

**Supplementary Table S1: Genomic alterations in components of the CDK4/6 pathway.** All data were compiled from The Cancer Genome Atlas (TCGA) in August 2021. Only studies with 10 or more samples and frequencies above 5% are shown.

Alteration type	Cancer type	Frequency of alteration	
<b>CCND1</b>			
<b>CNV gain</b>			
	Esophageal carcinoma	72 / 184	39.13%
	Head and Neck squamous cell carcinoma	174 / 521	33.40%
	Breast invasive carcinoma	301 / 1072	28.08%
	Bladder Urothelial Carcinoma	101 / 408	24.75%
	Ovarian serous cystadenocarcinoma	139 / 585	23.76%
	Lung squamous cell carcinoma	113 / 502	22.51%
	Uterine Carcinosarcoma	8 / 56	14.29%
	Stomach adenocarcinoma	55 / 432	12.73%
	Skin Cutaneous Melanoma	57 / 468	12.18%
	Sarcoma	31 / 260	11.92%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	35 / 294	11.90%
	Lung adenocarcinoma	57 / 513	11.11%
	Liver hepatocellular carcinoma	39 / 371	10.51%
	Uterine Corpus Endometrial Carcinoma	41 / 510	8.04%
<b>CNV loss</b>			
	Uterine Carcinosarcoma	3 / 56	5.36%
<b>3' UTR insertion/deletion</b>			
	Uterine Carcinosarcoma	8 / 105	7.62%
<b>3' UTR substitution</b>			
	Uterine Carcinosarcoma	10 / 105	9.52%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	2 / 39	5.13%
<b>Inframe insertion/deletion</b>			
	Uterine Carcinosarcoma	14 / 105	13.33%
<b>Missense substitution</b>			
	Brain Lower Grade Glioma	4 / 12	33.33%
	Uterine Carcinosarcoma	30 / 105	28.57%
	Colon adenocarcinoma	3 / 12	25.00%
	Uterine Carcinosarcoma	1 / 12	8.33%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	2 / 39	5.13%
<b>Stop codon gain</b>			
	Colon adenocarcinoma	1 / 12	8.33%
<b>CCND2</b>			
<b>CNV gain</b>			
	Ovarian serous cystadenocarcinoma	130 / 585	22.22%
	Uterine Carcinosarcoma	9 / 56	16.07%
	Lung squamous cell carcinoma	56 / 502	11.16%
	Head and Neck squamous cell carcinoma	37 / 521	7.10%
	Esophageal carcinoma	13 / 184	7.07%
	Breast invasive carcinoma	67 / 1,072	6.25%

	Sarcoma	16 / 260	6.15%
	Bladder Urothelial Carcinoma	24 / 408	5.88%
	Colon adenocarcinoma	23 / 448	5.13%
<b>CNV loss</b>			
	Sarcoma	26 / 260	10.00%
	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma	4 / 47	8.51%
	Ovarian serous cystadenocarcinoma	40 / 585	6.84%
	Stomach adenocarcinoma	27 / 432	6.25%
	Lung adenocarcinoma	30 / 513	5.85%
	Pancreatic adenocarcinoma	9 / 175	5.14%
<b>3' UTR insertion/deletion</b>			
	Uterine Corpus Endometrial Carcinoma	76 / 126	60.32%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	5 / 22	22.73%
	Esophageal carcinoma	6 / 28	21.43%
	Sarcoma	6 / 44	13.64%
<b>3' UTR substitution</b>			
	Uterine Corpus Endometrial Carcinoma	71 / 126	56.35%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	8 / 22	36.36%
	Esophageal carcinoma	6 / 28	21.43%
	Sarcoma	3 / 44	6.82%
	Breast invasive carcinoma	6 / 117	5.13%
<b>Frameshift mutation</b>			
	Prostate adenocarcinoma	1 / 12	8.33%
<b>Missense substitution</b>			
	Skin Cutaneous Melanoma	7 / 37	18.92%
	Uterine Corpus Endometrial Carcinoma	20 / 126	15.87%
	Liver hepatocellular carcinoma	3 / 22	13.64%
	Pancreatic adenocarcinoma	1 / 11	9.09%
	Uterine Carcinosarcoma	1 / 12	8.33%
	Stomach adenocarcinoma	4 / 52	7.69%

## **CCND3**

### **CNV gain**

	Ovarian serous cystadenocarcinoma	93 / 585	15.90%
	Esophageal carcinoma	28 / 184	15.22%
	Stomach adenocarcinoma	54 / 432	12.50%
	Lung adenocarcinoma	44 / 513	8.58%
	Bladder Urothelial Carcinoma	32 / 408	7.84%
	Pancreatic adenocarcinoma	13 / 175	7.43%
	Lung squamous cell carcinoma	37 / 502	7.37%
	Breast invasive carcinoma	77 / 1,072	7.18%
	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma	3 / 47	6.38%
	Rectum adenocarcinoma	10 / 164	6.10%

### **CNV loss**

	Ovarian serous cystadenocarcinoma	33 / 585	5.64%
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### **3' UTR insertion/deletion**

	Uterine Corpus Endometrial Carcinoma	12 / 56	21.43%
<b>3' UTR substitution</b>			
	Uterine Corpus Endometrial Carcinoma	8 / 56	14.29%
	Esophageal carcinoma	3 / 33	9.09%
	Liver hepatocellular carcinoma	1 / 18	5.56%
<b>Missense substitution</b>			
	Colon adenocarcinoma	4 / 17	23.53%
	Uterine Corpus Endometrial Carcinoma	7 / 56	12.50%
	Rectum adenocarcinoma	1 / 10	10.00%
	Bladder Urothelial Carcinoma	5 / 52	9.62%
	Pancreatic adenocarcinoma	1 / 14	7.14%
	Skin Cutaneous Melanoma	2 / 30	6.67%

### CDK4

#### CNV gain

	Sarcoma	56 / 260	21.54%
	Glioblastoma multiforme	98 / 596	16.44%
	Lung adenocarcinoma	61 / 513	11.89%
	Ovarian serous cystadenocarcinoma	53 / 585	9.06%
	Stomach adenocarcinoma	31 / 432	7.18%
	Skin Cutaneous Melanoma	28 / 468	5.98%
	Brain Lower Grade Glioma	27 / 497	5.43%

#### CNV loss

	Ovarian serous cystadenocarcinoma	35 / 585	5.98%
	Sarcoma	14 / 260	5.38%

#### 5' UTR substitution

	Cervical squamous cell carcinoma and endocervical adenocarcinoma	1 / 13	7.69%
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#### Missense substitution

	Uterine Corpus Endometrial Carcinoma	11 / 33	33.33%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	3 / 13	23.08%
	Skin Cutaneous Melanoma	10 / 45	22.22%
	Head and Neck squamous cell carcinoma	3 / 26	11.54%
	Colon adenocarcinoma	1 / 10	10.00%
	Bladder Urothelial Carcinoma	2 / 30	6.67%
	Stomach adenocarcinoma	2 / 40	5.00%

### CDK6

#### CNV gain

	Esophageal carcinoma	39 / 184	21.20%
	Ovarian serous cystadenocarcinoma	67 / 585	11.45%
	Stomach adenocarcinoma	48 / 432	11.11%
	Lung squamous cell carcinoma	55 / 502	10.96%
	Sarcoma	19 / 260	7.31%
	Uterine Carcinosarcoma	3 / 56	5.36%
	Pancreatic adenocarcinoma	9 / 175	5.14%
	Liver hepatocellular carcinoma	19 / 371	5.12%

#### CNV loss

	Uterine Carcinosarcoma	3 / 56	5.36%
<b>3' UTR substitution</b>			
	Uterine Corpus Endometrial Carcinoma	25 / 64	39.06%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	8 / 24	33.33%
	Esophageal carcinoma	3 / 47	6.38%
<b>Missense substitution</b>			
	Uterine Corpus Endometrial Carcinoma	18 / 64	28.13%
	Pancreatic adenocarcinoma	2 / 10	20.00%
	Bladder Urothelial Carcinoma	5 / 30	16.67%
	Colon adenocarcinoma	3 / 21	14.29%
	Lung adenocarcinoma	5 / 36	13.89%
	Glioblastoma multiforme	2 / 18	11.11%
	Stomach adenocarcinoma	5 / 59	8.47%
	Skin Cutaneous Melanoma	2 / 26	7.69%
<b>CDKN2A</b>			
<b>CNV gain</b>			
	Ovarian serous cystadenocarcinoma	46 / 585	7.86%
<b>CNV loss</b>			
	Glioblastoma multiforme	377 / 596	63.26%
	Esophageal carcinoma	89 / 184	48.37%
	Bladder Urothelial Carcinoma	152 / 408	37.25%
	Skin Cutaneous Melanoma	164 / 468	35.04%
	Head and Neck squamous cell carcinoma	181 / 521	34.74%
	Pancreatic adenocarcinoma	60 / 175	34.29%
	Lung squamous cell carcinoma	148 / 502	29.48%
	Cholangiocarcinoma	8 / 36	22.22%
	Lung adenocarcinoma	104 / 513	20.27%
	Sarcoma	48 / 260	18.46%
	Brain Lower Grade Glioma	81 / 497	16.30%
	Stomach adenocarcinoma	66 / 432	15.28%
	Liver hepatocellular carcinoma	44 / 371	11.86%
	Adrenocortical carcinoma	10 / 90	11.11%
	Ovarian serous cystadenocarcinoma	50 / 585	8.55%
	Thymoma	8 / 113	7.08%
	Kidney renal papillary cell carcinoma	15 / 269	5.58%
	Uterine Carcinosarcoma	3 / 56	5.36%
<b>3' UTR substitution</b>			
	Uterine Corpus Endometrial Carcinoma	9 / 61	14.75%
	Colon adenocarcinoma	4 / 35	11.43%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	1 / 18	5.56%
<b>Frameshift mutation</b>			
	Pancreatic adenocarcinoma	11 / 89	12.36%
	Adrenocortical carcinoma	1 / 11	9.09%
	Lung squamous cell carcinoma	19 / 236	8.05%
	Head and Neck squamous cell carcinoma	21 / 278	7.55%

	Liver hepatocellular carcinoma	3 / 54	5.56%
<b>Missense substitution</b>			
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	6 / 18	33.33%
	Cholangiocarcinoma	2 / 10	20.00%
	Lung squamous cell carcinoma	34 / 236	14.41%
	Pancreatic adenocarcinoma	12 / 89	13.48%
	Uterine Corpus Endometrial Carcinoma	8 / 61	13.11%
	Lung adenocarcinoma	19 / 145	13.10%
	Liver hepatocellular carcinoma	6 / 54	11.11%
	Stomach adenocarcinoma	10 / 96	10.42%
	Skin Cutaneous Melanoma	23 / 222	10.36%
	Bladder Urothelial Carcinoma	19 / 187	10.16%
	Head and Neck squamous cell carcinoma	23 / 278	8.27%
	Esophageal carcinoma	6 / 104	5.77%
<b>Splice donor/acceptor</b>			
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	1 / 18	5.56%
<b>Stop codon gain</b>			
	Head and Neck squamous cell carcinoma	59 / 278	21.22%
	Pancreatic adenocarcinoma	12 / 89	13.48%
	Skin Cutaneous Melanoma	24 / 222	10.81%
	Lung squamous cell carcinoma	23 / 236	9.75%
	Kidney renal papillary cell carcinoma	1 / 16	6.25%
	Stomach adenocarcinoma	5 / 96	5.21%
	Prostate adenocarcinoma	1 / 20	5.00%
<b>CDKN2B</b>			
<b>CNV gain</b>			
	Ovarian serous cystadenocarcinoma	46 / 585	7.86%
<b>CNV loss</b>			
	Glioblastoma multiforme	372 / 596	62.42%
	Bladder Urothelial Carcinoma	150 / 408	36.76%
	Pancreatic adenocarcinoma	58 / 175	33.14%
	Skin Cutaneous Melanoma	155 / 468	33.12%
	Lung squamous cell carcinoma	144 / 502	28.69%
	Lung adenocarcinoma	99 / 513	19.30%
	Brain Lower Grade Glioma	79 / 497	15.90%
	Stomach adenocarcinoma	63 / 432	14.58%
	Liver hepatocellular carcinoma	41 / 371	11.05%
	Adrenocortical carcinoma	9 / 90	10.00%
	Ovarian serous cystadenocarcinoma	49 / 585	8.38%
	Kidney renal papillary cell carcinoma	15 / 269	5.58%
	Uterine Carcinosarcoma	3 / 56	5.36%
<b>3' UTR substitution</b>			
	Colon adenocarcinoma	1 / 20	5.00%
<b>5' UTR substitution</b>			
	Uterine Corpus Endometrial Carcinoma	5 / 35	14.29%

	Adrenocortical carcinoma	1 / 11	9.09%
	Colon adenocarcinoma	1 / 20	5.00%
<b>Missense substitution</b>			
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	1 / 11	9.09%
	Uterine Corpus Endometrial Carcinoma	3 / 35	8.57%
	Colon adenocarcinoma	1 / 20	5.00%
<b>E2F1</b>			
<b>CNV gain</b>			
	Ovarian serous cystadenocarcinoma	75 / 585	12.82%
	Uterine Carcinosarcoma	6 / 56	10.71%
	Lung squamous cell carcinoma	45 / 502	8.96%
	Bladder Urothelial Carcinoma	36 / 408	8.82%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	20 / 294	6.80%
	Colon adenocarcinoma	25 / 448	5.58%
	Esophageal carcinoma	10 / 184	5.43%
	Head and Neck squamous cell carcinoma	27 / 521	5.18%
<b>3' UTR insertion/deletion</b>			
	Esophageal carcinoma	1 / 12	8.33%
	Uterine Corpus Endometrial Carcinoma	4 / 79	5.06%
<b>3' UTR substitution</b>			
	Uterine Corpus Endometrial Carcinoma	9 / 79	11.39%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	2 / 25	8.00%
<b>Frameshift mutation</b>			
	Uterine Corpus Endometrial Carcinoma	10 / 79	12.66%
	Prostate adenocarcinoma	1 / 14	7.14%
<b>Missense substitution</b>			
	Skin Cutaneous Melanoma	6 / 19	31.58%
	Uterine Corpus Endometrial Carcinoma	23 / 79	29.11%
	Liver hepatocellular carcinoma	3 / 15	20.00%
	Stomach adenocarcinoma	3 / 27	11.11%
	Esophageal carcinoma	1 / 12	8.33%
	Cervical squamous cell carcinoma and endocervical adenocarcinoma	2 / 25	8.00%
	Lung adenocarcinoma	3 / 39	7.69%
	Prostate adenocarcinoma	1 / 14	7.14%
	Breast invasive carcinoma	5 / 79	6.33%
	Lung squamous cell carcinoma	3 / 58	5.17%
<b>Stop codon gain</b>			
	Uterine Corpus Endometrial Carcinoma	5 / 79	6.33%
	Skin Cutaneous Melanoma	1 / 19	5.26%
<b>RB1</b>			
<b>CNV gain</b>			
	Ovarian serous cystadenocarcinoma	40 / 585	6.84%
	Stomach adenocarcinoma	28 / 432	6.48%
<b>CNV loss</b>			
	Sarcoma	81 / 260	31.15%

Prostate adenocarcinoma	133 / 487	27.31%
Uterine Carcinosarcoma	13 / 56	23.21%
Bladder Urothelial Carcinoma	91 / 408	22.30%
Ovarian serous cystadenocarcinoma	123 / 585	21.03%
Liver hepatocellular carcinoma	78 / 371	21.02%
Cervical squamous cell carcinoma and endocervical adenocarcinoma	56 / 294	19.05%
Glioblastoma multiforme	74 / 596	12.42%
Breast invasive carcinoma	125 / 1,072	11.66%
Lung squamous cell carcinoma	54 / 502	10.76%
Mesothelioma	9 / 84	10.71%
Head and Neck squamous cell carcinoma	55 / 521	10.56%
Rectum adenocarcinoma	17 / 164	10.37%
Esophageal carcinoma	16 / 184	8.70%
Lung adenocarcinoma	37 / 513	7.21%
Adrenocortical carcinoma	6 / 90	6.67%
Brain Lower Grade Glioma	29 / 497	5.84%
Colon adenocarcinoma	25 / 448	5.58%
Stomach adenocarcinoma	23 / 432	5.32%
<b>3' UTR substitution</b>		
Uterine Corpus Endometrial Carcinoma	15 / 104	14.42%
<b>Frameshift mutation</b>		
Bladder Urothelial Carcinoma	22 / 140	15.71%
Uterine Corpus Endometrial Carcinoma	15 / 104	14.42%
Glioblastoma multiforme	11 / 79	13.92%
Esophageal carcinoma	3 / 23	13.04%
Liver hepatocellular carcinoma	10 / 86	11.63%
Sarcoma	11 / 96	11.46%
Lung adenocarcinoma	9 / 79	11.39%
Skin Cutaneous Melanoma	5 / 45	11.11%
Kidney renal clear cell carcinoma	1 / 11	9.09%
Cervical squamous cell carcinoma and endocervical adenocarcinoma	6 / 71	8.45%
Lung squamous cell carcinoma	8 / 95	8.42%
Brain Lower Grade Glioma	3 / 36	8.33%
Colon adenocarcinoma	4 / 49	8.16%
Ovarian serous cystadenocarcinoma	7 / 131	5.34%
Head and Neck squamous cell carcinoma	4 / 76	5.26%
<b>Inframe insertion/deletion</b>		
Uterine Carcinosarcoma	1 / 16	6.25%
<b>Missense substitution</b>		
Uterine Corpus Endometrial Carcinoma	59 / 104	56.73%
Colon adenocarcinoma	10 / 49	20.41%
Rectum adenocarcinoma	4 / 24	16.67%
Lung adenocarcinoma	10 / 79	12.66%
Stomach adenocarcinoma	8 / 65	12.31%
Skin Cutaneous Melanoma	5 / 45	11.11%

Cervical squamous cell carcinoma and endocervical adenocarcinoma	7 / 71	9.86%
Kidney renal clear cell carcinoma	1 / 11	9.09%
Glioblastoma multiforme	7 / 79	8.86%
Lung squamous cell carcinoma	8 / 95	8.42%
Head and Neck squamous cell carcinoma	6 / 76	7.89%
Bladder Urothelial Carcinoma	11 / 140	7.86%
Uterine Carcinosarcoma	1 / 16	6.25%
Liver hepatocellular carcinoma	5 / 86	5.81%

**Splice donor/acceptor**

Bladder Urothelial Carcinoma	17 / 140	12.14%
Glioblastoma multiforme	8 / 79	10.13%
Lung adenocarcinoma	7 / 79	8.86%
Lung squamous cell carcinoma	8 / 95	8.42%
Sarcoma	7 / 96	7.29%
Liver hepatocellular carcinoma	6 / 86	6.98%
Skin Cutaneous Melanoma	3 / 45	6.67%
Uterine Carcinosarcoma	1 / 16	6.25%
Uterine Corpus Endometrial Carcinoma	6 / 104	5.77%
Brain Lower Grade Glioma	2 / 36	5.56%

**Stop codon gain**

Bladder Urothelial Carcinoma	38 / 140	27.14%
Glioblastoma multiforme	16 / 79	20.25%
Skin Cutaneous Melanoma	9 / 45	20.00%
Uterine Carcinosarcoma	3 / 16	18.75%
Uterine Corpus Endometrial Carcinoma	18 / 104	17.31%
Lung adenocarcinoma	13 / 79	16.46%
Lung squamous cell carcinoma	13 / 95	13.68%
Cervical squamous cell carcinoma and endocervical adenocarcinoma	8 / 71	11.27%
Sarcoma	9 / 96	9.38%
Esophageal carcinoma	2 / 23	8.70%
Breast invasive carcinoma	11 / 161	6.83%
Head and Neck squamous cell carcinoma	5 / 76	6.58%

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