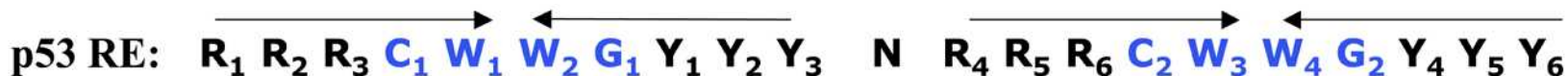


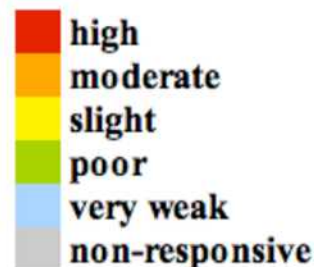
Supplementary information S1 | Rules for assessing functionality of p53 response elements



consensus RE

spacer length	0	1,2	>2
mismatch position			
CWWG sequence	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA

Transactivation score



1 mismatch at C or G

spacer length	0	≥1	0	≥1
mismatch position	C <sub>1</sub> or G <sub>2</sub>	C <sub>1</sub> or G <sub>2</sub>	G <sub>1</sub> or C <sub>2</sub>	G <sub>1</sub> or C <sub>2</sub>
CWWG sequence	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA

1 mismatch at W

spacer length	0		1,2		>2	
mismatch position	W <sub>1</sub> or W <sub>4</sub>	W <sub>2</sub> or W <sub>3</sub>	W <sub>1</sub> or W <sub>4</sub>	W <sub>2</sub> or W <sub>3</sub>	W <sub>1</sub> or W <sub>4</sub>	W <sub>2</sub> or W <sub>3</sub>
CWWG sequence	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA

1 mismatch at R or Y

spacer length	0			1,2	≥1	>2		
mismatch position	R <sub>1</sub> or R <sub>4</sub> or Y <sub>2</sub> or Y <sub>5</sub>	R <sub>3</sub> or R <sub>3</sub> or Y <sub>4</sub> or Y <sub>5</sub>	R <sub>2</sub> or R <sub>6</sub> or Y <sub>1</sub> or Y <sub>3</sub>	R <sub>1</sub> or R <sub>4</sub> or Y <sub>2</sub> or Y <sub>5</sub>	R <sub>2</sub> or R <sub>3</sub> or Y <sub>4</sub> or Y <sub>5</sub>	R <sub>3</sub> or R <sub>6</sub> or Y <sub>1</sub> or Y <sub>3</sub>	R <sub>1</sub> or Y <sub>4</sub>	R <sub>4</sub> or Y <sub>5</sub>
CWWG sequence	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA

2 mismatches at C or G

spacer length	same HS		different HS	
mismatch position				
CWWG sequence	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA

HS: half site

2 mismatches at W

spacer length	0		≥1	
mismatch position	same HS	different HS	same HS	different HS
CWWG sequence	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA	AT AA,TT,TA

Supplementary information S1 | Rules for assessing functionality of p53 response elements  
Presented are rules derived from experimental results obtained using yeast- and mammalian-based functional assays<sup>1-6</sup>, in which > 60 different p53 response elements (REs) were tested. At the top is the p53 consensus RE sequence. The CWWG core sequences of the two decamer half-sites are highlighted in blue. Transactivation score is summarized using a colour code and ranges from high (red) to non-responsive (grey) as illustrated in the legend. The criteria for functional scoring take into account the length of the spacer (N) separating the two half-sites (HS), the number and position of nonconsensus bases (mismatches), as well as the actual sequence of the CWWG core consensus. In the case of two mismatches from consensus, the impact on the functional score takes into account whether they both occur in the same HS, given that the remaining consensus HS could mediate p53 responsiveness, depending on its exact sequence<sup>6</sup>. Similarly, the impact of a mismatch at the conserved C or G positions is evaluated taking into account whether its position results in a consensus three-quarter site RE.

### References

1. Inga, A., Storici, F., Darden, T. A. & Resnick, M. A. Differential transactivation by the p53 transcription factor is highly dependent on p53 level and promoter target sequence. *Mol Cell Biol* **22**, 8612-25. (2002).
2. Resnick, M. A. & Inga, A. Functional mutants of the sequence-specific transcription factor p53 and implications for master genes of diversity. *Proc Natl Acad Sci U S A* **100**, 9934-9. Epub 2003 Aug 8. (2003).
3. Tomso, D. J. et al. Functionally distinct polymorphic sequences in the human genome that are targets for p53 transactivation. *Proc Natl Acad Sci U S A* **102**, 6431-6 (2005).
4. Menendez, D., Inga, A. & Resnick, M. A. The biological impact of the human master regulator p53 can be altered by mutations that change the spectrum and expression of its target genes. *Mol Cell Biol* **26**, 2297-308 (2006).
5. Jegga, A. G., Inga, A., Menendez, D., Aronow, B. J. & Resnick, M. A. Functional evolution of the p53 regulatory network through its target response elements. *Proc Natl Acad Sci U S A* **105**, 944-9 (2008).
6. Jordan, J. J. et al. Noncanonical DNA motifs as transactivation targets by wild type and mutant p53. *PLoS Genet* **4**, e1000104 (2008).