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Supplementary Figure 1. BCL6-GFP is a functional transcriptional repressor. A: 293T cells were transfected with lentiviral expression plasmids containing BCL6-GFP or GFP cDNA along with a BCL6 binding site reporter construct expressing luciferase. After 48 hours cells were harvested and dual luciferase assays performed to compare and contrast reporter activity in the different cell types. BCL6-GFP was able to powerfully repress the BCL6 reporter similar to the previously published activity of wild type BCL6. The Y axis shows the fold repression of BCL6-GFP or GFP vs. cells transfected with BCL6 reporter and empty lentiviral plasmid (i.e.: Ctrl). **B:** In order to show that BCL6-GFP can bind to an endogenous target gene, we performed chromatin immunoprecipitations in the context of a BCL6 negative DLBCL cell line (Toledo) after transduction with BCL6-GFP or GFP lentivirus. ChIP was performed with either BCL6 or actin (negative control antibodies). The Y axis shows the percent enrichment of BCL6 vs. input on the CCL3 promoter, which is a well characterized and useful target gene of BCL6 for promoter binding studies. Taken together, these data show that BCL6-GFP is a functional transcriptional repressor. **C:** The table shows the range of BCL6 protein expression relative to actin in centroblasts in which BCL6 is endogenously expressed, vs. the levels of BCL6 transduced in WI38 cells (from **Fig. 1**) or primary naïve B-cells (from **Fig. 6**). It can be observed that BCL6 expression in these three situations is roughly similar. The centroblast data are derived from our previously published data (see reference #4). D: Immunoblots were performed to detect expression level of ATM 48 hs after transduction of GFP-BCL6 vs. GFP control in WI38 cells. It can be observed that ATM expression increases after BCL6 transduction, although to a lesser extent than ATM mRNA.

Supplementary Figure 2. Cyclin D1 levels are not induced by ectopic BCL6 expression in WI38 diploid fibroblasts, MEFs or purified human naïve B-cells. Cellular lysates were obtained from WI38 cells, pMEFs and naïve B-cells (NBC) at baseline (WT) or 38 hours after transduction with BCL6-GFP or GFP control lentivirus respectively. Lysates were subjected to SDS-PAGE and immunoblotting for Cyclin D1 or actin as loading control.

Supplementary Figure 3. Model for the differential ability of BCL6 to control ATR and p53 checkpoints in centroblast and non-centroblast cells. A: In naïve B-cells and fibroblasts, genotoxic stress can activate checkpoint responses through p53 and ATR. Ectopic expression of BCL6 can prevent induction of ATR but not p53. p53 can then contribute to the triggering of cell death, growth arrest and senescence. **B:** in the centroblast context, endogenous expression of BCL6 can protect against checkpoint activation induced by rapid proliferation and AID induced genetic recombination. In this case additional cellular factors can contribute to suppress p53 and evade senescence, thus cooperating with BCL6 in mediating the unique centroblast phenotype. It is important to note that other BCL6 target genes that regulate DNA damage responses may also be involved in these effects of BCL6 in addition to ATR and p53.

Supp. Fig. 1

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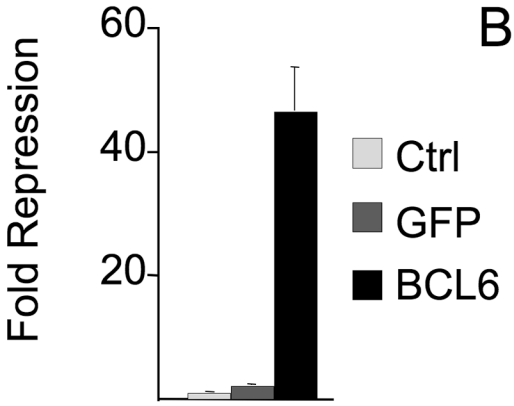
A



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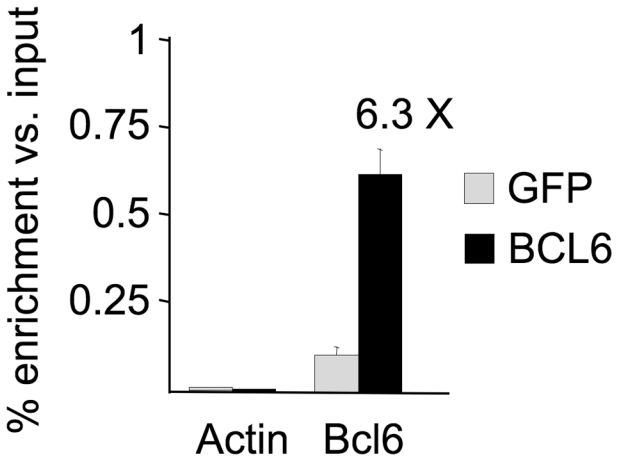
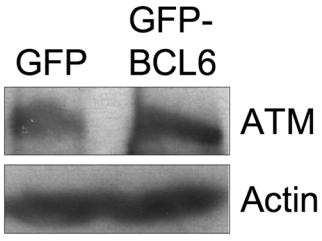


C

Cell type	BCL6 Source	BCL:Actin ratio (range)
Centroblast	Endogenous	1.35 - 1.29
WI38	Transduced	0.88 - 0.75
NBC	Transduced	1.00 - 0.83

D



Supp. Fig. 2

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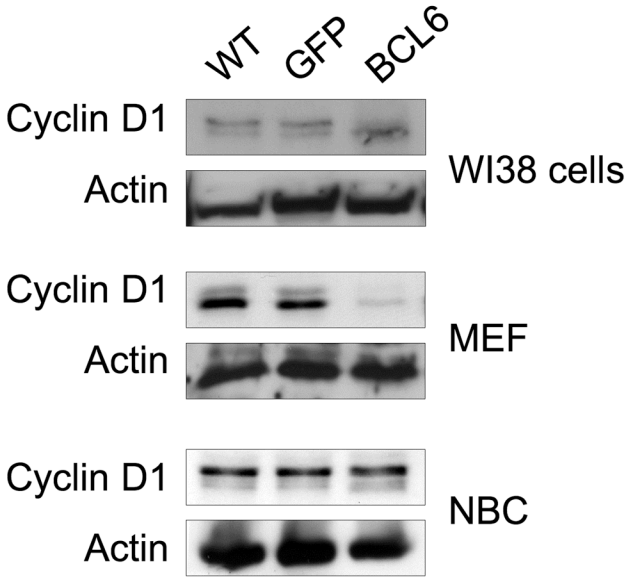

Supp Fig 3

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