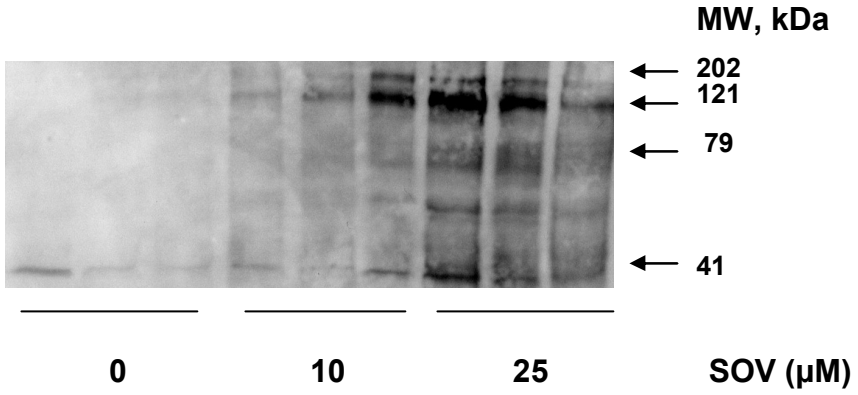
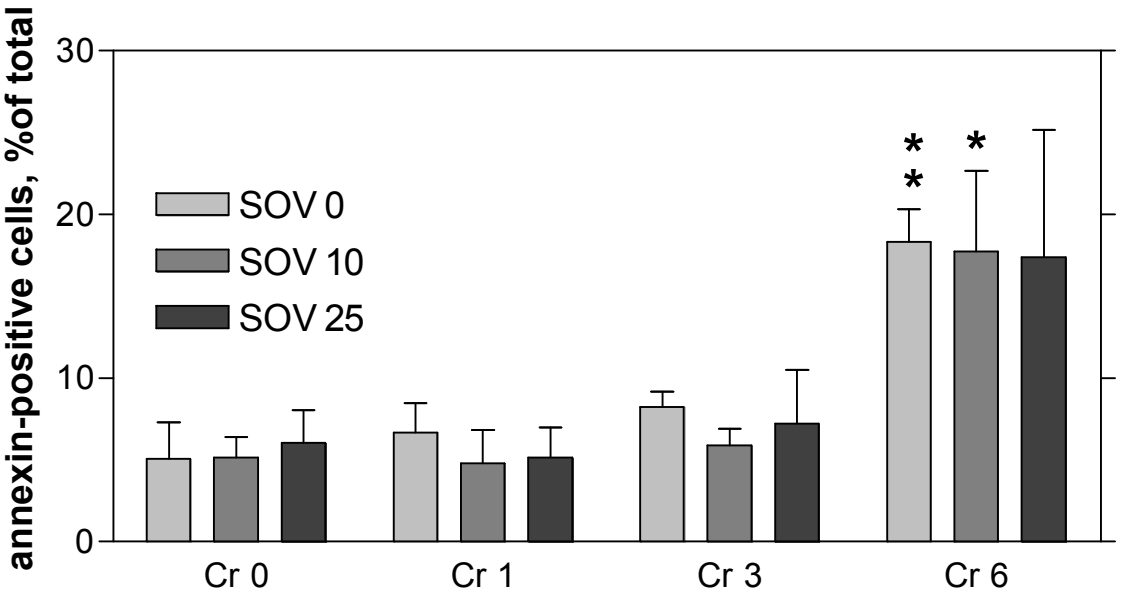


Supplemental Figure 1: Phosphotyrosine protein expression after SOV exposure: HLF cells were incubated with 10 or 25 μM SOV for 24h. Following this period, cells were gently scraped into RIPA buffer (1% Igepal, 0.5% sodium deoxycholate, and 0.1% sodium dodecyl sulfate) containing a cocktail of protease and phosphatase inhibitors, and cellular lysates were processed for immunoblotting. Equal amounts of protein from 3 independent experiments were separated by SDS-PAGE, and electroblotted onto PVDF membranes (Bio-Rad, Hercules, CA). Blots were probed with a monoclonal phosphotyrosine antibody (clone 4G10, Upstate Biotechnology, Lake Placid, NY), followed by a horseradish peroxidase-linked goat anti-mouse secondary antibody. The secondary antibody was detected by enhanced chemiluminescence (NEN, Boston, MA) after exposure to x-ray film.



Supplemental Figure 2: Effect of tyrosine phosphatase inhibition on apoptosis after exposure to Cr(VI): HLF cells were incubated without or with 1-6 μM Cr(VI) for 24 h in the absence or presence of 10 or 25 μM SOV followed by culture in complete medium without Cr(VI) for an additional 24 h. Apoptosis was assessed as the proportion of cells with translocated phosphatidylserine, as determined by binding of fluorescent annexin V. Data are expressed as % of apoptotic cells and are the means ± SE of 3 independent experiments. *, **: Statistically significant difference from control at $p<0.05$, $p<0.01$.

	Control	SOV, 10 μM
Cr, 1 μM	5.5 ± 0.3	6.0 ± 0.6
Cr, 2 μM	10.6 ±1.2	11.4 ± 0.6

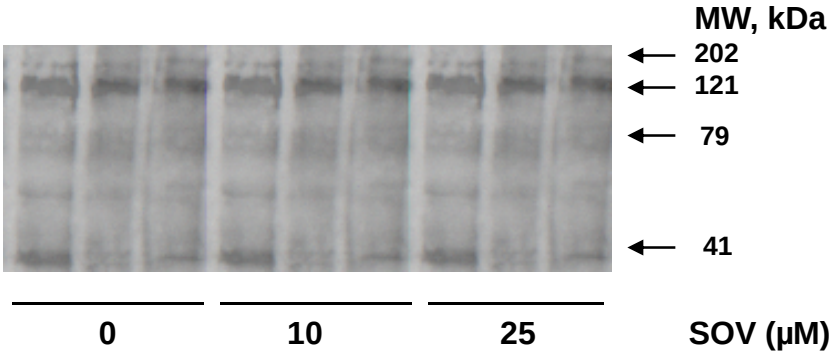
Supplemental Table 1: Effect of SOV on Cr-DNA adducts. HLF cells were incubated with 1 or 2 μM $Na_2{}^{51}CrO_4$ for 24 h, in the absence or presence of 10 μM SOV, and DNA was isolated. DNA-associated radioactivity (Cr adducts) was determined by scintillation counting. Data are expressed as pmol Cr/μg DNA, and are the means ± SE of 2 independent experiments, performed in triplicate.

Group	Effect on cell cycle progression	Gene Symbol	Description	GenBank ID	Treatment type		
					Ctl	Cr	SOV+ Cr
A	positive	CUL3	Cullin 3	AI797788	0.72	1.26	1.10
		RBBP6	retinoblastoma binding protein 6	BC029352	0.54	0.91	1.02
		GAS6	Growth arrest-specific 6	AI479082	0.81	1.22	1.47
		STAT1	Signal transducer and activator of transcription 1, 91kDa	AI539443	0.83	1.25	1.28
		CDC2L6	cell division cycle 2-like 6 (CDK8-like)	AI738802	0.57	0.83	1.00
		CENPF	centromere protein F, 350/400ka (mitosin)	NM_016343	0.62	1.06	1.38
		CCNB1	cyclin B1	N90191	0.64	1.01	1.36
	no/unknown	DST	Dystonin	AV702787	0.72	1.13	1.08
B	positive	OSMR	oncostatin M receptor	BC010943	1.07	2.10	0.98
		CUL4A	Cullin 4A	AL563297	1.18	2.12	0.75
	negative	DLEU2	deleted in lymphocytic leukemia, 2; candidate tumor suppressor	AF264787	1.18	2.04	0.95
		DLEU2	deleted in lymphocytic leukemia, 2; candidate tumor suppressor	AA905286	1.68	2.73	0.83
		ANAPC7	anaphase promoting complex subunit 7	AL137586	1.28	1.71	0.78
		EMP1	epithelial membrane protein 1	BF445047	0.87	1.51	0.89
		LOH11CR2A	loss of heterozygosity, 11, chromosomal region 2, gene A	BC001234	1.15	1.73	0.97
		CCNG2	Cyclin G2	AW134535	0.92	1.34	1.07
		HTATIP2	HIV-1 Tat interactive protein 2, 30kDa	AF092095	1.00	1.47	1.08
		RAD1	RAD1 homolog (S. pombe)	AI796010	1.09	1.51	0.94
	no/unknown	WDR39	WD repeat domain 39	NM_004804	1.01	1.30	0.72
		FTH1	ferritin, heavy polypeptide 1	AA083483	1.04	1.34	0.90
		TXNL4B	thioredoxin-like 4B	NM_017853	1.00	1.26	0.83
		NEDD9	neural precursor cell expressed, developmentally down-regulated 9	BC020686	1.11	2.18	0.74
		RAF1	V-raf-1 murine leukemia viral oncogene homolog 1	AI740571	0.94	1.64	0.84
		EDNRA	Endothelin receptor type A	AA573452	0.90	1.53	0.80
		SPATA5L1	spermatogenesis associated 5-like 1	AK022348	0.86	1.33	0.97
		PARD6A	par-6 partitioning defective 6 homolog alpha (C.elegans)	NM_016948	1.06	1.47	0.83
C	positive	RCC1	regulator of chromosome condensation 1	NM_001269	0.39	0.47	1.75
		TBRG4	transforming growth factor beta regulator 4 ;cell cycle progression 2 protein	NM_030900	0.59	0.65	1.43
		RCC1	regulator of chromosome condensation 1	X06130	0.58	0.63	1.39
		TBC1D8	TBC1 domain family, member 8 (with GRAM domain)	AI034387	0.45	0.44	1.63
		MAPK1	mitogen-activated protein kinase 1; erk2	NM_138957	0.53	0.65	1.11
		ANAPC1	Anaphase promoting complex subunit 1	AW205749	0.87	0.78	1.16
	negative	PTEN	Phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	BG403361	0.84	0.73	1.32
		RAD50	RAD50 homolog (S. cerevisiae)	AA877043	0.97	0.82	1.23
	no/unknown	MTSS1	metastasis suppressor 1	NM_014751	0.71	0.66	1.46
		SIAH1	Seven in absentia homolog 1 (Drosophila)	AV700132	0.80	0.68	1.06
		CYLD	Cylindromatosis (turban tumor syndrome)	AA555096	0.97	0.80	1.17
D	positive	JAG1	jagged 1 (Alagille syndrome)	U61276	1.14	1.37	0.68
		CUL7	cullin 7	AW081304	1.18	1.20	0.80
	negative	CDKN1C	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	R78668	1.35	1.30	0.61
		DAB2	disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila)	AF188298	1.05	1.25	0.86
		C9orf127	chromosome 9 open reading frame 127	NM_016446	1.12	1.29	0.86
		RECK	Reversion-inducing-cysteine-rich protein with kazal motifs	BC032240	1.08	1.24	0.86
		RECK	Reversion-inducing-cysteine-rich protein with kazal motifs	BC032240	1.09	1.25	0.85
		IRF1	interferon regulatory factor 1	NM_002198	1.10	1.21	0.80
		HEXIM1	hexamethylene bis-acetamide inducible 1	NM_006460	1.14	1.20	0.78
		IGFBP4	Insulin-like growth factor binding protein 4; BP4; IBP4	AI078033	1.42	1.48	0.80
		CDKN1C	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	D64137	1.23	1.23	0.83
		CDKN1C	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	NM_000076	1.23	1.23	0.80
		PMP22	peripheral myelin protein 22	L03203	1.26	1.24	0.85
		SEP6	septin 6	AL568374	1.30	1.22	0.69
		MAPK12	Mitogen-activated protein kinase 12	AK098058	1.26	1.05	0.67
	no/unknown	SPIN2	spindlin family, member 2 ; spindlin-like protein 2	AF356353	1.33	1.64	0.69
		TGFB2	Transforming growth factor, beta 2	AU145950	1.46	1.35	0.66
		TERF2	telomeric repeat binding factor 2	AW006832	1.24	1.48	0.91
		TERF2	Telomeric repeat binding factor 2	BE408975	1.13	1.25	0.78
		MAPRE2	Microtubule-associated protein, RP/EB family, member 2	BE671156	1.17	1.22	0.82

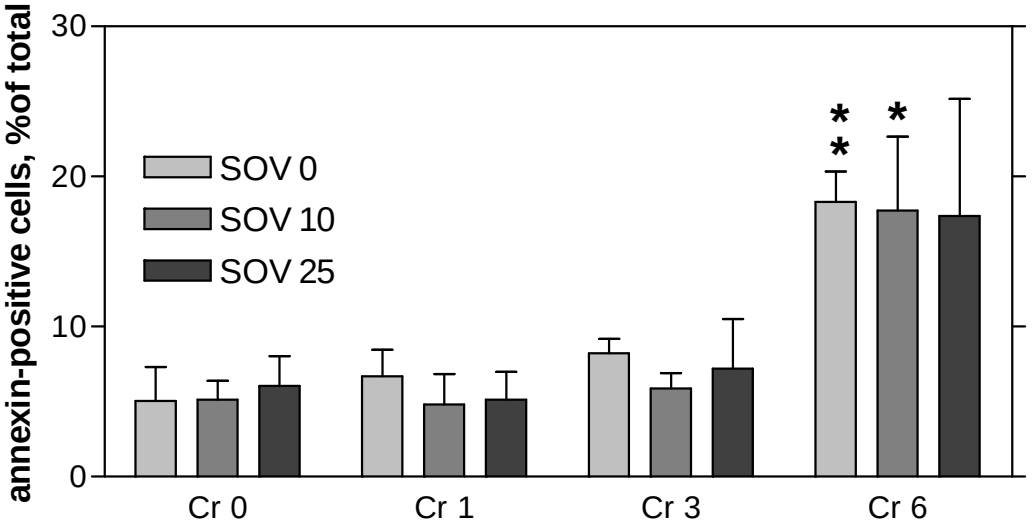
E	positive	PPP3CB	protein phosphatase 3 (formerly 2B), catalytic subunit, beta isoform (calcineurin A beta)	M29550	0.74	0.57	1.15
		IL11	interleukin 11	NM_000641	0.75	0.52	1.39
		IL6	interleukin 6 (interferon, beta 2)	NM_000600	0.86	0.59	1.33
		PDCD1LG1	CD274 antigen	AI608902	0.84	0.55	1.18
		CSF1	colony stimulating factor 1 (macrophage)	M76453	1.23	0.83	1.09
		MCM3	MCM3 minichromosome maintenance deficient 3 (S. cerevisiae)	NM_002388	1.10	0.69	0.92
		NEK1	NIMA (never in mitosis gene a)-related kinase 1	AV700007	1.02	0.60	0.93
		MCM6	MCM6 minichromosome maintenance deficient 6 (MIS5 homolog, S. pombe) (S. cerevisiae)	NM_005915	1.18	0.63	0.87
		CDCA7	cell division cycle associated 7	AY029179	1.06	0.44	0.98
		SUPT3H	suppressor of Ty 3 homolog (S. cerevisiae)	NM_003599	1.31	0.66	1.00
	negative	BCCIP	BRCA2 and CDKN1A interacting protein	NM_016567	0.71	0.55	1.25
		G0S2	G0/G1switch 2	NM_015714	0.86	0.66	1.32
		NF1	Neurofibromin 1 (neurofibromatosis, von Recklinghausen disease, Watson disease)	AW293356	1.03	0.75	1.10
	no/unknown	APBB2	Amyloid beta (A4) precursor protein-binding, family B, member 2 (Fe65-like)	BF115739	0.91	0.71	1.05

Supplemental Table 2: Transcripts associated with cell cycle and cell proliferation. HLF cells were incubated without or with 1 μM Cr(VI) for 24 h in the absence (control, Ctl) or presence of 10 μM SOV, and RNA was isolated using RNAbee followed by a secondary purification on Qiagen RNAeasy Mini columns. RNA quality was assessed by Agilent bioanalyzer and RNA Integrity Numbers (RIN) for all samples were >9.9. Labeled cRNA was hybridized to GeneChip Human Genome U133 Plus 2.0 Array and arrays were scanned with an Agilent laser scanner. The raw expression data were analyzed by GeneSpring (Silicon Genetics) for differentially regulated genes after respective treatment. Data set was filtered by 1-way ANOVA with 5% FDR and 1,880 genes out of total 54,675 transcripts were chosen. Transcripts associated with cell cycle and cell proliferation (according to GO Biological Process) were selected and further filtered by expression fold cutoff at 1.5. Expression data are the average of the normalized $\log_{10}$ values from 4 independent RNA samples per treatment, and are grouped as follows: A) genes upregulated by Cr(VI) treatment both in the absence and presence of SOV, as compared to control; B) genes upregulated by Cr(VI) treatment as compared to both control and Cr(VI) + SOV co-treatment; C) genes that were upregulated by Cr(VI) + SOV co-treatment, as compared to both control and Cr(VI) treatment alone; D) genes downregulated by Cr(VI) + SOV co-treatment, when compared to both control and Cr(VI) treatment alone; E) genes were downregulated by Cr(VI) treatment as compared to both control and Cr(VI) + SOV co-treatment. Genes were further

classified as either positive or negative regulators of cell cycle progression. A designation of no/unknown was used for the respective following criteria: no apparent cell proliferation function was identified; gene expression reported to correlate with both positive and negative regulation of cell cycle progression; relationship of gene expression to cell cycle progression was cell context-specific, with no known function in lung fibroblasts; no information could be obtained.



Supplemental Figure 1



Supplemental Figure 2