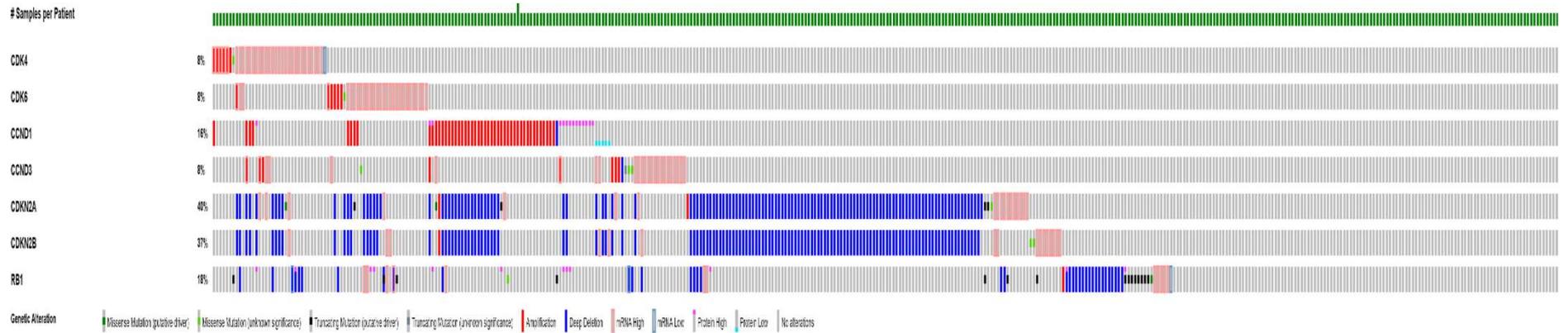


Supplement Figure Legends

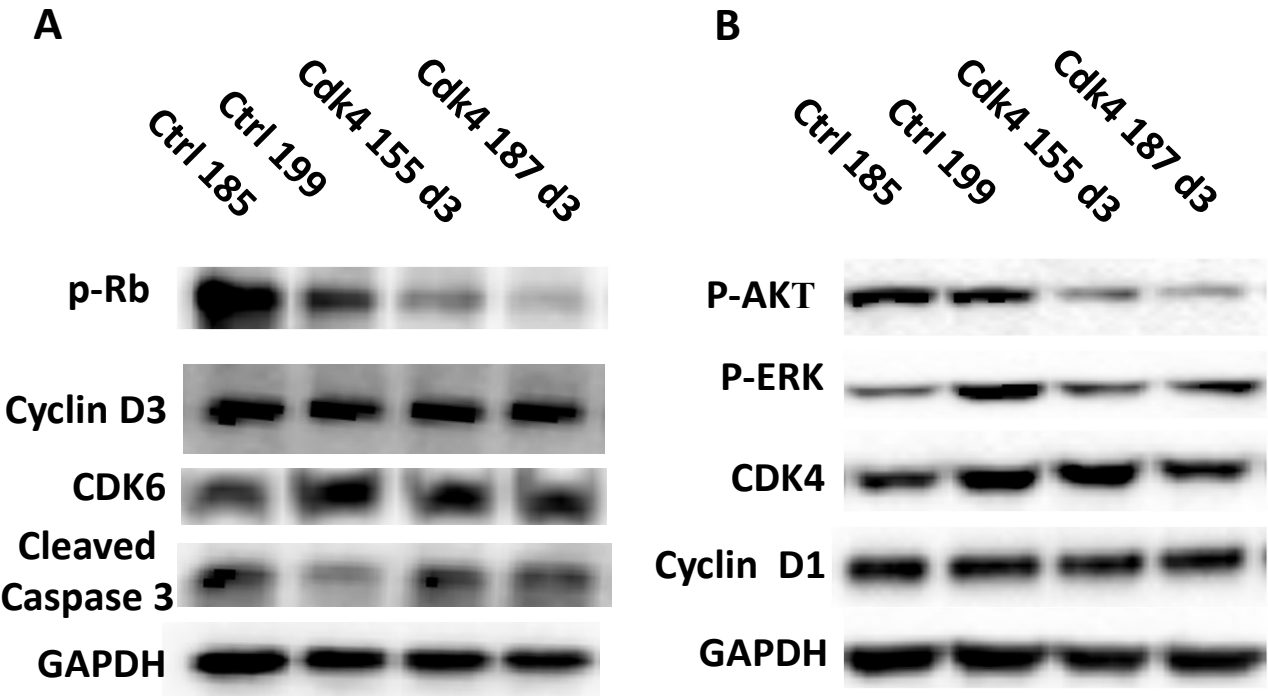
S-Figure 1. Alteration landscape of the cyclin-CDK4/6 pathway in bladder cancer. The genomic information of 413 bladder cancer specimens were analyzed for alterations of seven genes along the cyclin-CDK4/6 pathway: CDK4, CDK6, CCND1, CCND3, CDKN2A, CDKN2B and RB1. Each vertical bar represents one patient.

S-Figure 2. Palbociclib affected cell growth related proteins in bladder PDX models. A and B. Western blot analysis of tumors obtained three days after palbociclib treatment. The expression of p-Rb and p-Akt were suppressed in treatment group. However, the expression of p-ERK, CDK4, CDK6, cyclin D1, cyclin D3, Cleaved caspase-3 were not changed.

S-Figure 1



S-Figure 2



S-Table 1. Mutual exclusivity or co-occurrence among cell cycle regulators

A	B	Neither	A Not B	B Not A	Both	Log2 Odds Ratio	p-Value	Tendency
CDKN2A	CDKN2B	170	36	10	120	>3	<0.001	Co-occurrence
RB1	CDKN2B	132	74	106	24	-1.308	<0.001	Mutual exclusivity
CCND1	CDKN2B	171	35	92	38	1.013	0.006	Co-occurrence
CDKN2A	RB1	117	121	63	35	-0.896	0.008	Mutual exclusivity
CDKN2A	CCND1	150	113	30	43	0.928	0.011	Co-occurrence

Among 413 specimens, 336 specimens had the information available of all seven genes. The co-occurrence or mutual exclusivity was analyzed. Only the significant ones were presented in this table.

S-Table 2. Anti-PD1/PD-L1 antibodies that have been approved for bladder cancer treatment

Drug name	Approved date	Indications	ORR	Median OS	Median PFS	Grade $\frac{3}{4}$ irAEs
Atezolizumab	May 18, 2016	1, 2	13.4%	8.6 mos	2.1 mos	20%
Nivolumab	Feb 2, 2017	1	19.6%	8.7 mos	2.0 mos	18%
Durvalumab	May 1, 2017	1	17.8%	18.2 mos	1.5 mos	6.8%
Avelumab	May 9, 2017	1	17%	6.2 mos	1.5 mos	8%
Pembrolizumab	May 18, 2017	1, 2	21.1%	10.3 mos	2.1 mos	15%

1. Locally advanced or metastatic urothelial carcinoma that has disease progression during or following platinum-containing chemotherapy or has disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
2. Locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy

Abbreviation: ORR: overall response rate; OS: Overall survival; PFS: Progression-free survival; irAE: Immune-mediated adverse events.

Five anti-PD1/PD-L1 antibodies have been approved by the FDA for the treatment of advanced bladder cancer after disease progression of cisplatin-based chemotherapy or in those patients who are cisplatin-ineligible.