Clin. Lab. 2025;71:1-10

ORIGINAL ARTICLE

Identifying *TP53* Copy Number Variations in Hematologic Malignancies with a Digital PCR Method

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SUMMARY

Background: ***Tumor protein p53*** **(*TP53*) is a well-known tumor suppressor gene, of which allelic status has widely been raising concern in recent years. Copy number (CN) loss in this gene results in either haploinsufficiency or loss of function. Though detection methods like next generation sequencing (NGS) or array-based comparative genomic hybridization (aCGH) can be applied, the accurate and cost-effective identification of copy number variation (CNV) remains a challenge for in-hospital laboratories.**

Methods: **In this study, we developed a digital PCR method to quantify the *TP53* copy number in hematologic malignancies. Two Taqman probes were designed to be placed at the 5th and 7th exons of *TP53* gene, while another one was placed at the *RPP30* gene. By performing the experiments with the DNA of 102 healthy checkup individuals and two leukemia cell lines, we established the characteristics of the assay performance, including the limits of blank (LOB), the limits of detection (LOD), the linearities, and the coefficients of variation at the LOD levels. Forty-two samples from patients newly diagnosed with leukemia, lymphoma, myeloma, or myelodysplastic syndrome were further tested for validation. The results were then compared with other reports related to their allelic statuses of *TP53*.**

Results: **The lower LOB of the exon 5 and exon 7 were revealed to be 1.756 and 1.836 copies per genome, respectively, while the upper limits were 2.008 and 2.041. The LOD for CN loss of two exons were 1.692 and 1.777 copies per genome, respectively. Taking NGS results as reference, 1.716 and 1.786 copies per genome for exon 5 and exon 7, respectively, were decided as the cutoff values for CN loss using the receiver operator curve (ROC) method. The areas under curve (AUC) for both exons reached 1.**

Conclusions: **All in all, we consider dPCR an excellent tool for identifying *TP53* CNV status in hematologic malignancies.**

(Clin. Lab. 2025;71:1-10OI: 10.7754/Clin.Lab.2024.241051)

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Manuscript accepted November 6, 2024

Supplementary Data

Table S1. Raw experimental data.

Results for LOB establishment					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
1	**11,336.842**	**11,681.133**	**11,751.074**	**1.929**	**1.988**
2	**13,047.756**	**13,528.060**	**14,201.146**	**1.838**	**1.905**
3	**12,002.536**	**12,258.555**	**12,483.543**	**1.923**	**1.964**
4	**13,113.239**	**13,497.729**	**13,185.934**	**1.989**	**2.047**
5	**11,190.273**	**11,446.487**	**11,533.823**	**1.940**	**1.985**
6	**9,560.064**	**9,940.921**	**10,731.866**	**1.782**	**1.853**
7	**11,199.178**	**11,283.713**	**11,204.096**	**1.999**	**2.014**
8	**10,165.060**	**10,469.724**	**11,064.935**	**1.837**	**1.892**
9	**12,079.182**	**12,573.234**	**12,845.518**	**1.881**	**1.958**
10	**10,465.731**	**10,821.320**	**11,455.629**	**1.827**	**1.889**
11	**10,265.102**	**10,680.158**	**11,245.365**	**1.826**	**1.899**
12	**9,632.602**	**9,887.288**	**9,627.104**	**2.001**	**2.054**
13	**10,390.474**	**10,853.296**	**11,588.967**	**1.793**	**1.873**
14	**7,945.433**	**8,268.940**	**8,923.215**	**1.781**	**1.853**
15	**7,767.752**	**8,412.899**	**9,342.058**	**1.663**	**1.801**
16	**10,287.754**	**10,430.161**	**10,549.617**	**1.950**	**1.977**
17	**8,573.567**	**8,932.233**	**9,582.447**	**1.789**	**1.864**
18	**8,258.916**	**8,379.188**	**9,264.312**	**1.783**	**1.809**
19	**8,291.530**	**8,360.995**	**8,488.593**	**1.954**	**1.970**
20	**9,875.202**	**10,159.808**	**10,460.032**	**1.888**	**1.943**
21	**10,465.445**	**10,903.245**	**11,062.813**	**1.892**	**1.971**
22	**11,282.783**	**11,484.996**	**11,567.893**	**1.951**	**1.986**
23	**11,129.691**	**11,185.671**	**11,204.401**	**1.987**	**1.997**
24	**10,263.984**	**10,406.329**	**10,106.94**	**2.031**	**2.059**
25	**8,454.459**	**9,034.205**	**10,128.355**	**1.669**	**1.784**
26	**12,790.093**	**13,058.887**	**12,854.604**	**1.990**	**2.032**
27	**11,126.031**	**11,226.248**	**11,595.360**	**1.919**	**1.936**
28	**9,746.658**	**10,143.518**	**10,709.339**	**1.820**	**1.894**
29	**9,533.066**	**9,985.884**	**10,458.036**	**1.823**	**1.910**
30	**10,079.174**	**10,210.786**	**10,224.963**	**1.971**	**1.997**
31	**9,295.892**	**9,719.935**	**10,337.713**	**1.798**	**1.880**
32	**11,464.776**	**11,787.212**	**11,850.691**	**1.935**	**1.989**
33	**8,559.001**	**8,910.554**	**9,346.634**	**1.831**	**1.907**
34	**12,227.124**	**12,367.636**	**12,595.167**	**1.942**	**1.964**
35	**10,900.861**	**11,019.586**	**11,002.708**	**1.981**	**2.003**
36	**9,311.848**	**9.393.806**	**9,514.677**	**1.957**	**1.975**
37	**10,644.964**	**11,185.978**	**11,345.879**	**1.876**	**1.972**
38	**11,184.443**	**11,493.856**	**12,002.536**	**1.864**	**1.915**
39	**10,803.306**	**11,122.678**	**11,222.553**	**1.925**	**1.982**
40	**10,114.594**	**10,497.714**	**10,901.160**	**1.856**	**1.926**
41	**10,318.034**	**11,128.166**	**10,728.060**	**1.924**	**2.075**
42	**10,777.080**	**11,014.157**	**11,555.462**	**1.865**	**1.906**

Table S1. Raw experimental data (continued).

Results for LOB establishment					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
43	**11,519.530**	**11,670.169**	**11,926.155**	**1.932**	**1.957**
44	**14,026.926**	**14,233.961**	**14,631.,932**	**1.917**	**1.946**
45	**12,981.597**	**13,372.355**	**13,869.625**	**1.872**	**1.928**
46	**11,399.346**	**11,544.318**	**11,835.930**	**1.926**	**1.951**
47	**7,928.686**	**8,065.473**	**8,203.063**	**1.933**	**1.966**
48	**10,347.283**	**10,996.989**	**11,472.670**	**1.804**	**1.917**
49	**11,749.127**	**11,844.784**	**12,717.752**	**1.848**	**1.863**
50	**8,949.318**	**9,146.963**	**9,344.347**	**1.915**	**1.958**
51	**10,307.649**	**10,378.599**	**10,507.442**	**1.962**	**1.975**
52	**14,898.734**	**15,256.691**	**16,125.813**	**1.848**	**1.892**
53	**7,976.576**	**8,148.875**	**8,903.014**	**1.792**	**1.831**
54	**11,959.292**	**12,252.739**	**12,371.789**	**1.933**	**1.981**
55	**7,488.894**	**7,809.860**	**8,224.142**	**1.821**	**1.899**
56	**8,819.729**	**9,214.993**	**9,889.438**	**1.784**	**1.864**
57	**14,654.181**	**14,991.414**	**15,305.111**	**1.915**	**1.959**
58	**10,135.245**	**10,480.853**	**11,558.646**	**1.754**	**1.814**
59	**15,878.799**	**16,028.874**	**16,434.551**	**1.932**	**1.951**
60	**11,235.493**	**11,401.854**	**11,697.279**	**1.921**	**1.949**
61	**9,416.580**	**9,808.854**	**10,254.922**	**1.836**	**1.913**
62	**10,464.021**	**10,624.082**	**10,902.054**	**1.920**	**1.949**
63	**11,434.840**	**11,810.396**	**12,252.739**	**1.866**	**1.928**
64	**10,686.278**	**10,925.627**	**11,302.942**	**1.891**	**1.933**
65	**2,609.311**	**2,654.881**	**2,584.881**	**2.019**	**2.054**
66	**26,573.014**	**26,975.262**	**27,299.217**	**1.947**	**1.976**
67	**11,672.104**	**12,144.245**	**13.099,811**	**1.782**	**1.854**
68	**7,831.854**	**8,097.450**	**8,391.644**	**1.867**	**1.930**
69	**3,870.405**	**3,929.559**	**4,055.325**	**1.909**	**1.938**
70	**11,067.965**	**11,431.378**	**12,486.694**	**1.773**	**1.831**
71	**11,205.631**	**11,590.564**	**12,526.002**	**1.789**	**1.851**
72	**12,244.193**	**13,500.059**	**14,305.780**	**1.712**	**1.887**
73	**4,462.367**	**4,610.886**	**4,978.370**	**1.793**	**1.852**
74	**11,625.795**	**11,874.354**	**12,481.792**	**1.863**	**1.903**
75	**6,655.244**	**6,919.045**	**6,826.517**	**1.950**	**2.027**
76	**15,604.110**	**16,162.926**	**17,186.232**	**1.816**	**1.881**
77	**10,497.714**	**10,797.700**	**11,378.988**	**1.845**	**1.898**
78	**11,376.139**	**11,802.553**	**12,047.982**	**1.888**	**1.959**
79	**13,585.473**	**14,178.047**	**14,749.422**	**1.842**	**1.923**
80	**7,999.834**	**8,218.696**	**8,206.007**	**1.950**	**2.003**
81	**4,820.060**	**4,980.816**	**5,140.104**	**1.875**	**1.938**
82	**8,816.597**	**9,078.658**	**9,079.896**	**1.942**	**2.000**
83	**12,735.339**	**13,221.729**	**13,776.121**	**1.849**	**1.920**
84	**12,514.755**	**12,778.900**	**13,198.729**	**1.896**	**1.936**
85	**12,364.176**	**12,586.673**	**12,509.486**	**1.977**	**2.012**
86	**15,424.377**	**16,021.339**	**16,678.951**	**1.850**	**1.921**

Table S1. Raw experimental data (continued).

Results for LOB establishment					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
87	12,537.611	12,757.994	12,846.971	1.952	1.986
88	11,586.409	11,967.593	11,673.070	1.985	2.050
89	10,577.548	10,818.364	10,639.738	1.988	2.034
90	9,649.901	10,194.965	11,121.764	1.735	1.833
91	11,717.013	11,972.245	12,023.897	1.949	1.991
92	8,711.125	8,880.429	8,951.761	1.946	1.984
93	7,307.019	7,612.424	8,152.253	1.793	1.868
94	11,316.923	11,742.305	11,896.428	1.903	1.974
95	7,245.833	7,400.664	7,658.769	1.892	1.933
96	12,590.919	12,842.612	12,980.124	1.940	1.979
97	6,132.586	6,236.175	6,180.927	1.984	2.018
98	10,622.635	11,074.029	11,363.046	1.870	1.949
99	11,724.140	12,175.753	12,929.431	1.814	1.883
100	8,520.343	8,814.188	8,939.308	1.906	1.72
101	13,110.628	13,754.179	14,185.538	1.848	1.939
102	11,411.580	11,760.504	12,223.715	1.867	1.924
Results for LOD establishment					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
1	8,125.487	8,498.152	9,731.039	1.670	1.747
2	8,625.191	8,976.716	10,536.400	1.637	1.704
3	8,920.779	9,323.008	10,656.794	1.674	1.750
4	6,943.908	7,207.504	8,431.884	1.647	1.710
5	8,110.673	8,484.164	9,956.337	1.629	1.704
6	9,594.700	10,064.657	11,762.454	1.631	1.711
7	8,002.719	8,119.201	9,805.654	1.632	1.656
8	7,097.856	7,458.836	9,049.000	1.569	1.649
9	8,501.186	8,948.584	10,471.149	1.624	1.709
10	9,766.550	10,028.872	11,728.029	1.666	1.710
11	8,753.178	9,116.851	11,277.209	1.552	1.617
12	8,179.093	8,462.057	10,010.619	1.634	1.691
13	7,913.945	8,046.737	9.314,636	1.699	1.728
14	9,166.424	9,510.020	11,724.465	1.564	1.622
15	8,375.732	8,581.328	11,047.979	1.516	1.553
16	7,957.791	8,265.292	10,591.977	1.503	1.561
17	7,926.483	8,146.174	10,697.655	1.482	1.523
18	7,981.225	8,276.920	10,673.167	1.496	1.551
19	7,197.077	7,404.629	9,286.785	1.550	1.595
20	6,678.671	6,920.634	8,628.027	1.548	1.604
Results for linearity establishment					
HL60 DNA concentration	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
1	4.903,829	7.464	9,549.152	1.027	0.002
1	5,221.479	1.472	8,995.935	1.161	0.000
1	5,080.623	7.562	9,899.392	1.026	0.002
0.75	5,475.389	2,089.902	8,766.835	1.249	0.477

Table S1. Raw experimental data (continued).

Results for linearity establishment					
HL60 DNA concentration	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
0.75	**5,904.058**	**2,207.331**	**9,849.465**	**1.199**	**0.448**
0.75	**6,051.149**	**2,200.572**	**9,886.753**	**1.224**	**0.445**
0.75	**5,643.850**	**2,119.463**	**9,544.998**	**1.183**	**0.444**
0.5	**6,561.517**	**4,328.413**	**9,751.163**	**1.346**	**0.888**
0.5	**6,671.889**	**4,544.219**	**9,184.172**	**1.453**	**0.990**
0.5	**7,177.274**	**4,818.456**	**9,845.450**	**1.458**	**0.979**
0.5	**6,863.188**	**4,592.530**	**9,749.840**	**1.408**	**0.942**
0.25	**8,086.928**	**7,042.985**	**9,358.598**	**1.728**	**1.505**
0.25	**8,592.158**	**7,382.362**	**10,128.906**	**1.697**	**1.458**
0.25	**7,749.360**	**6,702.543**	**9,239.117**	**1.678**	**1.451**
0.25	**7,232.083**	**6,266.797**	**8,736.192**	**1.656**	**1.435**
0.05	**8,138.524**	**8,043.841**	**9,237.105**	**1.762**	**1.742**
0.05	**7,568.369**	**7,490.368**	**8,150.678**	**1.857**	**1.838**
0.05	**8,368.131**	**8,203.289**	**9,427.859**	**1.775**	**1.740**
Results for sensitivity verification					
exon 5					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
1	**10,468.298**	**10,945.364**	**12,463.605**	**1.680**	**1.756**
2	**10,028.600**	**10,385.101**	**12,463.258**	**1.609**	**1.667**
3	**9,844.112**	**10,191.915**	**11,531.600**	**1.707**	**1.768**
4	**9,621.608**	**10,016.862**	**11,443.023**	**1.682**	**1.751**
5	**9,998.651**	**10,390.474**	**11,797.655**	**1.695**	**1.761**
6	**9,773.721**	**10,159.256**	**11,588.007**	**1.687**	**1.753**
7	**9,653.838**	**9,986.155**	**11,417.232**	**1.691**	**1.749**
8	**10,533.242**	**10,880.321**	**12,117.561**	**1.739**	**1.796**
9	**9,790.206**	**10,134.970**	**11,419.745**	**1.715**	**1.775**
10	**9,856.696**	**10,169.208**	**11,637.029**	**1.694**	**1.748**
11	**10,026.146**	**10,562.224**	**11,628.360**	**1.724**	**1.817**
12	**10,250.589**	**10,443.521**	**12,332.062**	**1.662**	**1.694**
13	**10,151.521**	**10,320.845**	**12,004.537**	**1.691**	**1.719**
14	**10,500.286**	**10,593.709**	**12,504.924**	**1.679**	**1.694**
15	**10,877.051**	**10,989.169**	**12,897.240**	**1.687**	**1.704**
16	**10,748.283**	**10,827.233**	**12,451.384**	**1.726**	**1.739**
17	**10,321.126**	**10,352.638**	**11,749.774**	**1.757**	**1.762**
18	**9,989.142**	**10,072.599**	**11,936.745**	**1.674**	**1.688**
19	**6,863.384**	**6,928.983**	**8,150.452**	**1.684**	**1.700**
20	**7,681.714**	**7,810.076**	**9,087.573**	**1.691**	**1.719**
21	**6,739.922**	**8,464.381**	**9,261.283**	**1.456**	**1.828**
22	**6,909.912**	**8,655.253**	**9,559.806**	**1.446**	**1.811**
exon 7					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
1	**11,019.887**	**11,094.675**	**12,185.937**	**1.809**	**1.821**
2	**9,614.286**	**9,766.020**	**10,814.819**	**1.778**	**1.806**
3	**10,575.241**	**10,819.547**	**11,928.140**	**1.773**	**1.814**

Table S1. Raw experimental data (continued).

exon 7					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
4	**10,444.658**	**10,636.258**	**11,829.050**	**1.766**	**1.798**
5	**10,394.151**	**10,573.512**	**11,458.151**	**1.814**	**1.846**
6	**10,351.511**	**10,479.425**	**11,426.975**	**1.812**	**1.834**
7	**10,637.128**	**10,713.139**	**11,808.435**	**1.802**	**1.814**
8	**11,232.719**	**11,346.815**	**12,412.724**	**1.810**	**1.828**
9	**10,177.786**	**10,578.989**	**11,808.435**	**1.724**	**1.792**
10	**10,558.535**	**10,715.478**	**12,053.678**	**1.752**	**1.778**
11	**10,687.444**	**10,837.591**	**11,812.031**	**1.810**	**1.835**
12	**9,780.896**	**9,954.983**	**11,184.443**	**1.749**	**1.780**
13	**11,090.117**	**11,172.488**	**12,268.827**	**1.808**	**1.821**
14	**10,298.396**	**10,495.140**	**11,641.848**	**1.769**	**1.803**
15	**9,890.516**	**10,001.915**	**11,259.574**	**1.757**	**1.777**
16	**10,118.994**	**10,252.819**	**11,591.203**	**1.746**	**1.769**
17	**8,694.211**	**8,729.740**	**9,759.119**	**1.782**	**1.789**
18	**10,002.730**	**10,135.796**	**11,623.868**	**1.721**	**1.744**
19	**7,349.268**	**10,030.782**	**12,209.401**	**1.204**	**1.643**
20	**10,945.664**	**11,062.813**	**12,890.304**	**1.698**	**1.716**
21	**10,419.089**	**10,502.576**	**12,085.568**	**1.724**	**1.738**
22	**9,132.517**	**10,483.992**	**12,259.240**	**1.490**	**1.710**
Results of clinical sample validation					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
1	**8,176.834**	**8,695.163**	**9,739.772**	**1.679**	**1.785**
2	**458.317**	**604.548**	**2,676,778**	**0.342**	**0.452**
3	**2,841.137**	**2,966.371**	**3,035.543**	**1.872**	**1.954**
4	**7,691.166**	**7,947.637**	**8,162.169**	**1.885**	**1.947**
5	**4,310.578**	**4,518.362**	**4,516.029**	**1.909**	**2.001**
6	**7,755.416**	**8,255.956**	**8,299.301**	**1.869**	**1.990**
7	**6,205.464**	**6,459.195**	**10,753.274**	**1.154**	**1.201**
8	**6,079.739**	**6,333.193**	**11,188.125**	**1.087**	**1.132**
9	**5,695.623**	**5,823.421**	**5,998.014**	**1.899**	**1.942**
10	**13,893.444**	**14,332.375**	**14,492.604**	**1.917**	**1.978**
11	**5,686.683**	**5,820.756**	**10,265.382**	**1.108**	**1.134**
12	**5,793.795**	**5,954.524**	**6,173.559**	**1.877**	**1.929**
13	**10,481.425**	**10,899.073**	**11,460.675**	**1.829**	**1.902**
14	**12,266.087**	**12,271.226**	**11,624.511**	**2.110**	**2.111**
15	**10,142.966**	**10,292.514**	**10,325.340**	**1.965**	**1.994**
16	**6,898.606**	**7,323.357**	**13,993.793**	**0.986**	**1.047**
17	**6,161.231**	**7,430.752**	**7,290.914**	**1.69**	**2.038**
18	**3,572.236**	**6,747.337**	**3,929.266**	**1.818**	**3.434**
19	**7,924.502**	**8,218.470**	**8,669.964**	**1.828**	**1.896**
20	**6,827.895**	**7,165.453**	**7,201.165**	**1.896**	**1.990**
21	**10,160.638**	**10,655.422**	**11,487.844**	**1.769**	**1.855**
22	**3,234.297**	**3,243.151**	**3,309.364**	**1.955**	**1.960**
23	**12,415.853**	**12,645.584**	**12,470.947**	**1.991**	**2.028**

Table S1. Raw experimental data (continued).

Results of clinical sample validation					
ID	**CN of ChF**	**CN of ChH**	**CN of ChC**	**CN of exon 5**	**CN of exon 7**
24	**8,723.054**	**8,886.010**	**9,185.674**	**1.899**	**1.935**
25	**10,719.572**	**11,040.116**	**11,046.165**	**1.941**	**1.999**
26	**12,962.830**	**13,136.414**	**13,214.560**	**1.962**	**1.988**
27	**9,258.006**	**9,403.778**	**9,917.708**	**1.867**	**1.896**
28	**14,814.466**	**15,091.826**	**14,887.100**	**1.99**	**2.038**
29	**11,534.778**	**11,759.853**	**13,170.150**	**1.752**	**1.786**
30	**14,030.204**	**15,095.479**	**12,463.258**	**2.251**	**2.422**
31	**8,424.239**	**8,627.791**	**8,925.651**	**1.888**	**1.933**
32	**10,229.972**	**10,688.319**	**10,866.354**	**1.883**	**1.967**
33	**4,722.377**	**4,747.822**	**7,044.394**	**1.341**	**1.348**
34	**9,747.188**	**9,967.170**	**9,906.120**	**1.968**	**2.012**
35	**8,252.998**	**8,459.267**	**7,814.863**	**2.112**	**2.165**
36	**8,860.558**	**8,967.166**	**9,207.217**	**1.925**	**1.948**
37	**26,483.715**	**26,596.566**	**25,933.971**	**2.042**	**2.051**
38	**9,059.864**	**9,211.982**	**11,442.709**	**1.584**	**1.10**
39	**11,503.041**	**11,892.471**	**11,543.363**	**1.993**	**2.60**
40	**10,755.034**	**11,057.058**	**10,943.271**	**1.966**	**2.21**
41	**11,438.931**	**11,470.775**	**11,557.055**	**1.98**	**1.85**
42	**10,965.442**	**10,730.402**	**15,309.311**	**1.433**	**1.02**

Table S2. The test results of newly diagnosed patients and their related clinical history.

ID	Diagnosis	Sample source	NGS *TP53* mutation findings	NGS *TP53* CNV findings (copies/genome)	Karyotyping	CN of exon 5 (copies/genome)	CN of exon 7 (copies/genome)
1	MDS	PB	c.738G>A (60.50%)	NR	± 17 not found	1.679	1.785
2	Lymphoma	LN	c.370T>G (82.40%)	NR	NR	0.342	0.452
3	AML	BM	not found	NR	± 17 not found	1.872	1.954
4	MDS	BM	c.659A>G(37.20%) c.938del(33.40%)	NR	± 17 not found	1.885	1.947
5	AML	BM	c.578A>G(10.2%) c.659A>G(6.70%)	NR	± 17 not found	1.909	2.001
6	MDS	BM	not found	NR	± 17 not found	1.869	1.990
7	AML	PB	c.818G>T (61.00%)	NR	NR	1.154	1.201
8	AML	BM	c.799C>T (68.30%)	NR	-17[CP12]/[3]	1.087	1.132
9	MDS	BM	c.832C>T (90.30%)	NR	± 17 not found	1.899	1.942
10	MDS	BM	c.286del (93.0%)	not found	± 17 not found	1.917	1.978
11	MDS	BM	c.216del (72.5%)	1.20	-17[CP9]/[1]	1.108	1.134
12	AML	PB	not found	NR	± 17 not found	1.877	1.929
13	AML	BM	not found	NR	± 17 not found	1.829	1.902
14	MM	BM	NR	NR	± 17 not found	2.110	2.111
15	MM	BM	NR	NR	± 17 not found	1.965	1.994
16	Lymphoma	PB	NR	NR	± 17 not found	0.986	1.047
17	AML	BM	not found	NR	± 17 not found	1.690	2.038
18	Lymphoma	LN	c.626_627del(51.0%) c.844C>T(23.5%)	CN gain	-17[CP4]/[16]	1.818	3.434
19	Lymphoma	PB	c.742C>T(2.4%) c.403T>C(3.2%)	not found	± 17 not found	1.828	1.896
20	AML	BM	not found	not found	± 17 not found	1.896	1.990
21	aCML	PB	c.745A>G(48.8%)	not found	± 17 not found	1.769	1.855
22	MDS	BM	c.524G>A(46.9%) c.743G>A(45.8%)	not found	± 17 not found	1.955	1.960
23	MDS	BM	NR	NR	± 17 not found	1.991	2.028
24	AML	BM	not found	not found	± 17 not found	1.899	1.935
25	MDS	BM	not found	not found	NR	1.941	1.999
26	MDS	BM	not found	NR	± 17 not found	1.962	1.988
27	CMML	BM	not found	not found	± 17 not found	1.867	1.896
28	MDS	BM	NR	NR	± 17 not found	1.990	2.038
29	MDS	BM	not found	not found	± 17 not found	1.752	1.786
30	MDS	BM	not found	not found	± 17 not found	2.251	2.422
31	CMML	BM	not found	not found	NR	1.888	1.933
32	MDS	BM	not found	not found	± 17 not found	1.883	1.967
33	ALL	BM	not found	1.44	± 17 not found	1.341	1.348
34	MM	BM	NR	NR	± 17 not found	1.968	2.012

Table S2. The test results of newly diagnosed patients and their related clinical history (continued).

ID	Diagnosis	Sample source	NGS *TP53* mutation findings	NGS *TP53* CNV findings (copies/genome)	Karyotyping	CN of exon 5 (copies/genome)	CN of exon 7 (copies/genome)
35	Lymphoma	BM	NR	NR	± 17 not found	2.112	2.165
36	MM	BM	NR	NR	± 17 not found	1.925	1.948
37	MM	BM	NR	NR	± 17 not found	2.042	2.051
38	MM	BM	NR	NR	± 17 not found	1.584	1.610
39	Lymphoma	PB	not found	not found	± 17 not found	1.993	2.060
40	Lymphoma	BM	NR	NR	± 17 not found	1.966	2.021
41	Lymphoma	BM	not found	NR	± 17 not found	1.980	1.985
42	CLL	PB	NR	NR	± 17 not found	1.433	1.402

MDS, myelodysplastic syndrome; AML, acute myeloid leukemia; aCML, atypical chronic myelogenous leukemia; CMML, chronic myelomonocytic leukemia; MM, multiple myeloma; ALL, acute lymphoblastic leukemia; CLL, chronic lymphocytic leukemia; PB, peripheral blood; LN, lymphoid node; BM, bone marrow; NR, not reported; green shading indicates CN loss positive finding; orange shading indicates CN gain positive finding.

File S3. The detailed karyotypes of the patients involved.

1. Patient:
40-47,X,-X,del(5)(q13q33),-7,del(8)(q22),add(11)(q23),del(13)(q23q14),-22,+Mar[CP7]/46,XX[3].
2. Patient 3:
46,XY[20].
3. Patient 4:
43,XX,-3,-5,t(7;12)(p11;p12)[5]/44,XX,idem,+der(12)t(7;12)(p11;p12)[1]/43,XX,-3,-5,del(12)(q10)[1]/46,XX[3].
4. Patient 5:
47,XY,+del(1)(p11p32)[8]/46,XY[2].
5. Patient 6:
45-49,XY,del(5)(q12q33),+8,+del(8)(q21),+15,t(15;22)(q14;p13),add(18)(q21),+20,-22,der(22)t(15;22)(q14;p13),+Mar[CP10].
6. Patient 8:
43-49,X,add(X)(p22),der(1)del(1)(p31p32)t(1;17)(q12;p12),+2,i(3)(q10),del(5)(q13),del(5)(q13q33),del(7)t(1;7)(q25;p22),+8,-10,del(11)(q22)inv(11)(p15q24),-12,+14+,15,-17,-18,+20[CP12]/46,XX[3].
7. Patient 9:
43-45,XY,del(2)(q24q36),+del(5)(p10),del(5)(q13q33),?t(5;6)(q21;q16),-7,+del(8)(p21),+del(11)(q23),+del(11)(q14),add(12)(p13),?t(13;20)(q34;q12),-21,i(21)(q10)[CP7]/46,XY[3].
8. Patient 10:
44,XY,del(5)(q21),-14,-20[1]/44-46,XY,der(3)t(3;8)(p12;p12),del(5)(q21),-10,t(11;15)(p11;q24),+16,+Mar[CP9].
9. Patient 11:
40-45,XY,der(2)t(1;2)(p32;p25),-5,add(8)(p23),+del(11)(q13),add(12)(p12),del(13)(q13q21),t(14;22)(q11;q12),-17,-18,der(18)?t(8;18)(q10;p11),-21,del(21)(q22),+Mar[CP9]/46,XY[1].
10. Patient 12:
46,XY[20].
11. Patient 13:
46,XX[20].
12. Patient 14:
45,X,-Y[5]/46,XY[15].
13. Patient 15
46,XY[20].
14. Patient 16:
40-43,XX,t(1;2)(q10;q10),?del(2)(p23),del(2)(q22),+del(3)(q23),?t(4;19)(q28;p13),t(5;17)(q13;q25),t(11;14)(q13;32),-12,add(13)(q34),+14,add(16)q24,+der(19)?t(4;19)(q28;p13),-20,-21,-22,-22,+Mar[CP10].
15. Patient 17:
46,XX[6].

16. Patient 18:
41-44,XY,del(1)(p12p32),-2,+3,add(4)(q28),+?add(6)(p22),-9,-11,add(12)(p13),-13,add(13)(p10),t(16;?)(p10;?),-17,-21,Mar1,+Mar2[CP4]/46,XY,inv(9)(p11q12)[16].
17. Patient 19:
46,XX,t(1;5)(q22;p15),add(10)(p15)[3]/46,XX[7].
18. Patient 20:
46,XX[20].
19. Patient 21:
47,XY,del(3)(q21q25),+8[10].
20. Patient 22:
45-49,XY,del(5)(q12q33),+8,+del(8)(q21),+15,t(15;22)(q14;p13),add(18)(q21),+20,-22,der(22)t(15;22)(q14;p13),+Mar[CP10].
21. Patient 23:
46,XX[20].
22. Patient 24:
46,XY[20].
23. Patient 26:
46,XY,t(3;21)(q26;q22).
24. Patient 27:
46,XX[20].
25. Patient 28:
40-46,XY,add(3)(q29),-5,-7,dup(7)(q10q11),+8,del(12)(p12),-20,+Mar[CP14].
26. Patient 29:
46,XY[20].
27. Patient 30:
46,XX,9ph+[20].
28. Patient 31:
46,XX[20].
29. Patient 32:
45,X,-Y[13]/46,XY[7].
30. Patient 33:
46,XX[3].
31. Patient 34:
46,XX[20].
32. Patient 35:
46,XY[20].
33. Patient 36:
45,X,-Y[3]/46,XY[27].
34. Patient 37
46,XX[14].
35. Patient 38:
46,XY[20].
36. Patient 39:
46,X,del)X_(p11),t(1;3)(p36;p24),der(9)t(4;9)(q24;p23)×2,der(19)t(12;19)(q14;q13.2)[5]/46,X,idem,der(14)t(14;22)(q13;q13)[4]/45,XX,-20[1].
37. Patient 40:
46,XX[20].
38. Patient 41:
46,XX[20].
39. Patient 42:
7,XY,+12[20].