Simplified crude extraction	LwaCas13a	MUT	1.00	Fig. 5d

**Supplementary table 8**

Name	Description	Sequence	Target	Figure
FP17-RPA	Forward RPA Primer	GAAATTAATACGACTCACTATAGG gaataactaatgtttggaagttgtttgtttgct	CYP2C19*17	Fig. 2a
RP17-RPA	Reverse	gcccatcgtggcgcattatctctta	CYP2C19*17	Fig. 2a

	RPA Primer			
FP3-RPA	Forward RPA Primer	GAAATTAATACGACTCACTATAGG atcagcaatttctaacttgatggaaaaat	CYP2C19*3	Fig. 2a
RP3-RPA	Reverse RPA Primer	gtaagtggtttctcaggaagcaaaa	CYP2C19*3	Fig. 2a
FP2-RPA	Forward RPA Primer	GAAATTAATACGACTCACTATAGG ttgttttctcttagatatgcaataatttc	CYP2C19*2	Fig. 2a
RP2-RPA	Reverse RPA Primer	tttctcaaaaatatcactttccataaaagc	CYP2C19*2	Fig. 2a
FP2-PCR <sup>44</sup>	Forward PCR Primer	GAAATTAATACGACTCACTATAGGC AGAGCTTGGCATATTGTATC	CYP2C19*2	Fig. 3b,f
RP2-PCR <sup>44</sup>	Reverse PCR Primer	GTAACACAAAACTAGTCAATG	CYP2C19*2	Fig. 3b,f
FP3-PCR <sup>44</sup>	Forward PCR Primer	GAAATTAATACGACTCACTATAGGT GTGCTCCCTGCAATGTGAT	CYP2C19*3	Fig. 3c,g
RP3-PCR <sup>44</sup>	Reverse PCR Primer	TTTGGGGCTGTCACCAAAGT	CYP2C19*3	Fig. 3c,g
FP17-PCR <sup>44</sup>	Forward PCR Primer	GAAATTAATACGACTCACTATAGGG CCCTTAGCACCAAATTCTC	CYP2C19*17	Fig. 3d,h
RP17-PCR <sup>44</sup>	Reverse PCR Primer	ATTTAACCCCCTAAAAAACACG	CYP2C19*17	Fig. 3d,h

**Supplementary table 9**

Name	Sequence	Target	Figure
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gRNA 2-1	CYP2C19*2	tttcccactatcattgattattcccAGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-2	CYP2C19*2	ttcccactatcattgattattcccAgGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-3	CYP2C19*2	ttcccactatcattgattattcccAggGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-4	CYP2C19*2	tcccactatcattgattattcccAggaGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-5	CYP2C19*2	cccactatcattgattattcccAggaaGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-6	CYP2C19*2	ccactatcattgattattcccAggaacGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-7	CYP2C19*2	cactatcattgattattcccAggaaccGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-8	CYP2C19*2	actatcattgattattcccAggaaccGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-9	CYP2C19*2	ctatcattgattattcccAggaaccGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-10	CYP2C19*2	tatcattgattattcccAggaaccatGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-11	CYP2C19*2	atcattgattattcccAggaaccataGTTTTAGTCCCCTTCGT TTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a
gRNA 2-12	CYP2C19*2	tcattgattattcccAggaaccataaGTTTTAGTCCCCTTCGT TTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1a

gRNA 2-2R	CYP2C19*2	ttcccactatcattgattattcccAcGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 2c
gRNA 2-2L	CYP2C19*2	ttcccactatcattgattattccgAgGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 2c
gRNA 2-2LR	CYP2C19*2	ttcccactatcattgattattccgAcGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 2c
gRNA 3-1	CYP2C19*3	aaacatcaggattgaagcaccacctgAGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-2	CYP2C19*3	aacatcaggattgaagcaccacctgAaGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-3	CYP2C19*3	acatcaggattgaagcaccacctgAatGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-4	CYP2C19*3	catcaggattgaagcaccacctgAatcGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-5	CYP2C19*3	atcaggattgaagcaccacctgAatccGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-6	CYP2C19*3	tcaggattgaagcaccacctgAatccaGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-7	CYP2C19*3	caggattgaagcaccacctgAatccagGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-8	CYP2C19*3	aggattgaagcaccacctgAatccaggGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-9	CYP2C19*3	ggattgaagcaccacctgAatccaggtGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b

gRNA 3-10	CYP2C19*3	gattgtaagcaccctgAatccaggaGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-11	CYP2C19*3	attgtaagcaccctgAatccaggaGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 3-12	CYP2C19*3	ttgtaagcaccctgAatccaggaGTTTTAGTCCCCTTCG TTTTTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1b
gRNA 17-1	CYP2C19*17	tcaaattgtgtcttctgtctcaaagTGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-2	CYP2C19*17	caaattgtgtcttctgtctcaaagTaGTTTTAGTCCCCTTCGTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-3	CYP2C19*17	aaattgtgtcttctgtctcaaagTatGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-4	CYP2C19*17	aattgtgtcttctgtctcaaagTatcGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-5	CYP2C19*17	attgtgtcttctgtctcaaagTatctGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-6	CYP2C19*17	ttgtgtcttctgtctcaaagTatctcGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-7	CYP2C19*17	ttgtgtcttctgtctcaaagTatctcGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-8	CYP2C19*17	tgtgtcttctgtctcaaagTatctctgTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-9	CYP2C19*17	gtgtcttctgtctcaaagTatctctgaTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCctatagtgagtcgtattaatttc	Fig. 1c

gRNA 17-10	CYP2C19*17	tgcttctgttctcaaagTatctctgatGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-11	CYP2C19*17	gtcttctgttctcaaagTatctctgatgGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-12	CYP2C19*17	tcttctgttctcaaagTatctctgatgtGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 1c
gRNA 17-7R	CYP2C19*17	ttgtgtcttctgttctcaaaCTatctctGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c
gRNA 17-7L	CYP2C19*17	ttgtgtcttctgttctcaaagTTtctctGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c
gRNA 17-7LR	CYP2C19*17	ttgtgtcttctgttctcaaaCTTtctctGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c
gRNA 17-9R	CYP2C19*17	gtgtcttctgttctcaaagTTtctctgaGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c
gRNA 17-9L	CYP2C19*17	gtgtcttctgttctcaaaCTatctctgaGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c
gRNA 17-9LR	CYP2C19*17	gtgtcttctgttctcaaaCTTtctctgaGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c
gRNA 17-12R	CYP2C19*17	tcttctgttctcaaagTTtctctgatgtGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c
gRNA 17-12L	CYP2C19*17	tcttctgttctcaaagCTatctctgatgtGTTTTAGTCCCCTTCGTTT TTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c
gRNA 17-12LR	CYP2C19*17	tcttctgttctcaaagCTTtctctgatgtGTTTTAGTCCCCTTCGTT TTTGGGGTAGTCTAAATCcctatagtgagtcgtattaatttc	Fig. 2c

**Supplementary table 10**

Name	Sequence	Target	Figure
gRNA 2-5-1	CYP2C19*2	ttgttatgggtcccgggaaATCTACACTTAGTAGAAATTACCTA TAGTGAGTCGTATTAATTTTC	S1
gRNA 2-5-2	CYP2C19*2	aatttggatgggtcccggATCTACACTTAGTAGAAATTACCTA TAGTGAGTCGTATTAATTTTC	S1
gRNA 2-5-3	CYP2C19*2	taatttggatgggtcccgATCTACACTTAGTAGAAATTACCTAT AGTGAGTCGTATTAATTTTC	S1
gRNA 2-5-4	CYP2C19*2	gtaatttggatgggtcccATCTACACTTAGTAGAAATTACCTAT AGTGAGTCGTATTAATTTTC	S1
gRNA 2-3-1	CYP2C19*2	ctatcattgattattcccgATCTACACTTAGTAGAAATTACCTAT AGTGAGTCGTATTAATTTTC	S1
gRNA 3-5-1	CYP2C19*3	ttggccttacctggatccagATCTACACTTAGTAGAAATTACCT ATAGTGAGTCGTATTAATTTTC	S1
gRNA 3-5-2	CYP2C19*3	cttggccttacctggatccaATCTACACTTAGTAGAAATTACCTA TAGTGAGTCGTATTAATTTTC	S1
gRNA 3-5-3	CYP2C19*3	aacttggccttacctggatcATCTACACTTAGTAGAAATTACCT ATAGTGAGTCGTATTAATTTTC	S1
gRNA 3-3-1	CYP2C19*3	aagcaccctggatccaggATCTACACTTAGTAGAAATTACC TATAGTGAGTCGTATTAATTTTC	S1
gRNA 3-3-2	CYP2C19*3	ttgtaagcaccctggatcATCTACACTTAGTAGAAATTACCT ATAGTGAGTCGTATTAATTTTC	S1
gRNA 17-5-1	CYP2C19*17	acatcagagatgctttgagaATCTACACTTAGTAGAAATTACCT ATAGTGAGTCGTATTAATTTTC	S1

gRNA 17-5-2	CYP2C19*17	cttacatcagagatgcttgATCTACACTTAGTAGAAATTACCTA TAGTGAGTCGTATTAATTTTC	S1
gRNA 17-5-3	CYP2C19*17	tcttacatcagagatgctttATCTACACTTAGTAGAAATTACCTA TAGTGAGTCGTATTAATTTTC	S1
gRNA 17-5-4	CYP2C19*17	ctcttacatcagagatgcttATCTACACTTAGTAGAAATTACCTA TAGTGAGTCGTATTAATTTTC	S1
gRNA 17-3-1	CYP2C19*17	gttctcaaagcatctctgatATCTACACTTAGTAGAAATTACCTA TAGTGAGTCGTATTAATTTTC	S1

**Supplementary table 11**

Name	Sequence	Figure
CYP2C19 *2 WT	GAAATTAATACGACTCACTATAGGagttttaaattacaaccagagctggcatattgtatct atacctttattaaatgcttttaattaataaattattgtttctcttagatagcaataatccccactatcattgatt atccccgggaaccataaacaattacttaaaaacctgctttatggaaagtgatatttggagaaagta aaagaacaccaagaatcgatggacatcaacaaccctcgggactttattgattgcttctgat	Fig. 1a, 2a, 2c
CYP2C19 *2 MUT	GAAATTAATACGACTCACTATAGGagttttaaattacaaccagagctggcatattgtatct atacctttattaaatgcttttaattaataaattattgtttctcttagatagcaataatccccactatcattgatt atccccAggaaccataaacaattacttaaaaacctgctttatggaaagtgatatttggagaaagta aaagaacaccaagaatcgatggacatcaacaaccctcgggactttattgattgcttctgat	Fig. 1a, 2a, 2c
CYP2C19 *3 WT	GAAATTAATACGACTCACTATAGGggctgtgctccctgcaatgtgatctgctccattatctcc agaaacgttccgattataaagatcagcaatttctaactgatggaaaaattgaatgaaaacatcaggatt gtaagcaccctggatccaggaaggccaagttttgcttctgagaaaccacttacagtctttttctg ggaaatccaaaattctatattgaccaagccctgaagtacattttgaatactacagcttgcttaga	Fig. 1b, 2a
CYP2C19 *3 MUT	GAAATTAATACGACTCACTATAGGggctgtgctccctgcaatgtgatctgctccattatctcc agaaacgttccgattataaagatcagcaatttctaactgatggaaaaattgaatgaaaacatcaggatt	Fig. 1b, 2a

	gtaagcaccctgAatccaggtaaggccaagttttgctcctgagaaaccacttacagctcttttctg ggaaatccaaaattctatattgaccaagcctgaagtacattttgaatactacagctctgcctaga	
CYP2C19 *17 WT	GAAATTAATACGACTCACTATAGGttatgaacaggatgaatgggtatatattcagaata actaatgtttggaagtgtttggctaaaacaaagtttagcaaacgatttttttcaaattgtgtctctgt tctcaaagcatctctgatgaagagataatgcgccacgatgggcatcagaagacctcagctcaaatcc cagttctgccagctatgagctgtgtggcaccaacaggtgtcctgttctcccaggggtctcccttttc	Fig. 1c, 2a, 2c
CYP2C19 *17 MUT	GAAATTAATACGACTCACTATAGGttatgaacaggatgaatgggtatatattcagaata actaatgtttggaagtgtttggctaaaacaaagtttagcaaacgatttttttcaaattgtgtctctgt tctcaaagTatctctgatgaagagataatgcgccacgatgggcatcagaagacctcagctcaaatcc cagttctgccagctatgagctgtgtggcaccaacaggtgtcctgttctcccaggggtctcccttttc	Fig. 1c, 2a, 2c

**Supplementary table 12**

Name	Sequence	Fluorophore	Figure
Poly U FAM	/56-FAM/rUrUrUrUrU/3IABkFQ/	FAM	Fig. 1a-c
Texas Red	/5TEX615/T*A*rArUG*C*/3IAbRQSp/	Texas Red	Fig. 2-4, 5d
HEX	5HEX/TTATT/3IABkFQ	HEX	Fig. 3, 4, 5d, S1
Digoxigenin-FAM	56-FAM/TTATTATT/3DigN	FAM	Fig. 5b
Biotin-FAM	56-FAM/UUUUUUUUUUUUUU/3Bio	FAM	Fig. 5b