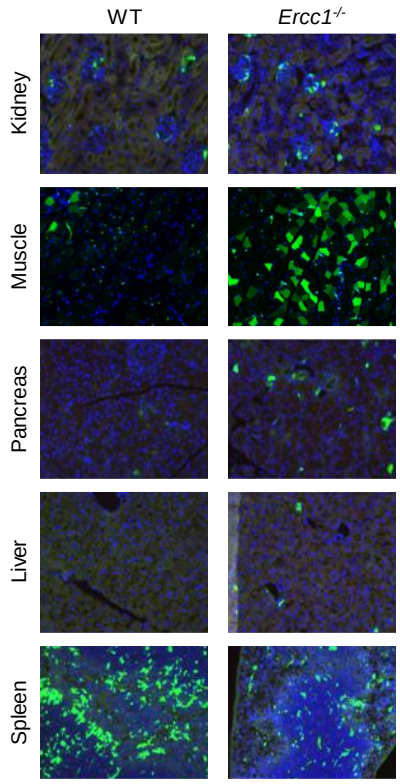
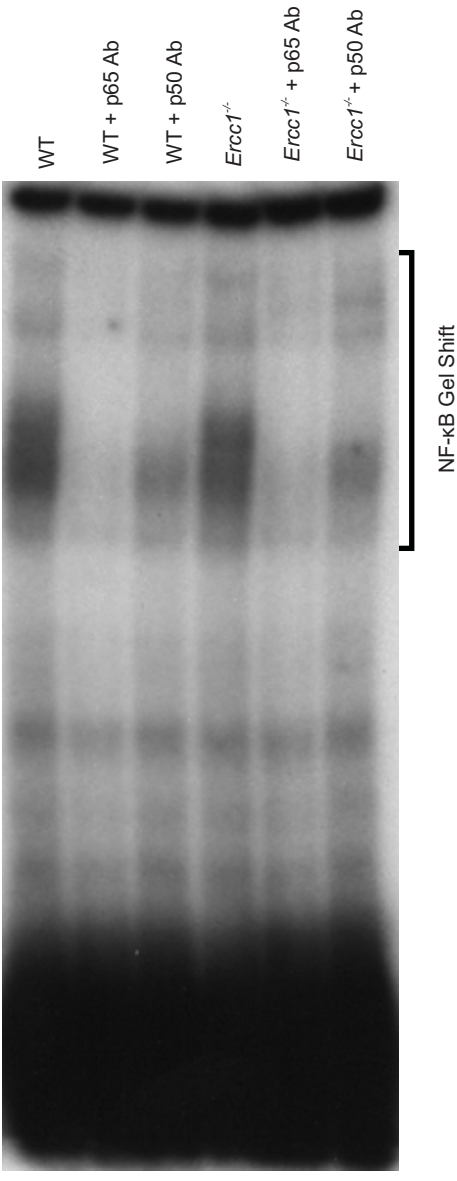


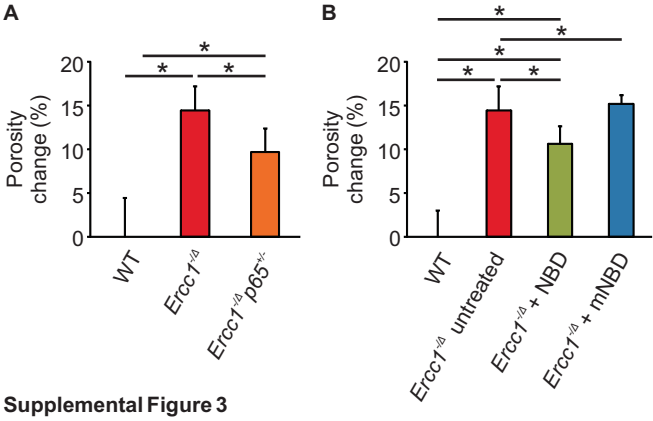
Supplemental Figure 1

NF-κB is activated in DNA repair-deficient, progeroid *Ercc1*$^{-/-}$ mice. Representative images of eGFP expression in tissue sections from 21 day-old progeroid *Ercc1*$^{-/-}$ mice and their normal littermates harboring the NF-κB^{eGFP} reporter knock-in construct. Kidney, skeletal muscle, pancreas, liver, and spleen sections from *Ercc1*$^{-/-}$ NF-κB^{eGFP} and WT NF-κB^{eGFP} mice were imaged using fluorescent microscopy to detect eGFP expression (green). Nuclei were counter-stained with Hoechst dye (blue; 20x objective).



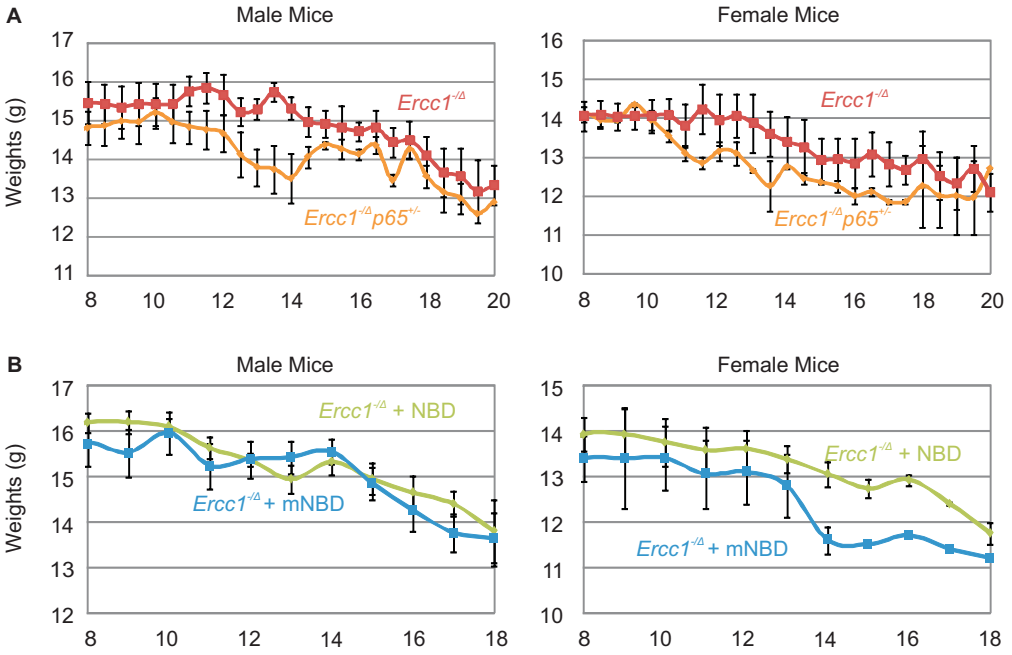
Supplemental Figure 2

EMSA of NF-κB activity. EMSA was performed using nuclear extracts from WT and *Ercc1*$^{-/-}$ primary MEFs, passage 5 and a 5'-^{32}P end-labeled duplex oligonucleotide containing a centrally located NF-κB binding sequence. Some extracts were pre-incubated with antibodies against p65 and p50 to determine which NF-κB subunits are mediating NF-κB binding activity.



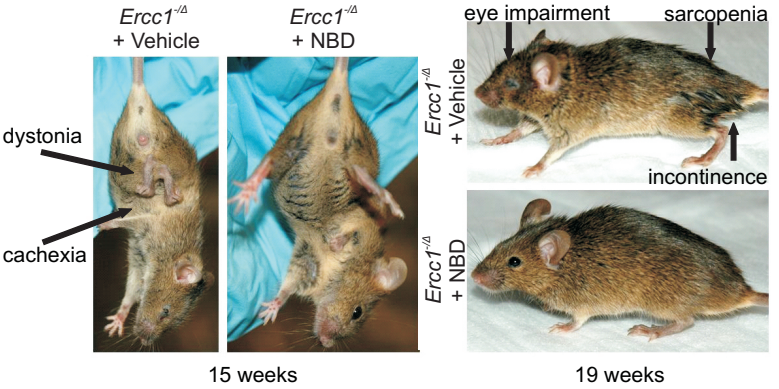
Supplemental Figure 3

Quantitation of bone porosity (osteoporosis) in *Ercc1*$^{-/\Delta}$ mice following genetic or pharmacologic inhibition of NF-κB. Micro-computed tomography of spines isolated from mice using a VivaCT 40 (Scanco Medical) with 15 μm isotropic voxel size resolution, 55 kVp of energy and 145 μA of current. (**A**) The percent change in porosity in *Ercc1*$^{-/\Delta}$ and *Ercc1*$^{-/\Delta}$*p65*$^{+/-}$ mice compared to age-matched WT mice. '*', $p < 0.05$, Tukey-Kramer test. The values denote the mean ± S.D. of 9 mice per group. (**B**) The percent change in porosity in *Ercc1*$^{-/\Delta}$ mice treated with 8K-NBD or 8K-mNBD compared to age-matched WT mice. '*', $p < 0.05$, Tukey-Kramer test. The values denote the mean ± S.D. of 3 mice per group.



Supplemental Figure 4

Weight changes associated with genetic and pharmacologic inhibition of NF-κB. Mice were weighed bi-weekly starting at 8 weeks of age. (**A**) Female and male *Ercc1*$^{-/\Delta}$ and *Ercc1*$^{-/\Delta}$*p65*$^{+/-}$ mice. (**B**) Female and male *Ercc1*$^{-/\Delta}$ mice treated with either 8K-NBD or 8K-mNBD. The weights at each time point reflect the average of at least 6 mice per group ± S.E.M.



Supplemental Figure 5

Chronic treatment of *Ercc1*$^{-/\Delta}$ mice with the NF-κB inhibitor, 8K-NBD, significantly delayed aging-related symptoms and chronic degenerative diseases. *Ercc1*$^{-/\Delta}$ mice were treated with 8K-NBD, 10 mg/kg, i.p., 3X per week, beginning at 5 weeks of age and continuing throughout their lifespan. Representative images of *Ercc1*$^{-/\Delta}$ mice treated with 8K-NBD or PBS at 15 and 19 weeks of age. Aging-related phenotypes are labeled with arrows.

Supplemental Table 1

Chronic treatment of *Ercc1*$^{-/\Delta}$ mice with the NF-κB inhibitor 8K-NBD significantly delayed progeroid symptoms and pathologies

Symptoms	Age at onset (weeks)		Change of onset (weeks)	Number of *Ercc1*$^{-/\Delta}$ mice (Vehicle, NBD)
	Vehicle	NBD		
Dystonia	8.0	9.1	1.1	17, 17
Trembling*	7.8	9.8	2.0	17, 17
Kyphosis	11.3	12.1	0.8	17, 15
Ataxia**	13.9	16.4	2.5	17, 13
Sarcopenia***	14.0	16.9	2.9	16, 11
Spontaneous activity	17.8	18.4	0.6	8, 2
Urinary incontinence	13.6	18.5	4.9	5, 2

Ercc1$^{-/\Delta}$ mice were treated with 8KNBD,10 mg/kg, i.p., 3X per week, beginning at 5 weeks of age and continuing throughout their lifespan. Shown are the average age-at-onset of each symptom for mice treated with the peptide inhibitor or vehicle only (phosphate buffered saline) and the differences between the group averages. Yellow shaded cells indicate symptoms delayed in mice treated with the NF-κB inhibitor, 8K-NBD, versus vehicle-treated mice. *p*-values were determined using Student's *t*-test. '*', $p < 0.05$; '**', $p < 0.01$; '***', $p < 0.001$.