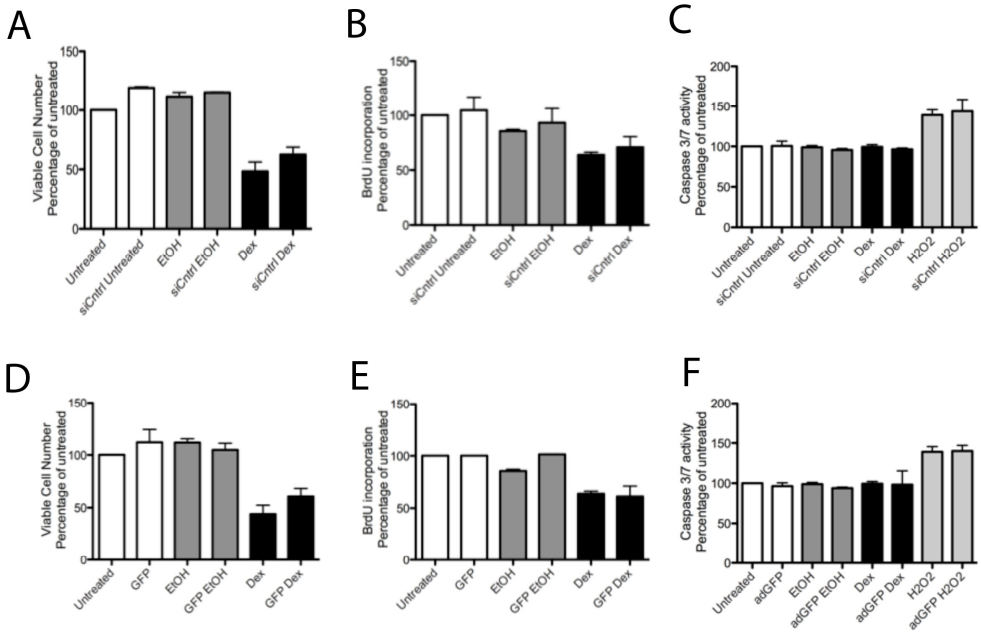
Supplementary Figure 1

Validation of RNAi and adenoviral-mediated gene transduction protocols.

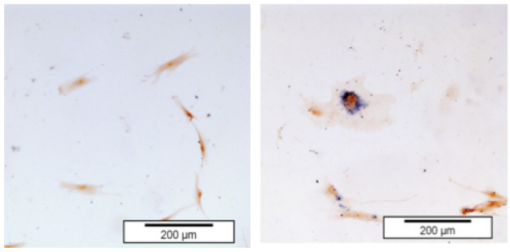
There was no significant difference in **A** viable cell number (determined using the Alamar Blue assay; Life Technologies, Paisley, UK), **B** cell proliferation (measured by BrdU incorporation) or **C** apoptosis (determined by measuring caspase 3/7 activity using the Apo-One Homogeneous Caspase 3/7 Assay, Promega Corporation, Madison, WI, USA) between non-transfected and transfected (siCntrl) ethanol- or dexamethasone- (1μM) treated cells. Similarly, there was no significant difference in the cell response to ethanol or dexamethasone treatment in terms of **D** viable cell number, **E** cell proliferation or **F** apoptosis between cells infected with a GFP-bearing adenoviral construct (adGFP) and uninfected cells. Hydrogen peroxide was used as a positive control for apoptosis induction. Experiments were repeated three times using tenocytes isolated from a different patient for each experimental replicate.



Supplementary Figure 2

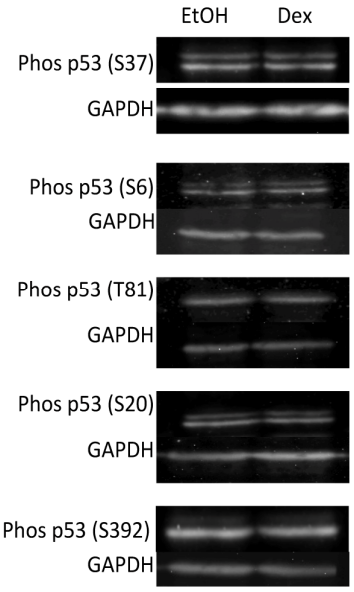
Senescence-associated β-galactosidase activity (SA-βgal) in glucocorticoid-treated tenocytes.

Photomicrographs showing increased SA-βgal activity (blue staining) following treatment of primary human tenocytes with dexamethasone (1μM) for 72h. (Left ethanol; Right dexamethasone).



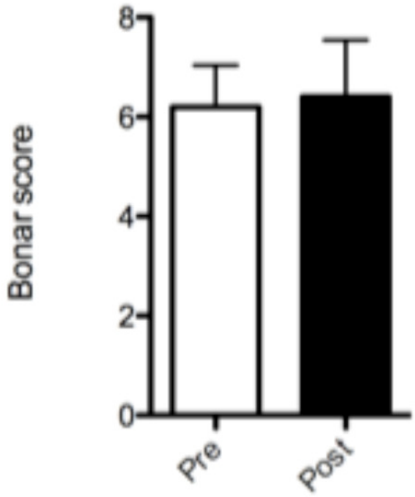
Supplementary Figure 3

Western blots showing levels of phosphorylated p53 in dexamethasone-treated tenocytes. There was no difference in the levels of p53 phosphorylated on serines 37, 6, 30 or 392 or on threonine 81 in protein lysates from tenocytes treated with 1μM dexamethasone for 48h compared to tenocytes treated with the corresponding amount of ethanol carrier. p53 phosphorylated on serine 15 was not detectable in lysates from either ethanol-treated or dexamethasone-treated tenocytes (not shown).



Supplementary Figure 4

Mean Bonar scores pre- and post- glucocorticoid injection. There was no significant difference in mean Bonar score, as assessed by H&E and Alcian Blue histological staining of tissue sections, between pre- and post-injection samples.



Supplementary Figure 5

Glucocorticoids induce senescent-like changes in primary human chondrocytes and osteoblasts. The percentage of SA-βgal positive cells was significantly higher ($p<0.05$) following 72h of treatment with dexamethasone (1μM) in **A** primary human chondrocytes and **B** primary human osteoblasts compared to ethanol carrier-treated controls (n=3).