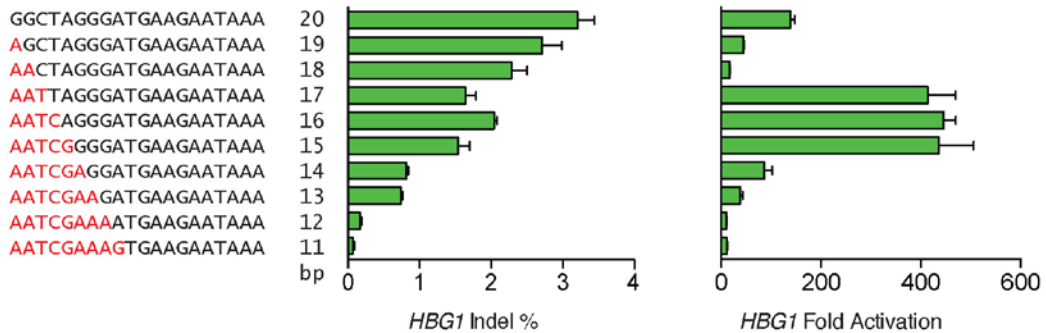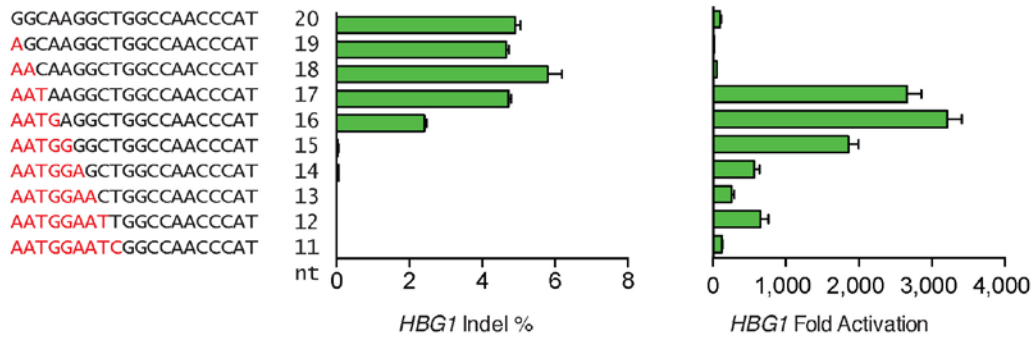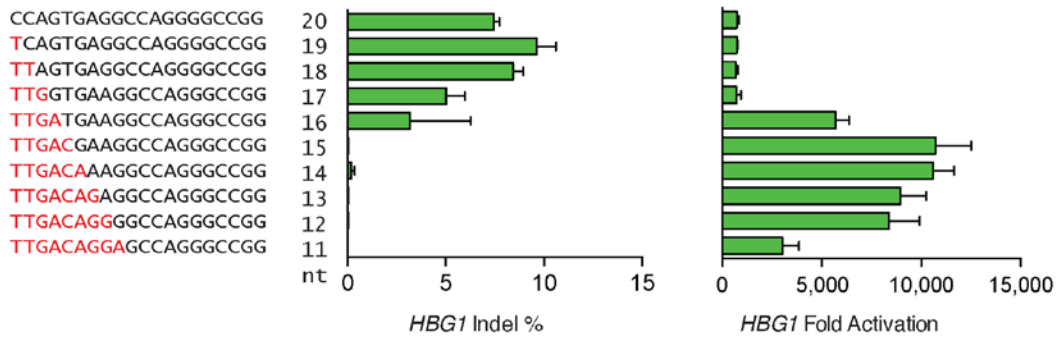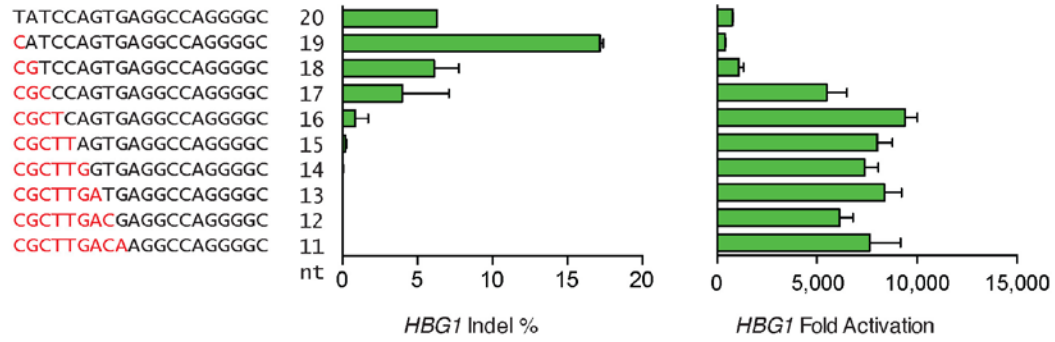**Supplementary Figure 1**

dRNAs can mediate robust gene activation using an active Cas9.

Three different dRNAs targeting the *HBG1* promoter region were designed. The length of the RNA targeting sequence was varied from 11nt to 20nt. *HBG1* mRNA (normalized to *GAPDH*, and compared to cells transfected with GFP plasmid) was quantified, as well *HBG1* indel frequency. In all cases, guides were designed with MS2 binding loops in the tetraloops and stem loop two[11], and were co-transfected with active Cas9 and the MPH transcriptional activation complex. Average +/- SEM is plotted, N=2-3 replicates group.

Supplementary Figure 2

20bp dRNAs with mismatches at the 5' end can activate transcription.

Four dRNAs were designed to target the *HBG1* promoter region with a series of 5' end mismatches (red). Target indel formation occurred consistently when sixteen or more nucleotides were matched to target DNA.

Gene activation was observed with as few as 11 bp of homology to the target DNA. Average +/- SEM is plotted, N=2-3 replicates/ group.
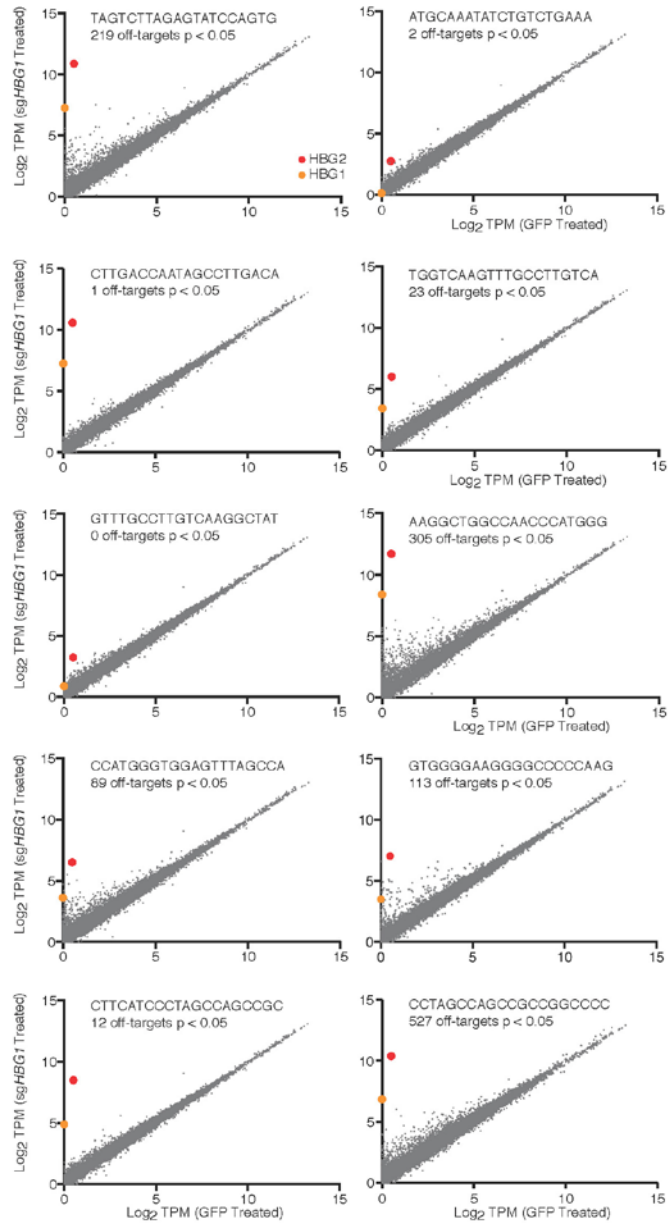
Supplementary Figure 3

Transcriptome-wide mRNA profiles for ten different sgRNAs targeting *HBG1/2*

20nt sgRNAs with MS2 binding loops were co-transfected with dCas9 and the MPH complex. A previously published nuclease OT score[13] did not significantly correlate with guide specificity. (In all cases, N=3 replicates / group).
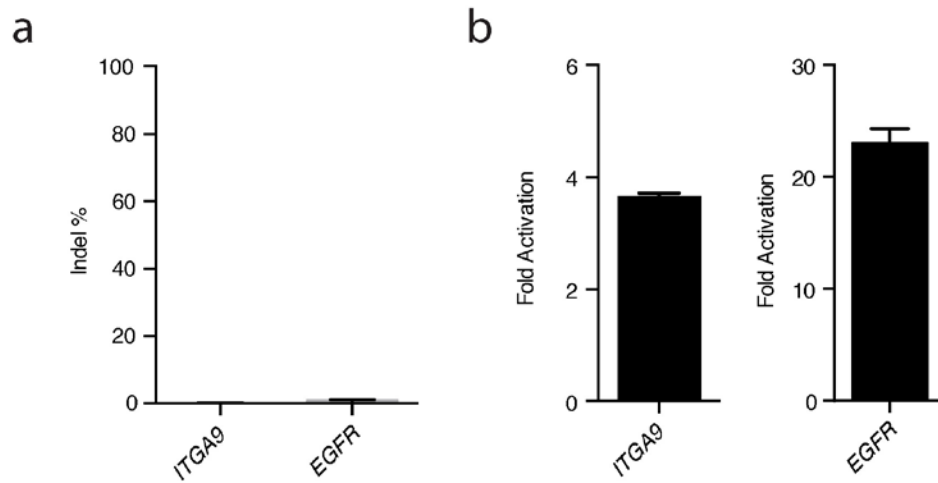
Supplementary Figure 4

dRNAs activate target gene expression with active Cas9

A375 cells were transduced with lentivirus containing a dRNA. (a) Indel formation was measured at 0.6% and 0.05% for DNA sites targeted by *ITGA9* and *EGFR* dRNAs, respectively. (b) *ITGA9* and *EGFR* mRNA levels (normalized to *GAPDH)* were quantified. In all cases, average + / - SEM is plotted, and N=3 replicates / group.

Click inside this box and insert a single image for Supplementary Figure 5. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

Supplementary Figure 5

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 6. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 6

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 7. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 7

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 8. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 8

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 9. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 9

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 10. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 10

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 11. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 11

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 12. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 12

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 13. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 13

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 14. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

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Supplementary Figure 14

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Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.

Click inside this box and insert a single image for Supplementary Figure 15. For best results, use Insert menu to select a saved file; do not paste images. Source images must be JPEGs (no larger than 10 MB) saved in RBG color profile, at a resolution of 150–300 dpi. Optimize panel arrangement to a 2:3 height-to-width ratio; maximum online display is 600h x 900w pixels. Reduce empty space between panels and around image. Keep each image to a single page.

Delete these instructions before inserting the image.

Supplementary Figure 15

Insert figure title here by deleting or overwriting this text; keep title to a single sentence.

Insert figure caption here by deleting or overwriting this text; captions may run to a second page if necessary.