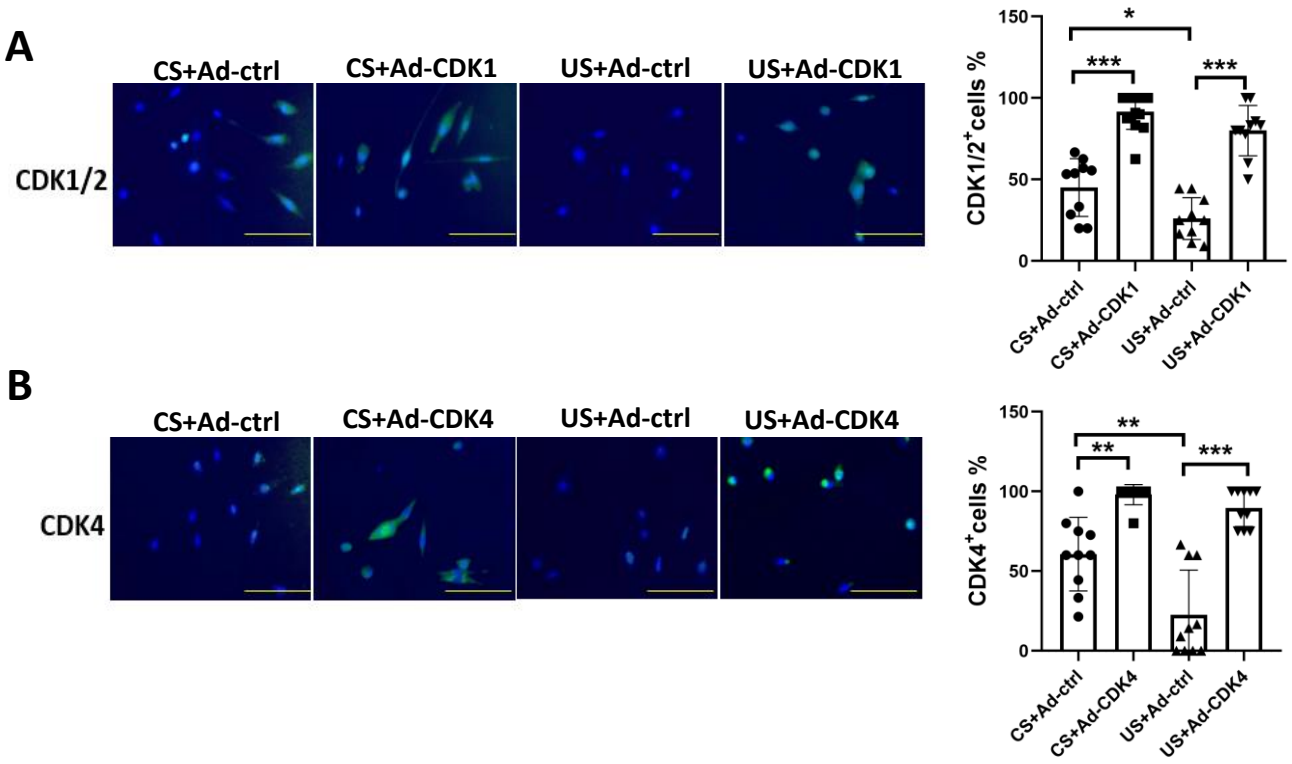
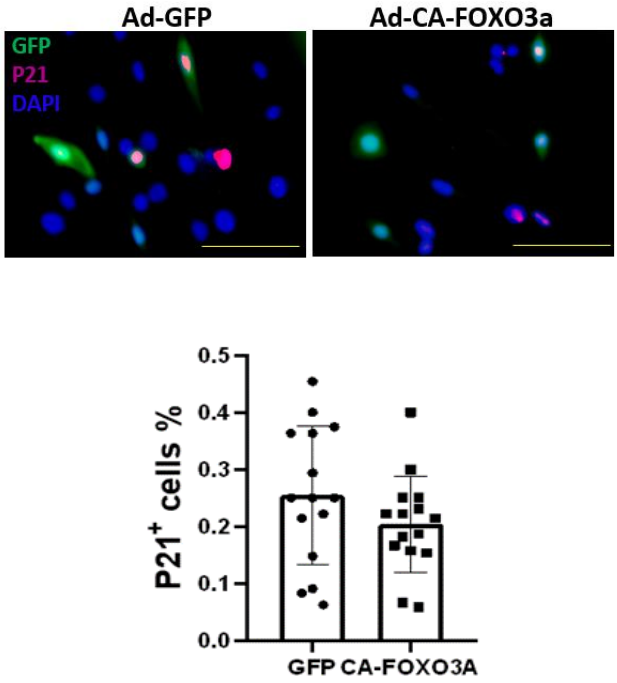


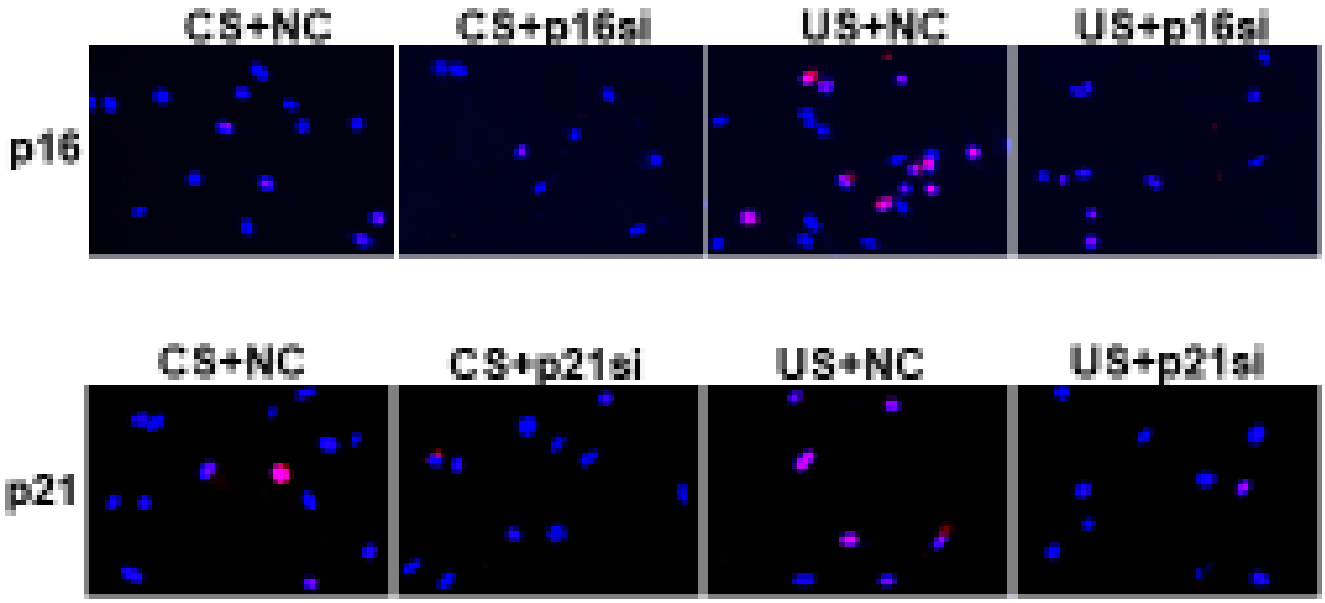
Supplementary Figure 1. Uremic serum (US) decreased the amount of cyclin-dependent kinase (CDK).

MPCs were transduced with Ad-ctrl, Ad-CDK1 (A) or Ad-CDK4 (B) and treated with either control (CS) or uremic serum (US) for 48 hours. Immunofluorescence staining showed that CDK1/2+ and CDK4+ cells were increased after adenovirus transduction. DAPI staining was used to determine the number of nuclei (total cell population). The percent of CDK1+ (**A**) or CDK4+ (**B**) cells in total cell population were calculated and summarized in bar/point graph. (Bars: mean ± s.e.; scale bar = 50μm; n = 6/group; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$).



Supplementary Figure 2. p21 was not regulated by FOXO3a in MPCs.

MPCs were transduced with constitutive activation Ad-(CA)-FOXO3a-GFP or Ad-GFP adenovirus for control. **(A)** The shape of adenovirus transduced MPCs were shown (scale bar = 100μm). **(B)** p21 positive cells were measured by immunofluorescence. The percent of p21 positive cells (red) in total cell population were calculated and summarized in bar/point graph. (Bars: mean ± s.e.; scale bar = 50μm; n = 6/group).



Supplementary Figure 3. confirmation of knockdown by the siRNAs in uremic serum treated MPCs

MPCs were treated in 2% control or uremic serum for 48 hours. The siRNA of control (NC), p16 (p16si) or p21 (p21si) were transfected into the cells. Immunofluorescence staining showed that p16 and p21 positive cells were decreased in uremic treated group. DAPI staining was used to determine the number of nuclei (total cell population).

Supplementary Table 1-A

ID	Age	Gender	Race	Weight (kg)	BMI	Smoking	Veteran	CKD stage	CKD Etiology	Hypertension	Diabetes	Family Hx of HTN
CKD_001	61	1	1	95.3	31	1	1	4	unspecified	1	0	1
CKD_002	61	1	0	91.4	30.6	2	0	4	kidney stones	1	1	unknown
CKD_003	70	1	0	89	28.2	2	1	4	Pt. says he has plaque build	1	0	1
CKD_004	55	1	1	95.2	31.1	2	0	4	diabetes	1	1	1
CKD_005	70	1	1	66.3	23.5	2	1	4	HTN	1	1	1
CON_001	55	1	1	77.4	25.9	1	1	N/A	N/A	unspecified	unspecifie	1
CON_002	59	1	1	101.2	34.2	1	1	N/A	N/A	1	0	1
CON_003	62	1	1	95	30	0	1	N/A	N/A	1	0	1
CON_004	66	1	1	65.1	21.2	0	1	N/A	N/A	1	0	1
CON_005	57	1	1	68.4	22.9	0	1	N/A	N/A	0	0	0

Supplementary Table 1-B

CAD	PTSD	Beta Blockers	ACE/ARB	DCCB	NDCCB	Diuretics	PDE	Alpha blocker	Hydralazine	Statin	Sodium Bicarb
0	1	carvedilol	0	Amlodipin	0	0	sildenafil	0	1	0	650mg
1	0	carvedilol	lisinopril	amlodipin	0	0	0	0	0	0	650mg
0	0	metoPROLOL	lisinopril	0	0	0	0	0	0	atorvastatin	0
0	0	carvedilol	captopril	0	0	0	0	0	0	atorvastatin	0
0	0	Carvedilol	0	Nifedipine	0	0	tadalafil	0	0	atorvastatin	0
unspecifie	0	0	0	0	0	0		0	0	0	
0	0	0	lisinopril	0	0	0		0	0	0	
0	0	0	losartan	0	0	hydrochlorothiazide		0	0	0	
0	0	0	0	amlodipin	0	0	sildenafil	0	0	0	
0	1	0	0	0	0	0	sildenafil	0	0	0	

Supplementary Table 2. Antibody list

antibody	Company	catalog number
p53	Santa Cruz Biotechnology, Inc.	sc-6243
p16	Santa Cruz Biotechnology, Inc.	sc-1207
p16	Abcam	ab211542
p21	Abcam	ab188224
CDK1/2	Santa Cruz Biotechnology, Inc.	sc-53219
CDK4	Santa Cruz Biotechnology, Inc.	sc-23896
γ-H2AX		ZRB05636
Mac-2	Santa Cruz Biotechnology, Inc.	sc-30157
Arginase 1	Santa Cruz Biotechnology, Inc.	sc-20150
IL-1b	Santa Cruz Biotechnology, Inc.	sc-7884
CCN1	R&D system	mab4864
TNF-a	Cell signaling Technology	3707
Murf1	Abcam	ab77577
atrogin1	Abcam	ab168372
myostatin	Abcam	ab71808
p-AKT	Cell signaling Technology	4060
AKT	Cell signaling Technology	4691
Foxo3a	Cell signaling Technology	2491
Foxo1a	Sigma-Aldrich	F2303
KI67	Millipore	AB9260
Rb	BD Pharmingen	554136
Pax7	Developmental Studies Hybridoma Bank	Pax 7
GAPDH	Santa Cruz Biotechnology, Inc.	SC-365062

Supplementary Table 3. Primer list

Name	Sequence
IL-6	Forward GGAGATGGATGTGCCAAACG
	Reverse CGAGCTCACTCTCTGTGGTGTT
TNFα	Forward TGCTGATGGGAGGAGATGTCT
	Reverse TTTCTTTCAGGGACAGCCTGTT
IL-1β	Forward AACACGGCAGTGGCTTTAAC
	Reverse GAGGAGAAGGCGTTTGCTTA
IFN-γ	Forward CCAGAGCGAAAGCATTTGCCAAGA
	Reverse TCGGCATCGTTTATGGTCGGAACT

Supplementary Table 4. The effect of D&Q treatments on body or muscle weights, BUN, creatinine, and grip strength

	Sham	CKD	CKD/Vehicle	CKD/D&Q
B.W.(Initial)	24.7±1.4	25.2±1.1	24.5±0.4	27.3±1.4
B.W. (harvest)	33.7±0.7	19.0±1.1***	19.8±0.4	23.2±1.2
BUN (mM)	9.5±1.1	33.6±6.0**	36.8±0.9	21.9±4.7
Creatinine(mg/dL)	0.49±0.09	1.34±0.19**	1.62±0.24	1.16±0.15
Gastrocnemius (mg)	189.7±7.9	111.0±7.1***	106.2±4.9	137.3±6.6#
Soleus (mg)	11.1±0.6	7.4±0.6**	8.1±0.5	9.3±0.7
TA (mg)	57.3±2.8	33.6±1.2***	34.0±1.6	41.8±1.6#
EDL (mg)	12.2±0.9	6.5±0.9***	7.5±0.3	8.9±0.3
muscle grip strength (KGF2)	0.139±0.002	0.065±0.005***	0.080±0.004	0.114±0.005###

B.W.: body weight; BUN: blood urea nitrogen; TA: Tibialis anterior muscle; EDL: Extensor digitorum longus muscle; *: $p < 0.05$ compared with sham group; **: $p < 0.01$ compared with sham group; ***: $p < 0.001$ compared with sham group; #: $p < 0.05$ compared with CKD + Vehicle group; ###: $p < 0.001$ compared with CKD + Vehicle group by one-way ANOVA.