

| Category of PBM motif                             | total # TFs | perturbation exists* | sig. effect on targets** | % sig. |
|---|-------------|----------------------|--------------------------|--------|
| <i>All motifs</i>                                 | 89          | 79                   | 44                       | 55.7   |
| <i>Different from literature PWM</i>              | 17          | 17                   | 10                       | 58.8   |
| <i>Different from literature PWM or consensus</i> | 20          | 20                   | 12                       | 60.0   |
| <i>No previous binding information</i>            | 30          | 24                   | 13                       | 54.2   |
| <i>Novel binding motif (all new or different)</i> | 50          | 44                   | 25                       | 56.8   |
| <i>Closely matches literature PWM</i>             | 31          | 31                   | 17                       | 54.8   |
| <i>Matches literature PWM or consensus</i>        | 39          | 35                   | 19                       | 54.3   |

| Category of PBM motif                              | total # TFs | Genetic interactor perturb.*** | sig. effect on targets** | % sig. |
|--|-------------|--------------------------------|--------------------------|--------|
| <i>TF has no self-perturbation expression data</i> | 10          | 5                              | 3                        | 60.0   |

\* # of TFs for which expression data exist for a mutation, deletion, or overexpression of that TF

\*\* significant enrichment of predicted TF targets among genes whose expression is affected by perturbation

\*\*\* # of TFs for which a genetic interactor has expression data for a mutation, deletion, or overexpression

**Table S7.** This table summarizes the effect of mutating or deleting a TF (using expression data available from the literature) on the PBM-predicted target genes of that TF. TFs are broken down into different motif categories to emphasize the similar results for novel motifs as compared to known motifs.