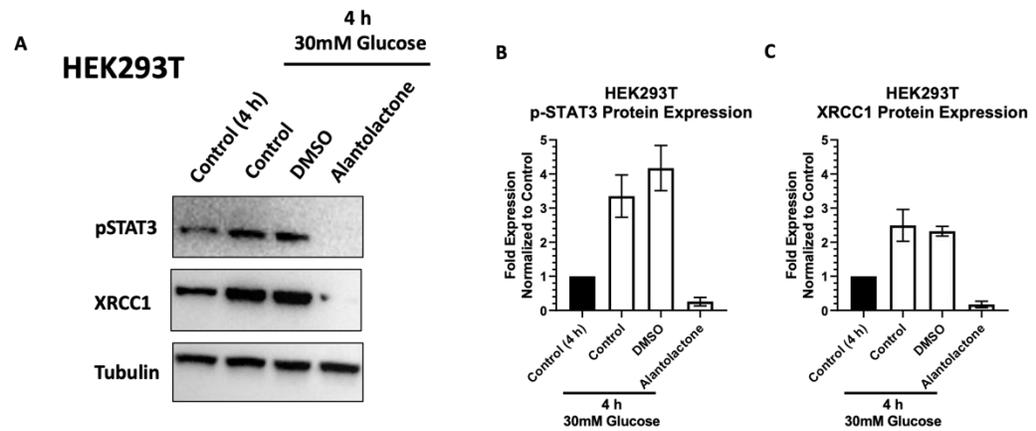
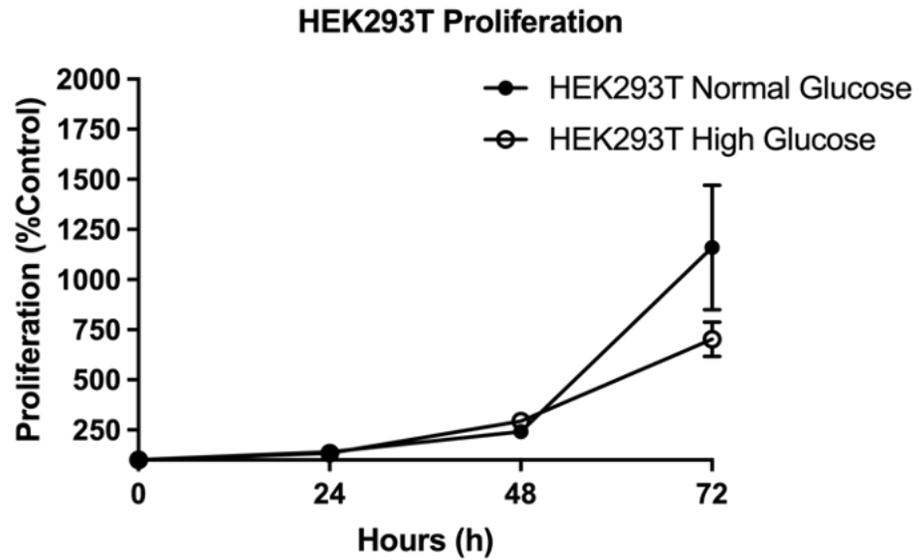
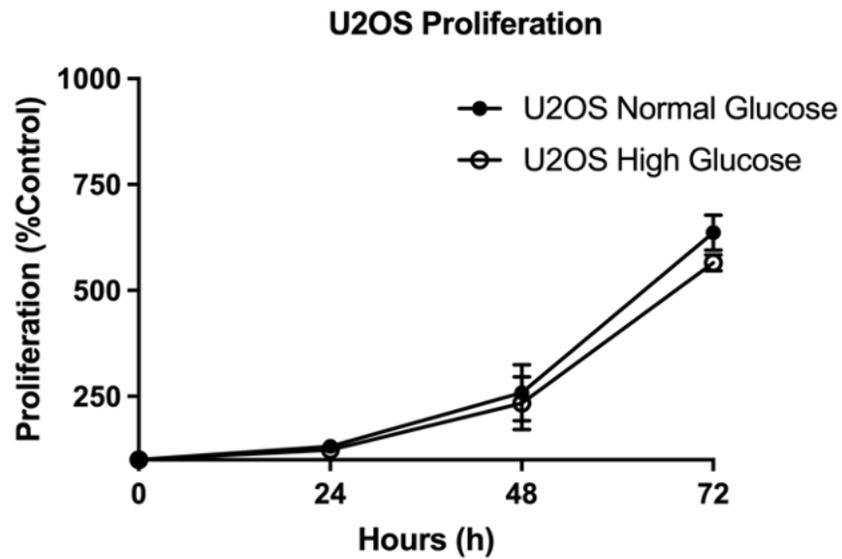


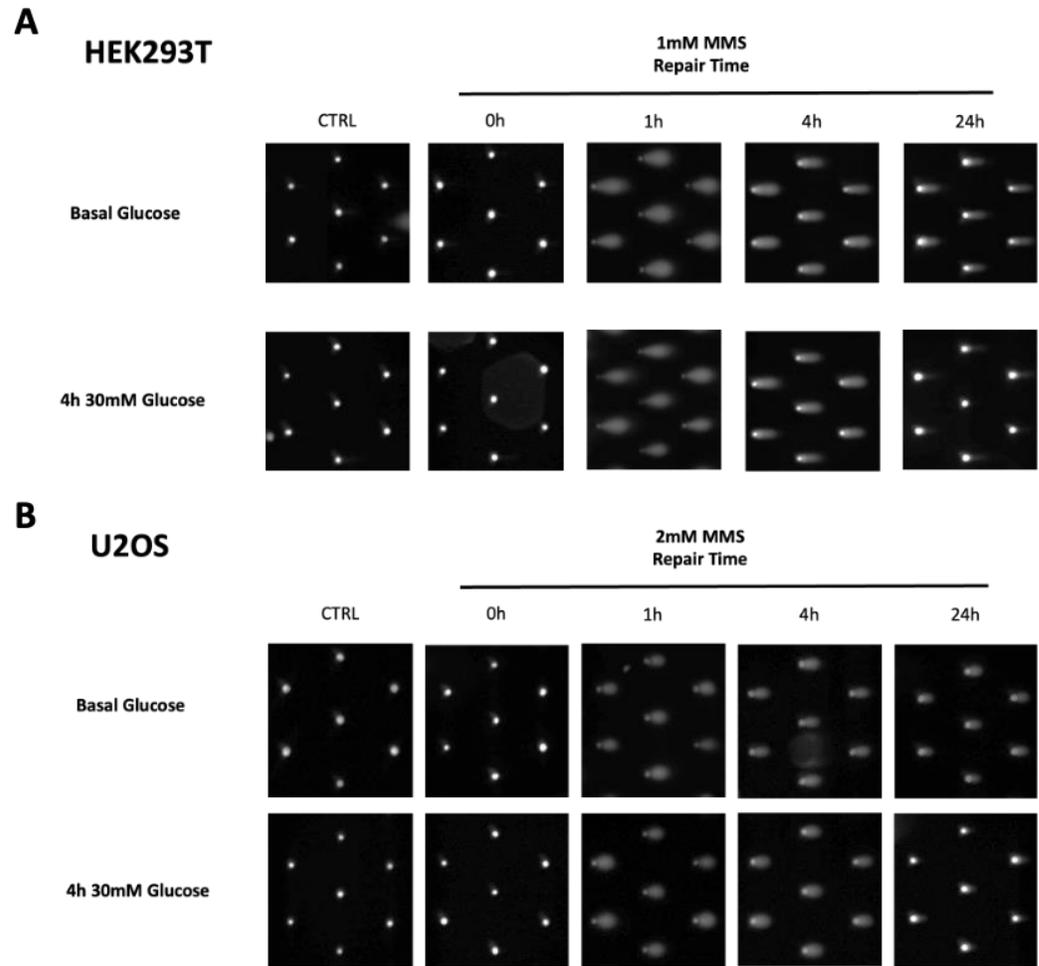
Supplementary Information:



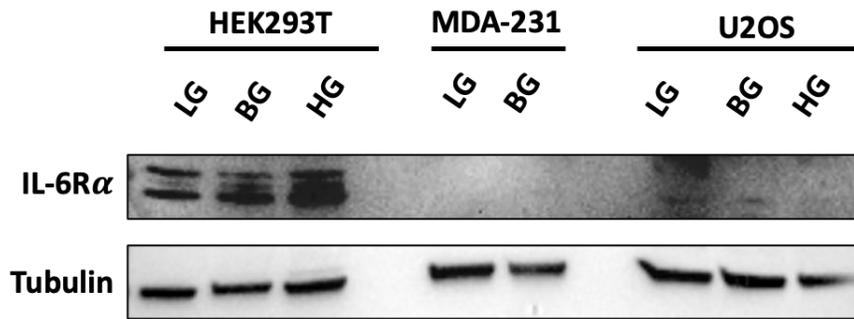
**Figure S1.** Alantolactone reverses acute high glucose induced increases in XRCC1 expression (A) Representative immunoblot for pSTAT3 and XRCC1 following 30 mM high glucose for 4h and 4h 30mM high glucose with 15  $\mu$ M alantolactone co-exposure. Tubulin is the loading control. (B) pSTAT3 protein for control, control 4 h 30 mM glucose, DMSO 4 h 30 mM glucose, and 4 h 30 mM glucose with 15  $\mu$ M alantolactone co-exposure ( $n = 2$ ). pSTAT3 levels are normalized to the loading control, then to the control, untreated. (C) XRCC1 protein for control, control 4 h 30 mM glucose, DMSO 4 h 30 mM glucose, and 4 h 30 mM glucose with 15  $\mu$ M alantolactone co-exposure ( $n = 2$ ).

**A****B**

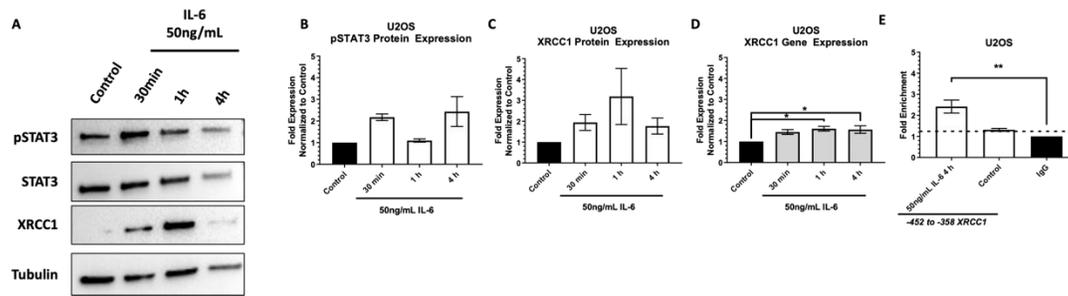
**Figure S2.** Doubling time for HEK293T (**A**) and U2OS (**B**) in basal glucose and high glucose is similar up to 72 h. Values presented as the mean cell count % of control  $\pm$  the standard error of the mean (SEM) at each time point ( $n = 3$ ).



**Figure S3.** Comet Chip analysis following MMS exposure. (A) Representative Comet Chip images for basal glucose HEK293T and 4 h pre-treatment with high glucose (30 mM) HEK293T followed by 1mM MMS exposure with 0, 1, 4, 24 h of repair time. (B) Representative Comet Chip images for basal glucose U2OS and 4 h pre-treatment with high glucose (30 mM) U2OS followed by 2 mM MMS exposure with 0, 1, 4, 24 h of repair time.



**Figure S4:** Immunoblot with increased exposure time showing IL-6R $\alpha$  expression in U2OS and MDA-231 following harsh strip and re-probe.



**Figure S5.** Acute IL-6 exposure in basal glucose U2OS. **(A)** Representative immunoblot for pSTAT3, STAT3, and XRCC1 following 50 ng/mL IL-6 exposure for 30 min, 1, and 4 h, tubulin as the loading control. **(B)** pSTAT3 protein following 50 ng/mL of IL-6 exposure for 30 min, 1, and 4 h. pSTAT3 levels are normalized to the loading control, then to the control, untreated. **(C)** XRCC1 protein expression following 50 ng/mL of IL-6 exposure for 30 min, 1, and 4 h. **(D)** XRCC1 gene expression following 50 ng/mL of IL-6 exposure for 30 min, 1, and 4 h. **(E)** CHIP analysis of STAT3 occupancy of the XRCC1 promoter following 50 ng/mL of IL-6 exposure for 4 h. \*  $p < 0.5$ , \*\*  $p < 0.01$

**Table S1.** IL-6 stimulation of XRCC1 protein, gene expression and STAT3 occupancy in HEK293T, MDA-231 and U2OS

<b>XRCC1 Protein Expression</b>	<b>Control</b>	<b>30 min</b>	<b>1 h</b>	<b>4 h</b>
HEK293T	1 ± 0	1.6 ± 0.33	1.7 ± 0.17	3.0 ± 0.20
MDA-231	1 ± 0	1.5 ± 0.16	1.15 ± 0.15	1.2 ± 0.056
U2OS	1 ± 0	1.6 ± 0.36	3.5 ± 0.42	3.3 ± 0.59
<b>XRCC1 Gene Expression</b>	<b>Control</b>	<b>30 min</b>	<b>1 h</b>	<b>4 h</b>
HEK293T	1 ± 0	1.5 ± 0.13	1.6 ± 0.13	1.8 ± 0.15
MDA-231	1 ± 0	1.8 ± 0.25	1.7 ± 0.14	1.6 ± 0.14
U2OS	1 ± 0	1.5 ± 0.14	1.7 ± 0.091	1.6 ± 0.20
<b>STAT3 Occupancy of the <i>XRCC1</i> promoter</b>	<b>Control</b>	<b>30 min</b>	<b>1 h</b>	<b>4 h</b>
HEK293T	1.49 ± 0.28	----	----	2.20 ± 0.26
MDA-231	2.4 ± 0.11	----	----	----
U2OS	1.3 ± 0.034	----	----	2.4 ± 0.27