## Supporting Information for

# A DNA base-specific sequence interposed between CRX and NRL contributes to RHODOPSIN expression.

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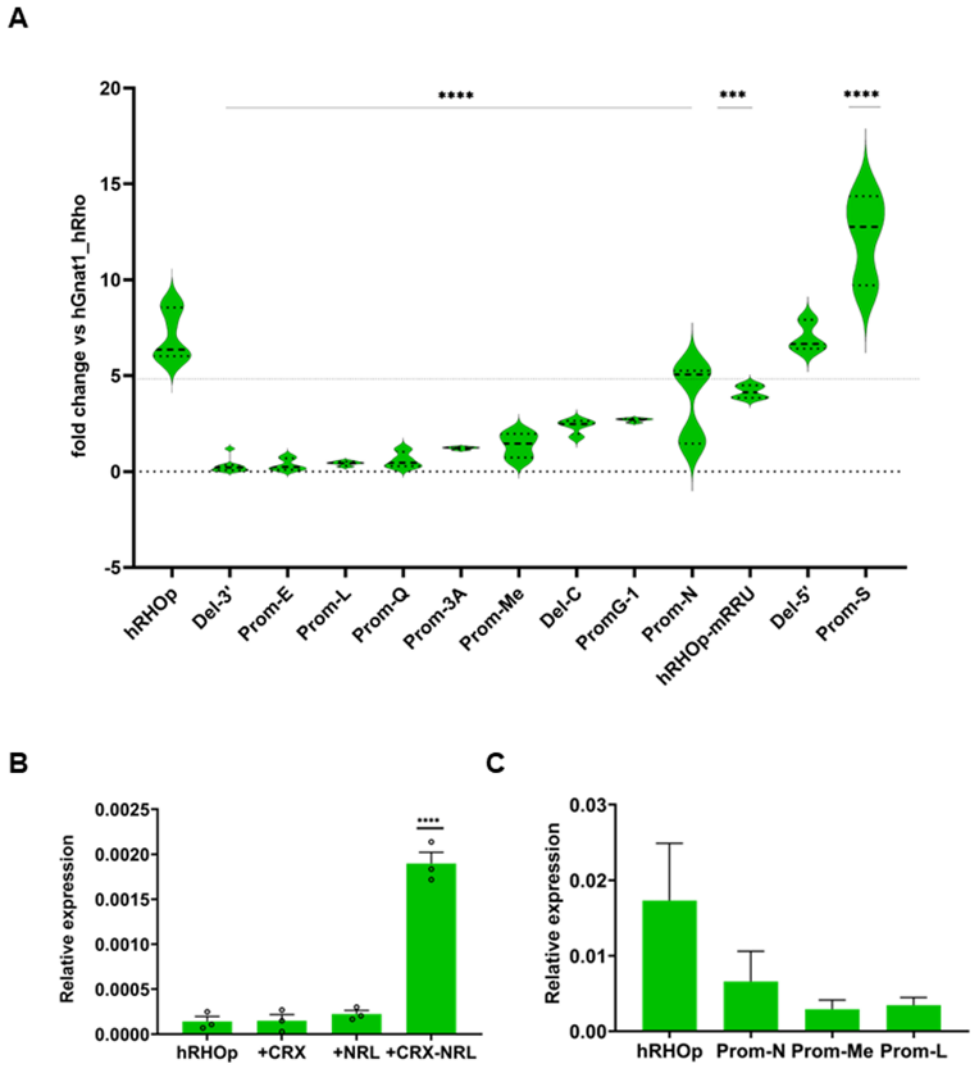


**Fig. S1.** (*A*) Cumulative eGPF variations across the promoters tested in vivo, normalized to wild-type promoter. (*B*) To test promoter activation in vitro the cells HEK-293 were transfected with hRHOp and its transactivating transcription factors CRX and NRL. (*C*), In vitro (HEK-293) transfection of hRHOp and mutants as indicated.

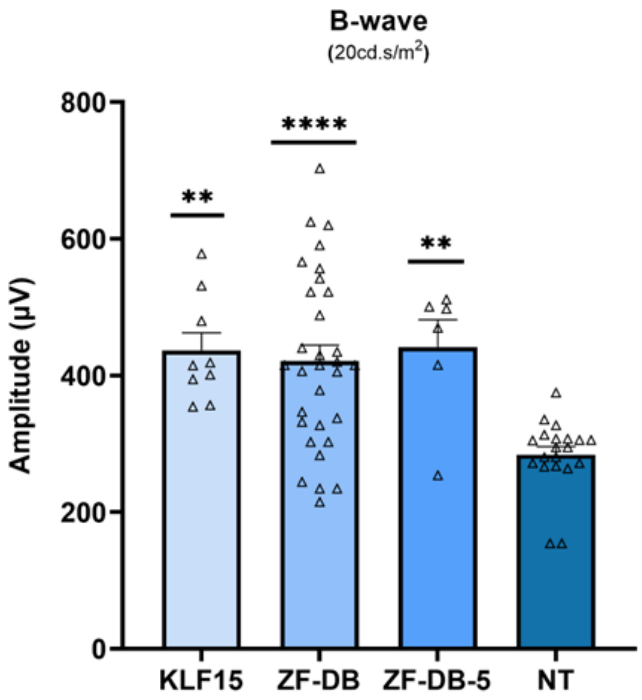


**Fig. S2.** Electroretinography (ERG) analysis on P347S mice subretinally injected at post-natal day 14 (PD14) with AAV8-CMV-ZF-DB (n=10), AAV8-CMV-ZF-DB-5 (n=6), AAV8-CMV-KLF15 (n=9), or AAV8-CMV-eGFP (n=20) and analysed at P30. Preservation of retinal maximal responses, scotopic (dim light) B-waves amplitudes evoked by light flash at +1.3 log cd*s/m2 (which correspond to 1x10-5.2 to 20.0 cd*s/m2), were preserved in AAV8-CMV-ZF-DB, ZF-DB-5 and KLF15 compared to eGFP control.

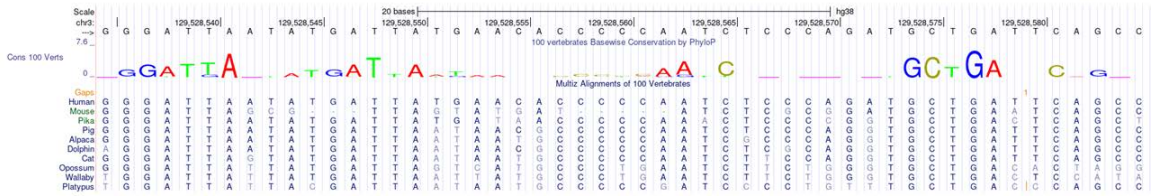


**Fig. S3.** Evolutive conservation of RHO promoter. Upper panel: logo of basewise conservation by PhyloP. Lower panel: multiple sequence alignment of representative mammalian species among 100 vertebrates.

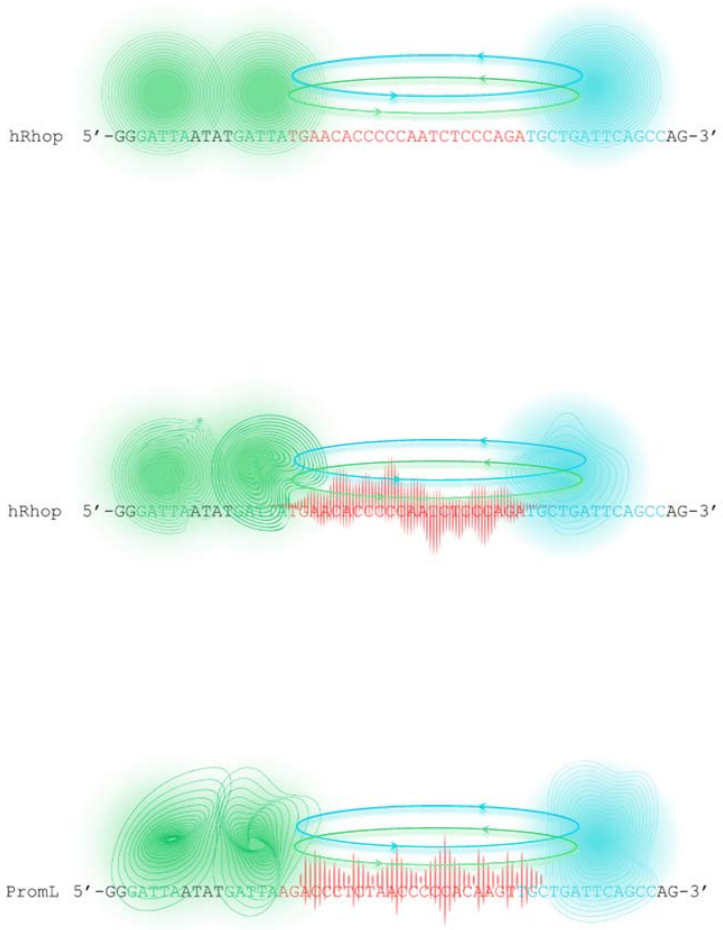


**Fig.S4.** Graphical representation modelling the novel DNA-TF interaction mechanism proposed. Top drawing shows standard model (TFs binding-dependent mechanisms) of TFs interaction with their respective binding sites. CRX and NRL TFs and their binding sites are represented in green and light blue respectively, and their TF-TF interaction is represented by light blue and green arrows. In the middle and bottom drawings, the binding-independent interaction mechanism proposed, mediated by the DNA itself. Distinct DNA bases composition (and length) of the DNA-linker (red sequence; middle drawing, hRHOp DNA-linker; bottom, hRHOp DNA-linker arranged in the opposite orientation 5'-3', Prom-L in the text) differentially impact (red waves) on TF-TF activity adding to TFs binding-dependent mechanisms (top drawing), eventually leading to differential gene expression levels.