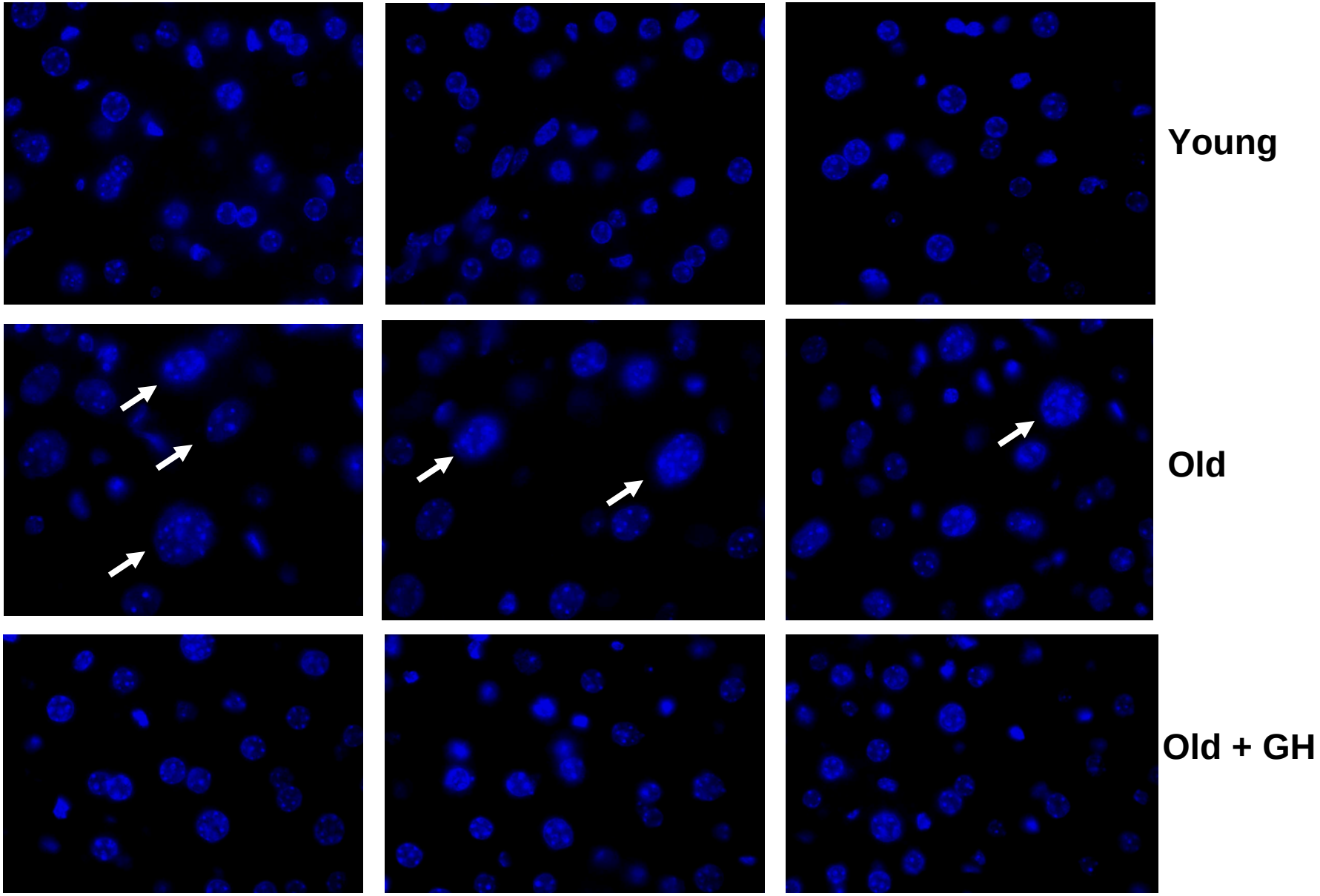
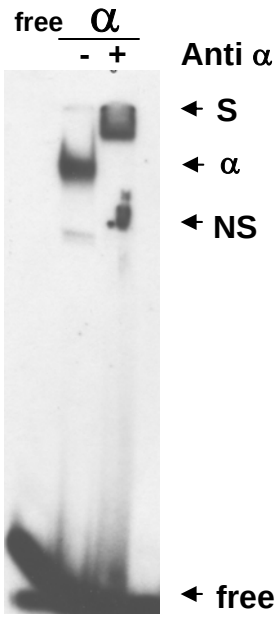


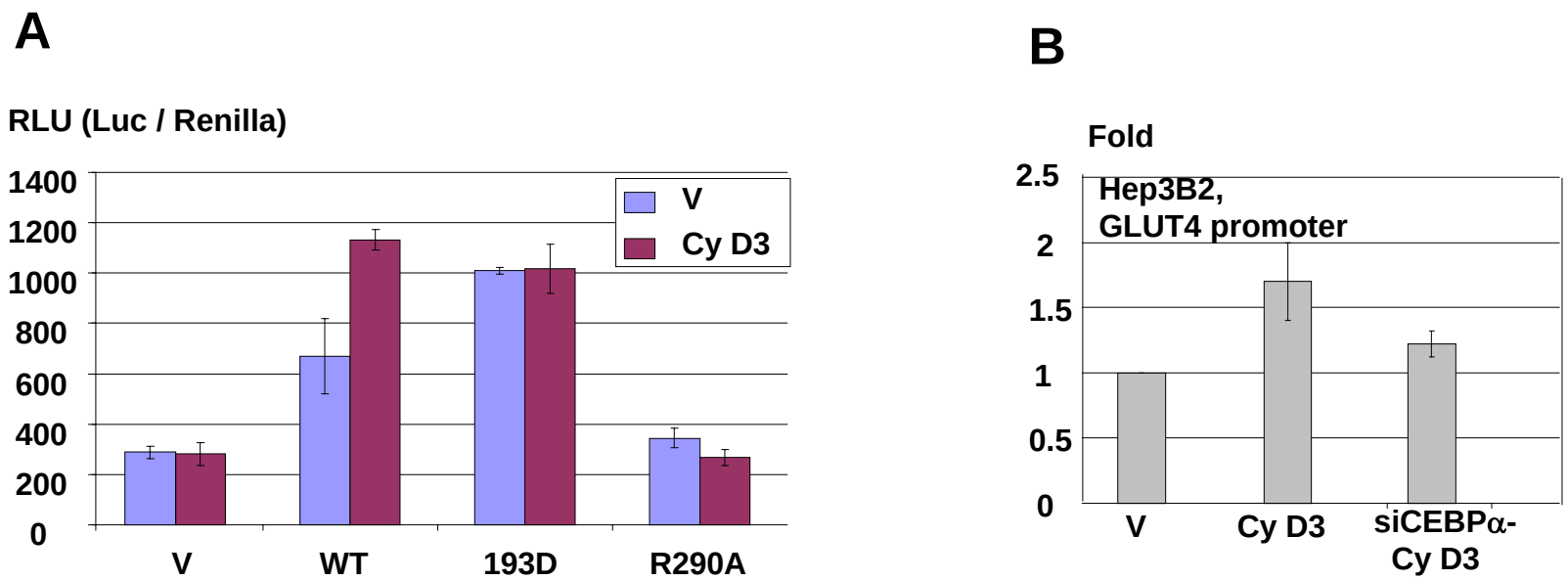
Supplemental figure 1. GH-mediated elimination of C/EBPα-HDAC1 complex reduces size of the nuclei and alters chromatin structure of the nuclei in hepatocytes of old mice. DAPI staining of livers of three young, old and old GH-treated mice. Arrows show nuclei in old livers which are enlarged and have changed chromatin structure.

Cyclin D1 promoter

3481 AGACAAATCTCAGATCCCACCCCACCCCCCCAGCGAGGAGGAATAGATGAAATAATGGCC
3541 ACCATCTTGAGCTGTTGCTGGAATTTTCGGGGTTTTATTTTATTTTTGAGCGAGCGCATG
3601 CTAGGCTGGGGATCCTTTAAAGTTCAGATACCCCTCTGGCCCTTTGCAACCACCCCAGTG
3661 CGCCAGGATGGAGCCTGCACGAGAGCTTAGGGCTCGTCTGGCATCTTCGGGTGTTACACA
3721 GTTCCTGAATTTTACACGTGTTGATGAAATTGAAAGAAGACAGGGACGCTGGGATTTCTA
3781 AGCAATGGGTCCGCCTGTGGGTGCCTCGTGGCGTACTCGGAAACGCACCCATTCTCCCGG
3841 TTTAAGAACAGGGTGTCCTTGCACCCCCAGGCTCCCCTTCCATACATTCTTCCTTGGCTT
3901 GCGTGTGGCCTGGCCTCCCTCCTAGCTGTCCTCCTGTCCAGAGCCGCCACTACCCCACCT
3961 CCACAGGTCTCGGAGGACCCTCTTAGGGAAAGAAGCCCCCCTCCCCCTTGCCCCGCTCTT
4021 TCCCAGTTTGGAGAGAAGCAGTCCGAGCGATTTGCATATCTACGAAGGCTGAGGGGGAAG
4081 GGTTTGGGCTTGCCCCCCCCCCGCCGCCCCCCCCCCTCACTGCTCCCGAGCCCCCTCCCC
4141 CTGCACCCGCCTCGGCCCTCCCCCTCCCCCTTTTCTCTGCCCGGCTTTGATCTCTGCTTA



Supplemental figure 2. The cyclin D1 promoter contains binding site for C/EBPα.
Left part shows the sequence of the cyclin D1 promoter. The start of transcription is shown in blue. C/EBPα site is shown by red bold letters. Arrows show the positions of primers used in ChIP analysis.
Right part shows EMSA analysis with DNA probe from the cyclin D1 promoter (underlined on the left part). Antibodies to C/EBPα were added before the probe addition.



Supplemental figure 3. A. Cyclin D3-cdk4-mediated phosphorylation of C/EBPα at S193 enhances the ability of C/EBPα to activate the Glut4 promoter. The Glut4 promoter was co-transfected with WT, C/EBPα-S193D and C/EBPα-R290A with or without cyclin D3. B. Phosphorylation of endogenous C/EBPα in Hep3B2 activates the Glut4 promoter. Glut4 promoter was co-transfected with empty vector, with cyclin D3 and with Cyclin D3 + siRNA to C/EBPα.

Description of results in supplemental figure 3.

Because S193D mutation mimics phosphorylation status of C/EBPα, we determined if phosphorylation of WT C/EBPα at S193 by cyclin D3-cdk4 will change the ability of C/EBPα to activate the Glut4 promoter. For this goal, we have used cyclin D3-mediated activation of cdk4 which increases phosphorylation of C/EBPα at S193 (Wang *et al.*, 2006; 2008b; 2008c). Cyclin D3 was co-transfected with WT C/EBPα and with the Glut4-reporter. Our data show that, similar to S193D mutation, the cyclin D3-cdk4-mediated phosphorylation of C/EBPα increases the ability of C/EBPα to activate the Glut4 promoter (SF 3A). The DNA binding deficient mutant R290A does not bind to DNA (Wang *et al.*, 2004) and does not activate the Glut4 promoter. This mutant also can not be activated by cyclin D3. Because overexpression studies do not reflect precisely biologically relevant conditions, we next examined if cyclin D3-cdk4-mediated phosphorylation of C/EBPα expressed from endogenous promoter might enhance its ability to activate the Glut4 promoter. For this goal, we have used Hep3B2 cells since endogenous C/EBPα is not phosphorylated in these cells (Wang *et al.*, 2004; 2008c). Supl Fig 3B shows that the ectopic expression of cyclin D3 increases the activity of the Glut4 promoter in Hep3B2 cells. This activation occurs through C/EBPα because the inhibition of the endogenous C/EBPα abolishes the cyclin D3-medaited activation of the Glut4 promoter.