

Supporting Texts for "On Statistical Significance of Combinatorial Regulations" by Terada, A., Okada-Hatakeyama, M., Tsuda, K., Sese, J.

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Supporting Text 1: Mann-Whitney U Test

Decrease of the minimum p -value with respect to the number of genes in the Mann-Whitney U Test

In this paper, we used Fisher's exact test as the statistical test. LAMP can be applicable to any statistical test as long as it satisfies the following two properties: the existence of a non-zero minimum p -value and decrease of the minimum value to the number of target genes. Here, we prove that the Mann-Whitney U test satisfies these properties to show that it can be used in LAMP.

Suppose that we have N genes and that we know their expression ranks under a specific condition. Given a binding motif combination, the set of genes whose regulatory regions contain all the motifs is defined as J . N genes are classified into $x = |J|$ targeted and $N - x$ untargeted genes. Mann-Whitney U is defined as the probability that the ranks achieves more biased than J .

The p -value is achieved at the smallest value when expression levels of genes in J are larger than the others, or they are smaller than the others. The probability to appear the case is described as

$$1 / \binom{N}{x}.$$

This is the minimum p -value of Mann-Whitney U .

This value decreases with increase of x for $1 \leq x \leq N/2$, and takes the minimum value when $x = \lfloor N/2 \rfloor$, which is non-zero value. Therefore, Mann-Whitney U can be used in LAMP.

Supporting Text 2: Comparison of LAMP with Bonferroni correction with four thresholds

Summary of the numbers of significant combinations detected by LAMP and Bonferroni correction with four different thresholds

We compared LAMP and Bonferroni correction on one yeast and two human datasets with four thresholds that is used to divide the gene expressions in up-regulated and unregulated. Tables in Section A show the summary of the results. Figures in Section B show the number of samples in which at least one significant combination was found. Figures in Section C show the number of significant combinations. The combinations found by the combinations are in Table S1.

A. Statistics of the number of significant combinations

The rows are:

- # of detected samples: The number of samples in which at least one motif combination is significant over all conditions (173 for yeast, 27 for EGF and 28 for HRG).
- # of significant combinations: The sum of the numbers of statistically significant motif combinations over all conditions.
- Maximum arity: The largest arity over all conditions.
- Avg. # of up-regulate genes: The average number of up-regulated genes over all conditions.
- Average, minimum and maximum of m' : The average, minimum and maximum value of m' over all conditions.

A. Yeast (The details are in Table S1A)

Threshold (log2 ratio)		0.5	1	1.5	2
Avg. # of up-regulated genes		990.86	363.62	171.36	95.29
# of detected samples	LAMP	157	135	113	95
	Bonferroni (<=2)	134	111	95	78
	Bonferroni (<=3)	103	95	71	57
# of significant combinations	LAMP	513	449	326	235
	Bonferroni (<=2)	308	264	192	137
	Bonferroni (<=3)	187	176	108	82
Stats of LAMP	Maximum arity	3	3	4	3
	Avg. of m'	243.30	366.43	446.30	498.34
	Min. of m'	132	183	233	290
	Max of m'	554	556	702	703

B. EGF induced sample (The details are in Table S1B)

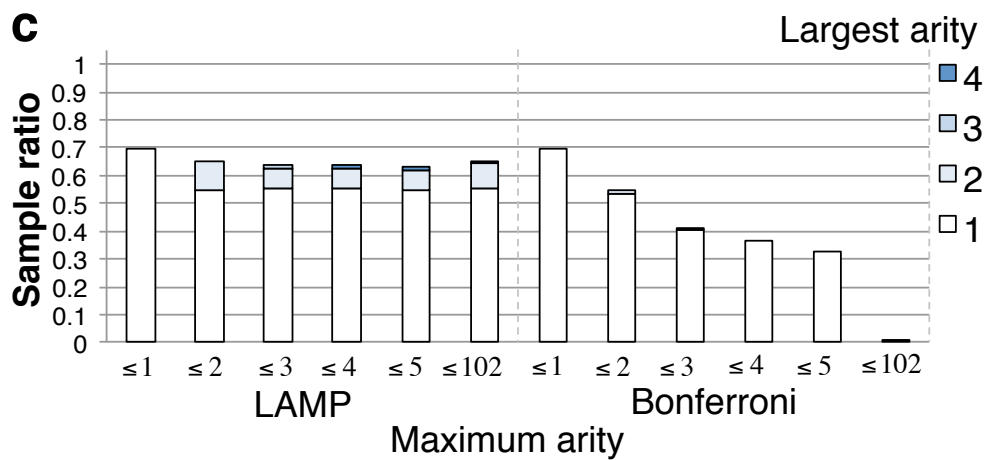
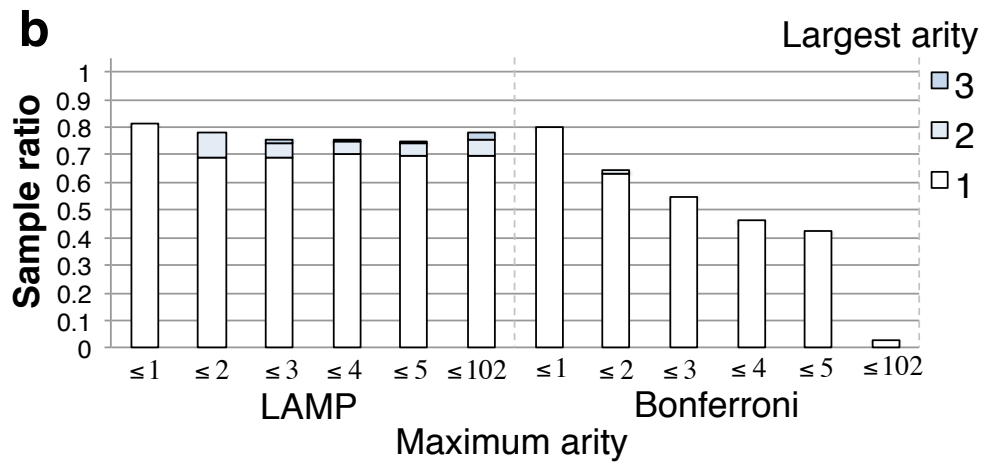
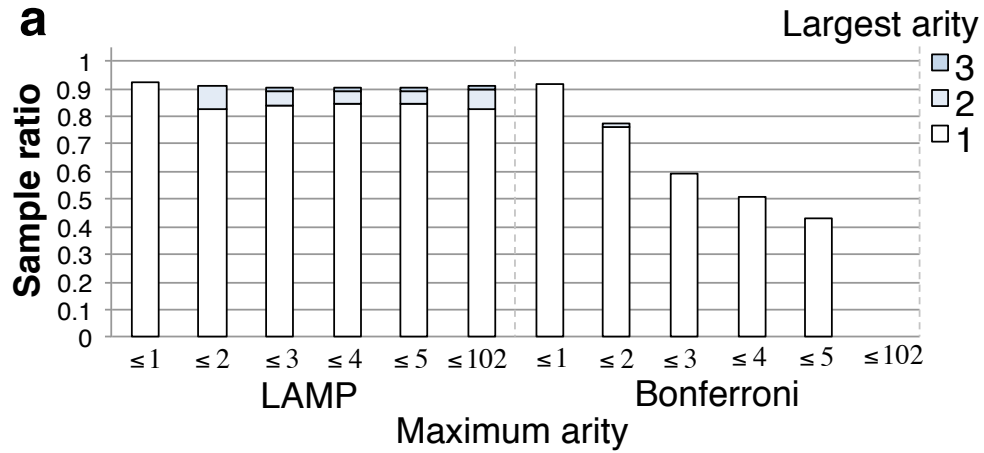
Threshold (log2 ratio)		0.5	1	1.5	2
Avg. # of up-regulated genes		2359.81	1226.67	777.04	491.26
# of detected samples	LAMP	17	20	16	10
	Bonferroni (<=2)	21	23	22	16
	Bonferroni (<=3)	8	14	13	6
# of significant combinations	LAMP	46	43	23	24
	Bonferroni (<=2)	78	70	41	38
	Bonferroni (<=3)	20	19	14	8
Stats of LAMP	Maximum arity	5	8	7	8
	Avg. of m'	1,742,870	3,669,596	5,180,881	7,169,767
	Min. of m'	1,459,869	2,700,718	3,750,336	5,238,103
	Max of m'	2,700,718	3,750,336	5,238,103	7,247,034

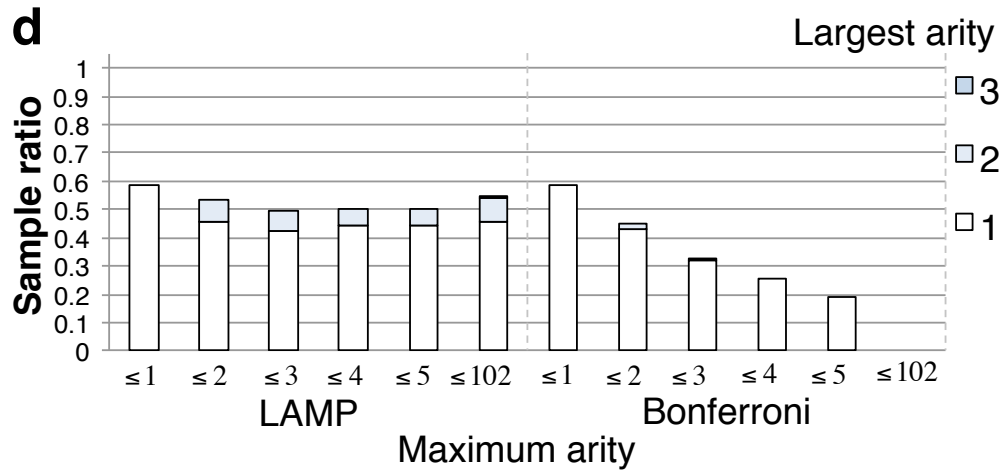
C. HRG induced sample (The details are in Table S1C)

Threshold (log2 ratio)		0.5	1	1.5	2
Avg. # of up-regulated genes		4189.54	2337.36	1277.00	758.68
# of detected samples	LAMP	18	12	10	7
	Bonferroni (<=2)	25	21	12	12
	Bonferroni (<=3)	5	6	4	1
# of significant combinations	LAMP	26	23	16	11
	Bonferroni (<=2)	40	43	26	19
	Bonferroni (<=3)	5	7	7	1
Stats of LAMP	Maximum arity	6	5	5	6
	Avg. of m'	579,531	1,790,220	3,800,657	5,561,464
	Min. of m'	359,149	1,174,198	2,874,627	3,982,295
	Max of m'	1,174,108	2,874,627	5,542,428	7,635,557

B. Comparisons of the numbers of samples in which at least one motif combination is significant between LAMP and Bonferroni correction.

B-1. Yeast

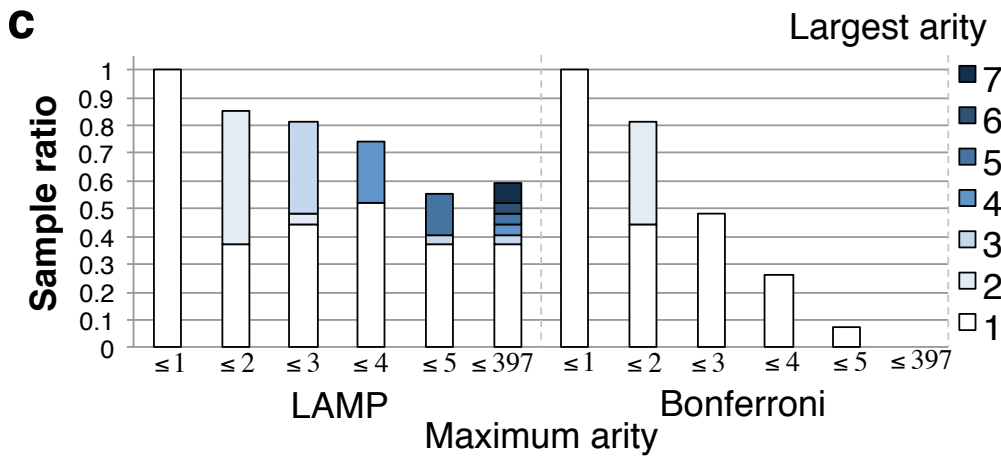
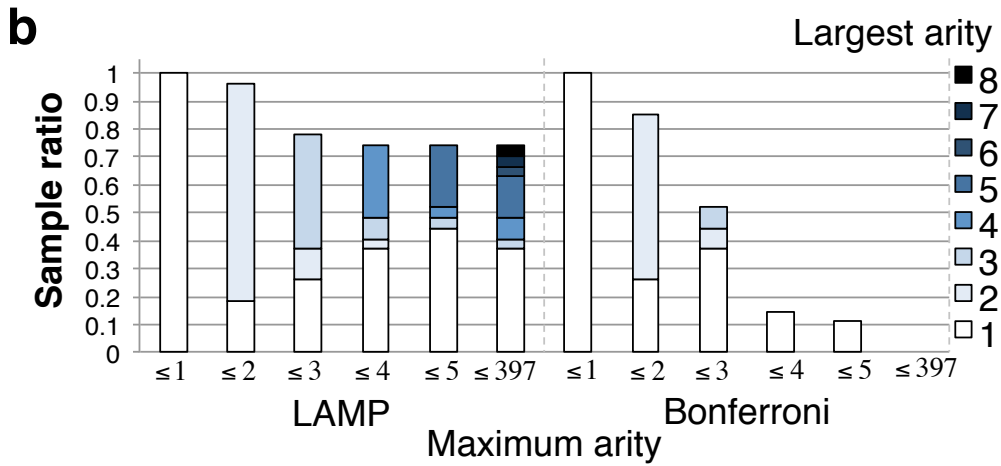
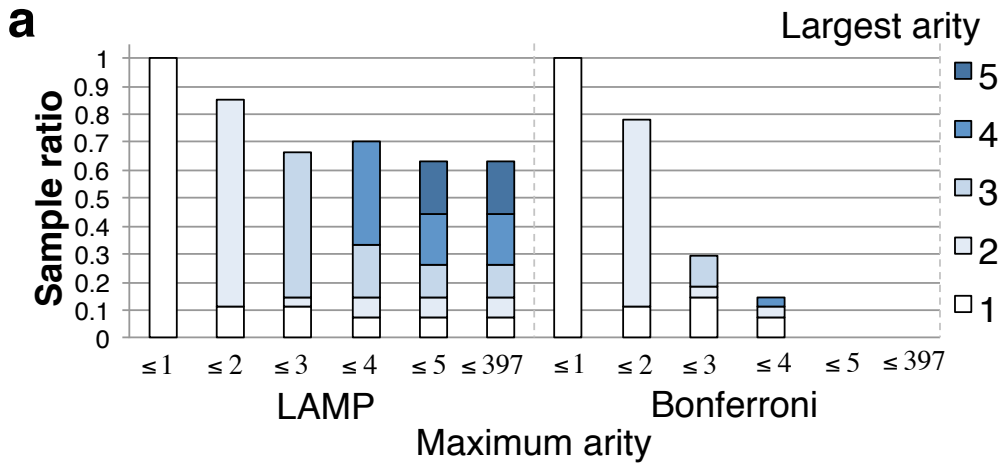


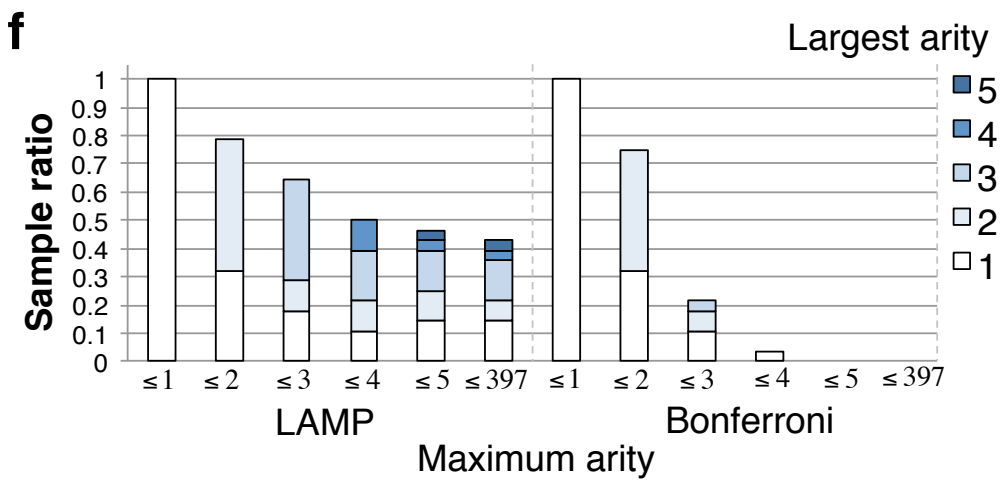
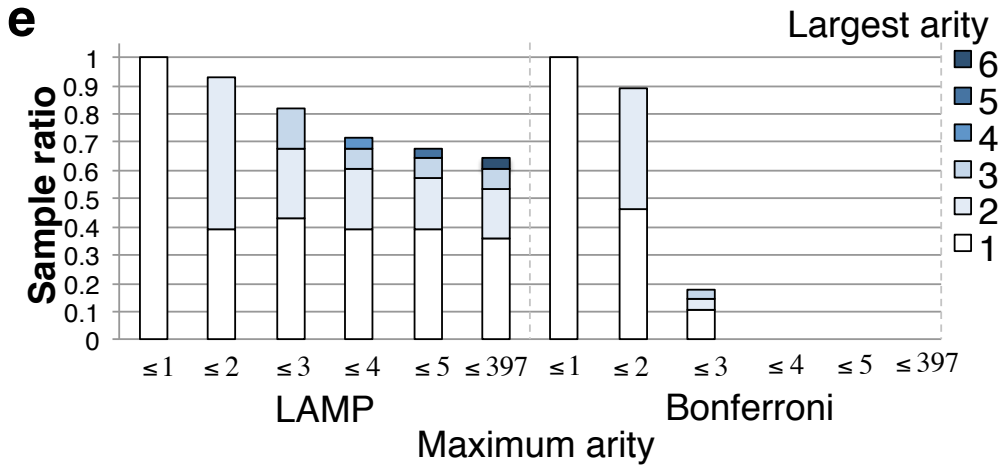
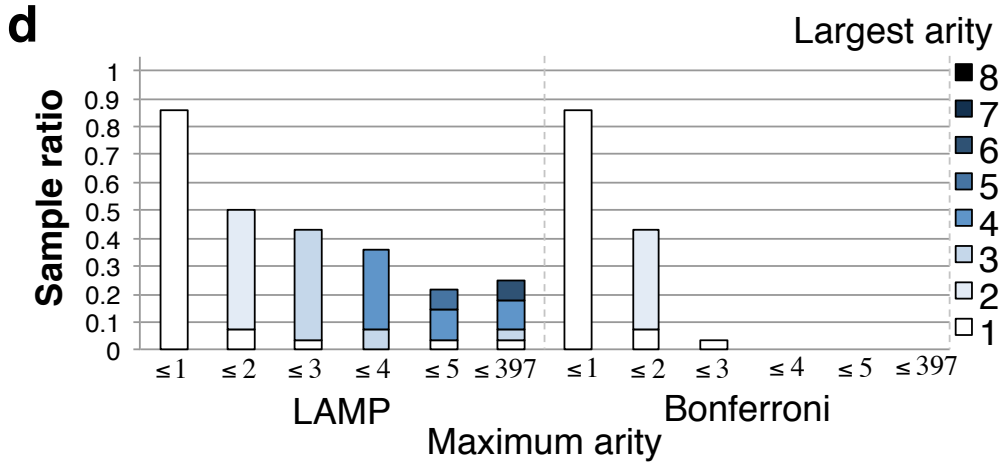


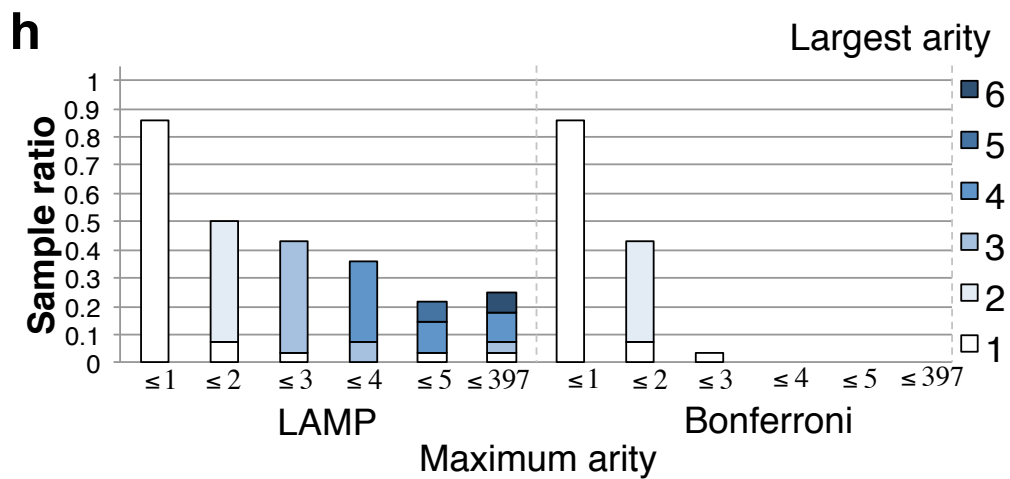
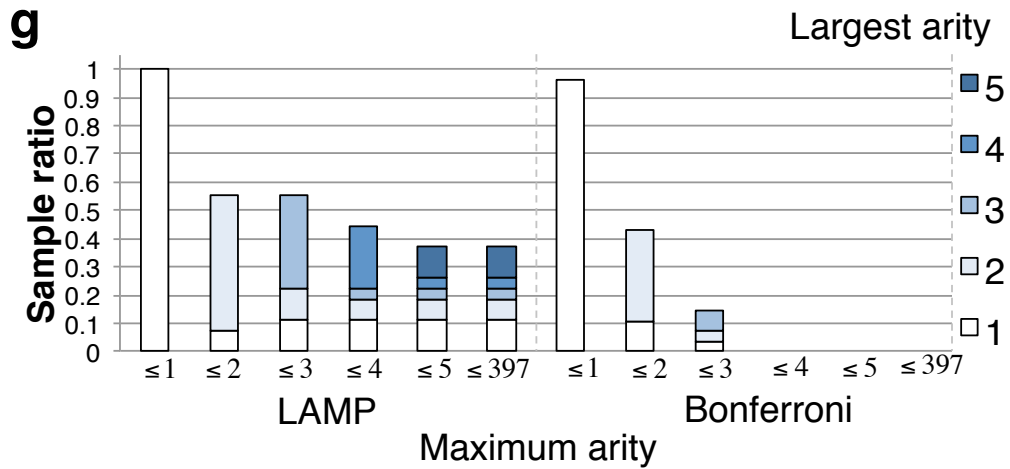
Sample ratios in which at least one motif combination is significant over 173 yeast stress environments. We varied the arity limit and computed the number of samples in which at least one sample was deemed significant for the specified arity limit. The number of motifs we used was 102. The significant level α was set to 0.05. We also used the Bonferroni correction to compute the motif combinations under three different expression thresholds, which correspond to the data shown in Supporting Table S1. For any threshold, the LAMP found at least one motif combination from at least half the samples even when the arity limit was removed. However, the number of samples detected using the Bonferroni correction decreased with the increasing arity limit, and the Bonferroni correction found significant combinations from only a few samples when the arity limit was removed. The colors indicate the largest arity. The LAMP discovered at most four-motif combinations, whereas the Bonferroni correction found at most two-motif combinations.

(a) Expression threshold = 0.5. (b) Expression threshold = 1.0. (c) Expression threshold = 1.5. (d) Expression threshold = 2.0.

B-2. Human MCF-7





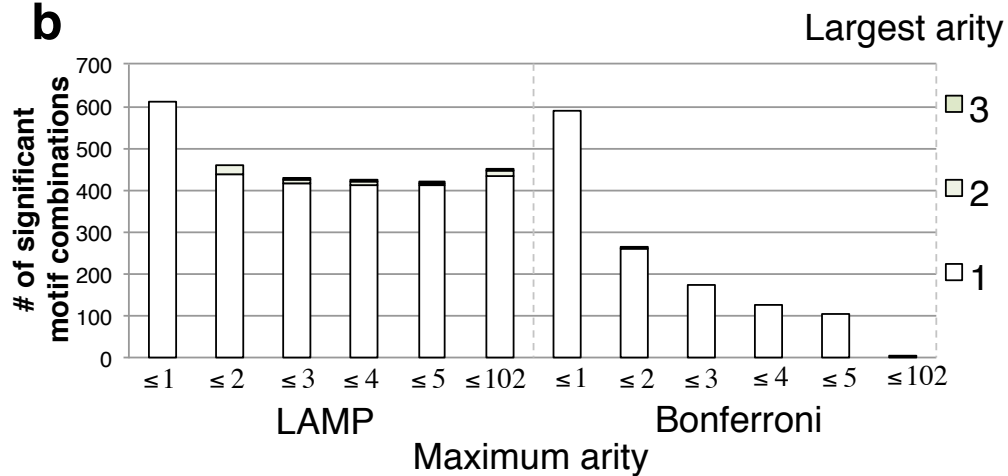
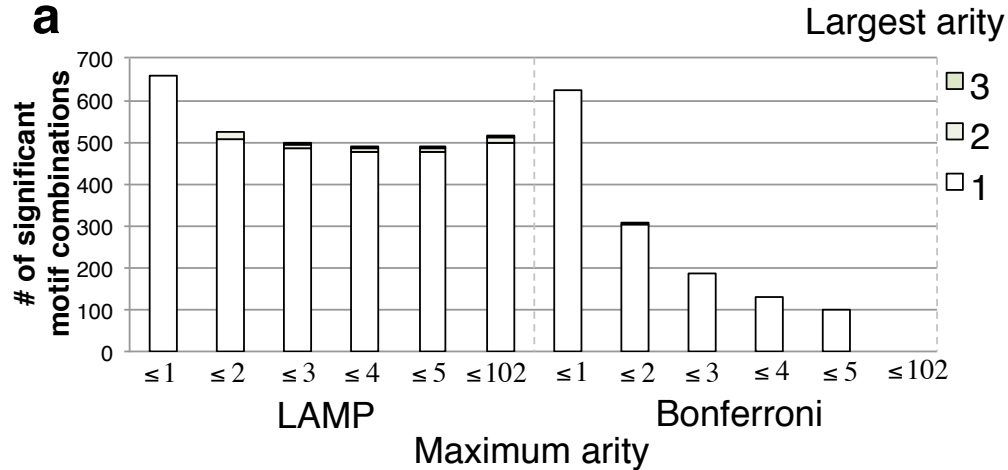


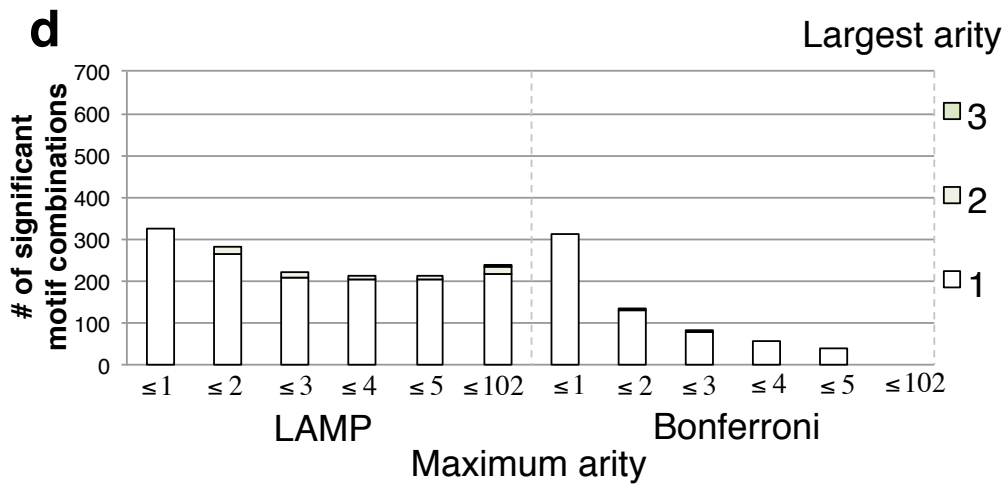
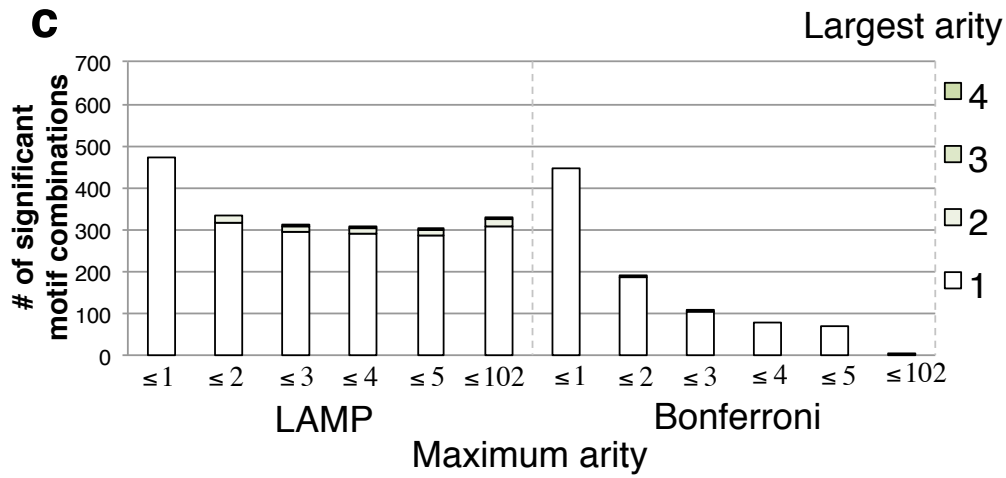
Sample ratios in which at least one motif combination was deemed significant in 27 HRG⁻ and 28 HRG⁻induced MCF-7 cell samples. We varied the arity limit and computed the number of samples in which at least one sample deemed significant for the specified arity limit. The number of motifs was 397. The significance level α was set to 0.05. We computed the combinations under three different thresholds for performing Fisher's exact test. The colors indicate the largest arity.

- (a) EGF, expression threshold = 0.5. (b) EGF, expression threshold = 1.0.
- (c) EGF, expression threshold = 1.5. (d) EGF, expression threshold = 2.0.
- (e) HRG, expression threshold = 0.5. (f) HRG, expression threshold = 1.0.
- (g) HRG, expression threshold = 1.5. (h) HRG, expression threshold = 2.0.

C. Comparison of the numbers of significant combinations between LAMP and Bonferroni correction.

C-1. Yeast

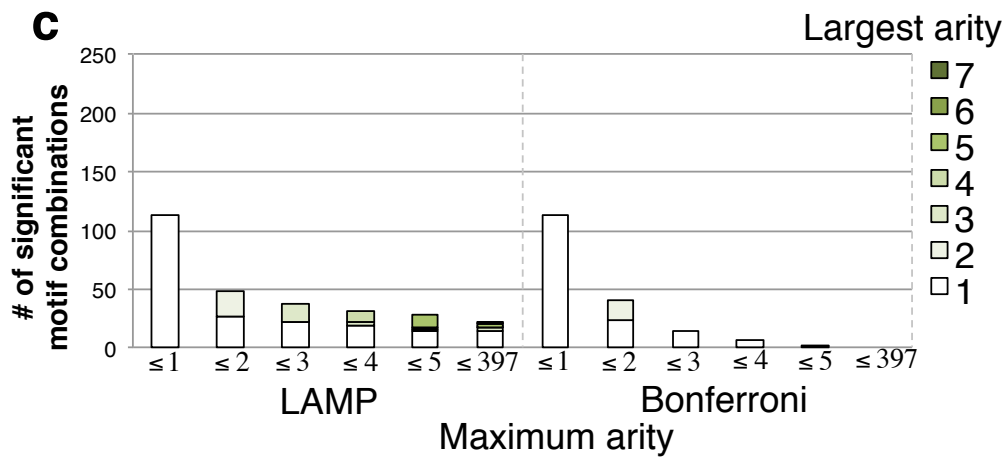
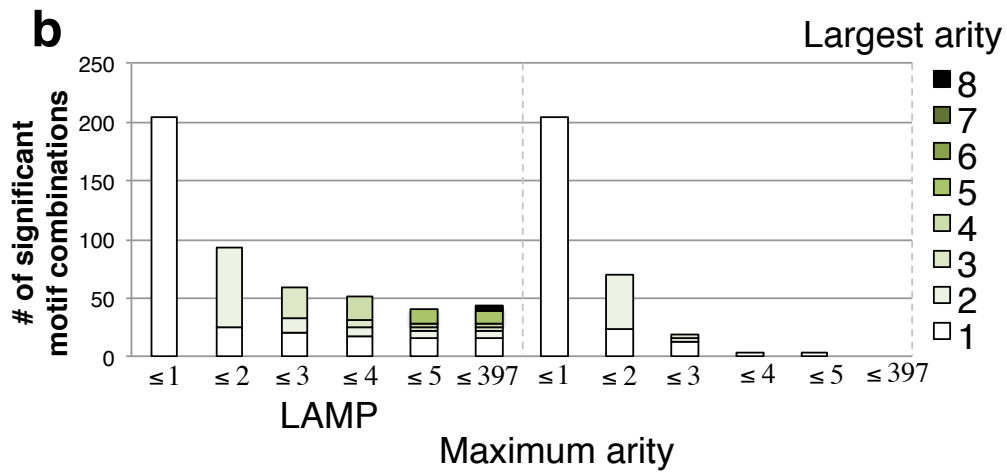
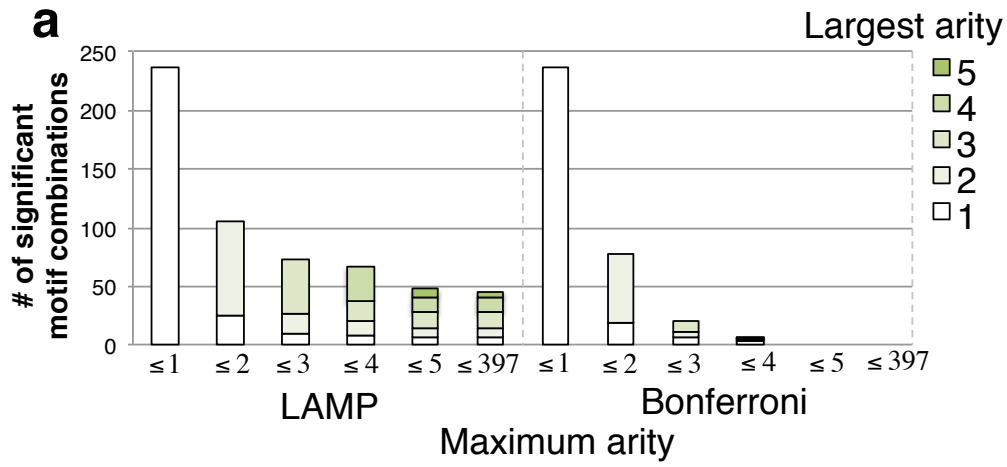


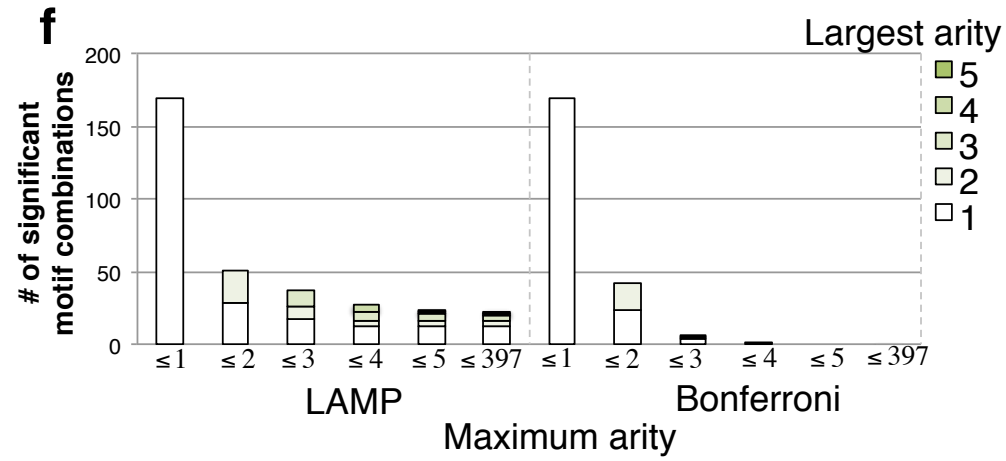
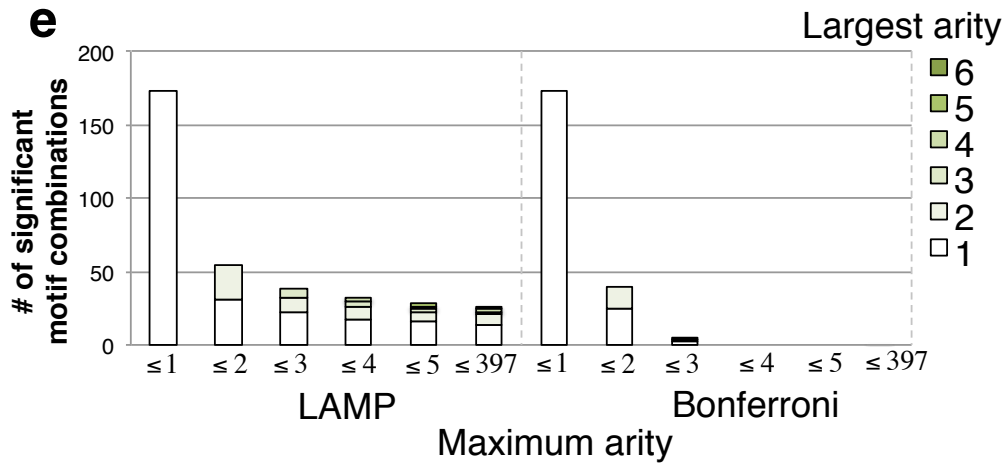
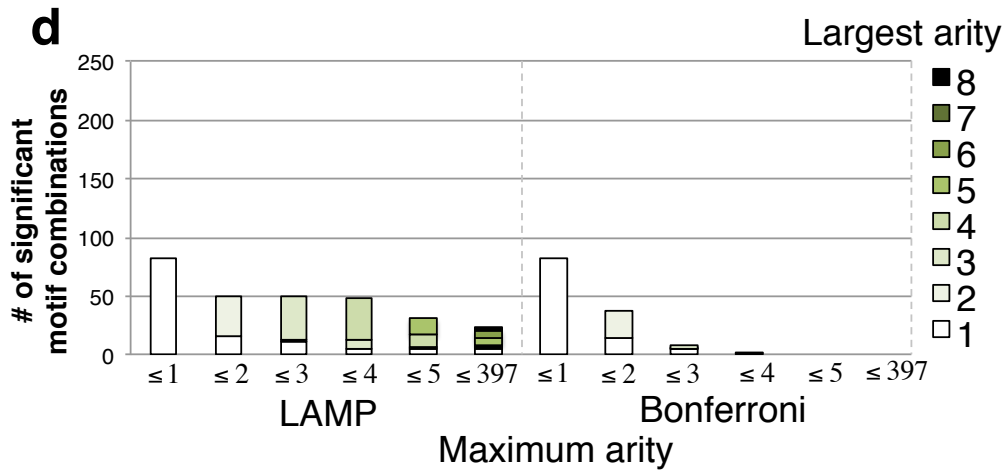


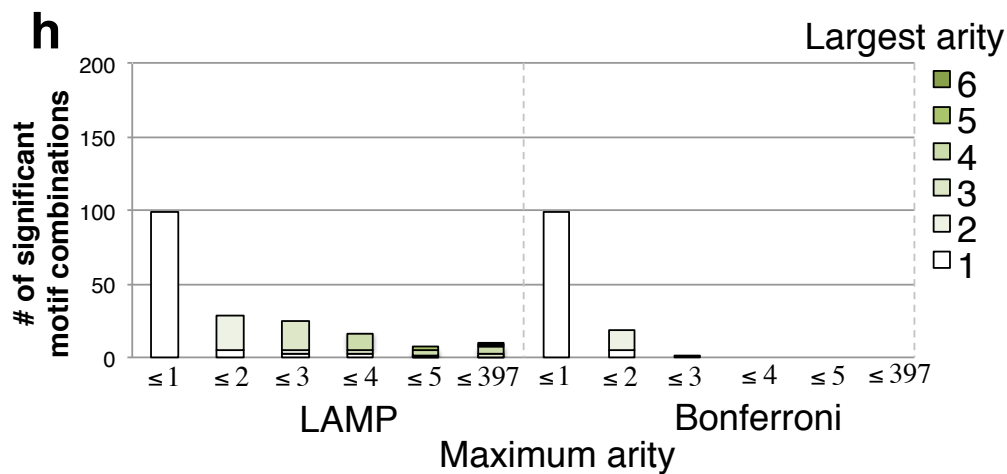
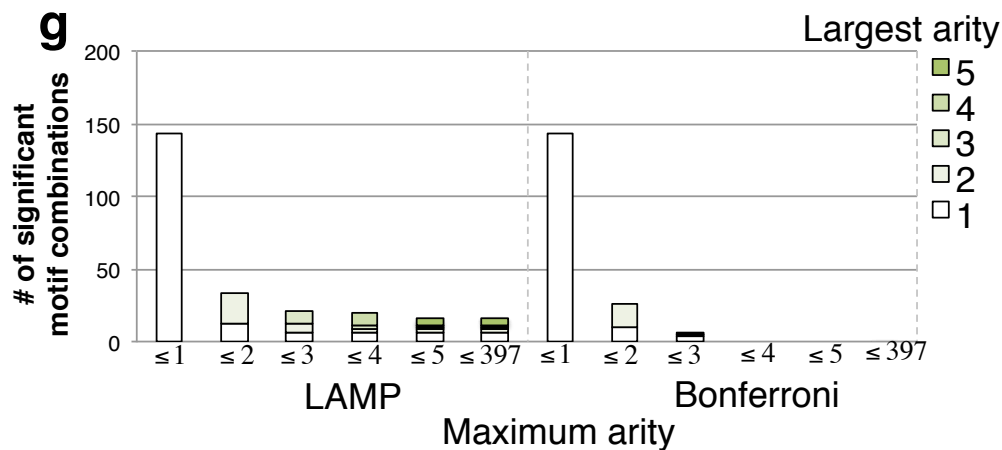
The number of statistically significant motif combinations in the 173 yeast stress environments. Each bar indicates the number of statistically significant motif combinations for a specific arity limit. Within the bar, the colors indicate the largest arity. We computed these combinations under three different expression thresholds for Fisher's exact test. The LAMP found more than 200 motif combinations even when the arity limit was removed, whereas the Bonferroni correction found 9 combinations under any threshold.

(a) Expression threshold = 0.5. (b) Expression threshold = 1.0. (c) Expression threshold = 1.5. (d) Expression threshold = 2.0.

C-2. Human MCF-7







The number of statistically significant motif combinations in 27 EGF and 28 HRG induced MCF-7 cell samples. Each bar indicates the number of statistically significant motif combinations for the specified arity limit. Within the bar, the colors indicate the largest arity. We computed the combinations under three different thresholds for performing Fisher's exact test. Whereas the Bonferroni correction detected only a few combinations when up to 5-motif combinations were considered, the LAMP found more than 16 combinations, including one 8-motif combination.

- (a) EGF, expression threshold = 0.5. (b) EGF, expression threshold = 1.0.
- (c) EGF, expression threshold = 1.5. (d) EGF, expression threshold = 2.0.
- (e) HRG, expression threshold = 0.5. (f) HRG, expression threshold = 1.0.
- (g) HRG, expression threshold = 1.5. (h) HRG, expression threshold = 2.0.

Supporting Text 3: Details of the TFs that bind to the motifs in Fig. 4

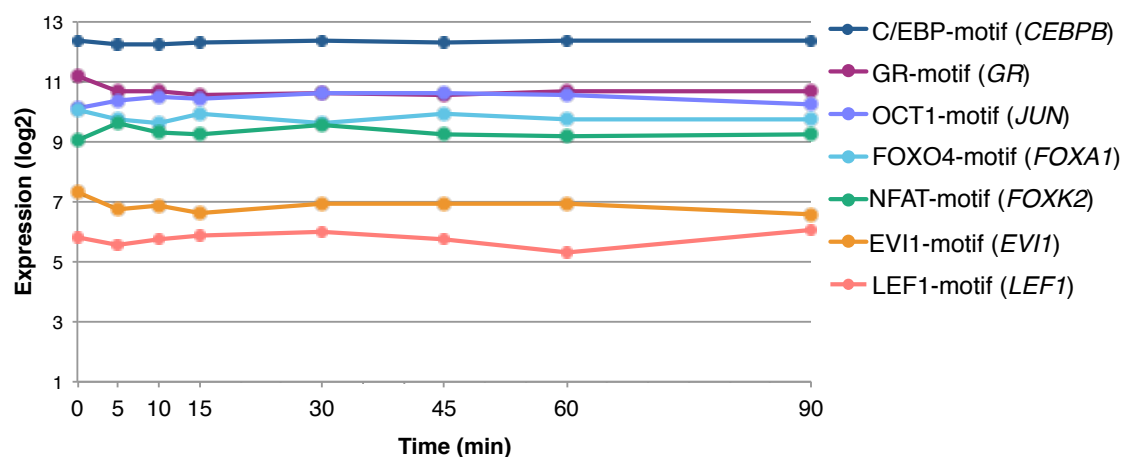
TFs that bind to the motifs in Fig. 4 and their expression levels.

A. The eight-motif combination

A-1. The list of TFs that can bind to the motif

Motif	TFs that bind to the motif
CTTTAAR	-
C/EBP	<i>C/EBP, CEBPB</i>
EVI1	<i>EVI1</i>
FOXO4	<i>FOXA1, FOXA2, FOXO1, FOXO4, HMGA1</i>
GR	<i>GR</i>
LEF1	<i>LEF1</i>
NFAT	<i>ELOF1, FOXK2, NFATC1, NFATC2, NFATC3, NFATC4</i>
OCT1	<i>GATA1, JUN, NFYA, NFYB, NFYC, OCT1, OCT2, SP1</i>

A-2. The expression levels of TFs that bind to the motifs.



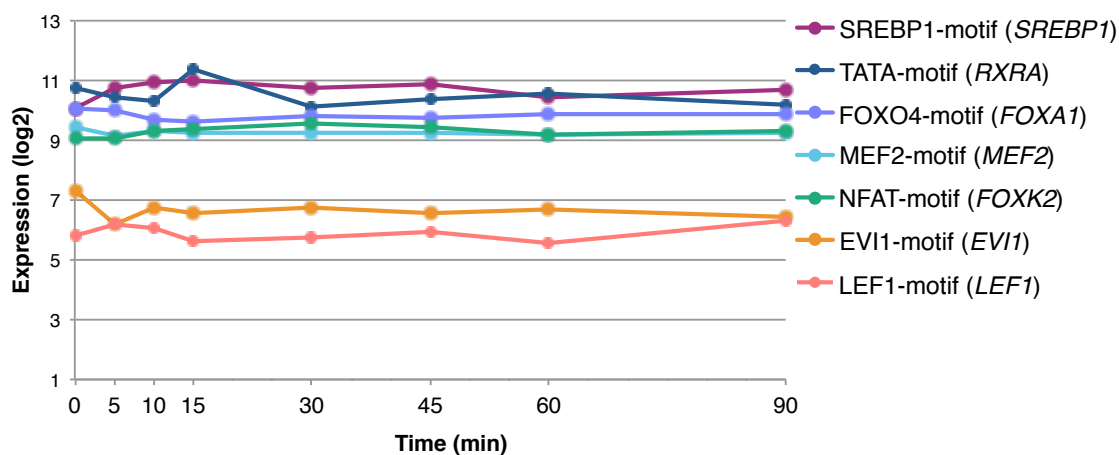
Expression levels of TFs that bind to the motifs in the eight-motif combination. Each line corresponds to one motif and shows the expression levels of a TF that can bind to the motif. When single motif is recognized by multiple TFs, we selected the TF whose expression level under control (0 min) among TFs that can bind to the motif is the highest one. The name on each line is the motif name, and the TF name is in parentheses. For example, since *CEBPB* can bind to the C/EBP-motif and the expression of *CEBPB* is higher than that of *C/EBP* at 0 min, the expression levels of *CEBPB* are described in the figure as a blue line. When the TF has multiple probes in Affimetrix chip, the probe that has the highest expression level at 0 min is used. The motif "CTTTAAR" is not shown because no TF bound to the motif is identified yet.

B. The seven-motif combination

B-1. The list of TFs that can bind to the motifs.

Motif	TFs that bind to the motif
EVI1	<i>EVI1</i>
FOXO4	<i>FOXA1, FOXA2, FOXO1, FOXO4, HMGA1</i>
LEF1	<i>LEF1</i>
MEF2	<i>MEF2, MEF2D</i>
NFAT	<i>ELOF1, FOXK2, NFATC1, NFATC2, NFATC3, NFATC4</i>
SREBP1	<i>SREBP1</i>
TATA	<i>GTF2B, HINFP, RXRA, TBP, THRB, TMF1</i>

B-2. The expression levels of the TFs that bind to the motifs.



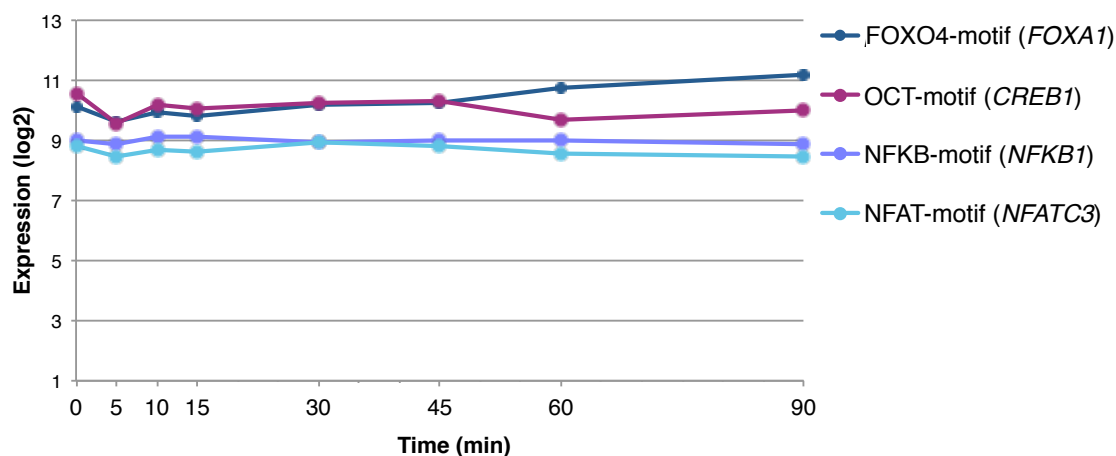
Expression levels of the TFs that bind to the motifs in seven-motif combination. Each line indicates the expression levels of the TF that binds to the motif. If multiple TFs can be bound to the motif, the expression levels of the TF whose expression level at control sample is the highest are shown. The name of the TF is in parentheses.

C. The five-motif combination

C-1. The list of TFs that can bind to the motifs

Motif	TFs that bind to the motif
AACTTT	-
FOXO4	<i>FOXA1, FOXA2, FOXO1, FOXO4, HMGA1</i>
NFKB	<i>NFKB1, NFKB2, REL, RELA</i>
OCT	<i>CREB1, GATA1, JUN, NFYA, NFYB, NFYC, POU5F1, POU5F1B, SP1</i>
NFAT	<i>ELOF1, FOXK2, NFATC1, NFATC2, NFATC3, NFATC4</i>

C-2. The expression levels of the TFs that bind to the motifs.



Expression levels of the TFs that bind to the motifs in the five-motif combination. Each line indicates the expression levels of the TF that binds to the motif. If multiple TFs can be bound to the motif, the expression levels of the TF whose expression level at control sample is the highest are shown. The name of the TF is in parentheses. The motif "AACTTT" is not shown because no TF bound to the motif is identified yet.

Supporting Text 4: Monotonicity of the minimum p -value

Our algorithm takes advantage of the fact that the minimum p -value decreases to its occurrence frequency. In this section, we show the detail of the minimum p -value.

Suppose that we have N genes. Only one expression level is available for each of the N genes. Given a motif combination, the genes are partitioned in two ways. In one way, the genes are classified into x targeted and $N - x$ untargeted genes, depending on whether they are targeted by all of the members of the motif combination or not. In the other way, they are classified into n_u up-regulated genes and $N - n_u$ unregulated genes. Let n be the number of genes that are targeted and upregulated.

Using One-sided Fisher's exact test, the p -value of the motif combination is computed as

$$p = \sum_{n_x=n}^B P(n_x), P(n_x) = \binom{n_u}{n_x} \binom{N - n_u}{x - n_x} / \binom{N}{x},$$

where $B = \min\{n_u, x\}$. If we regard that n is a variable, the minimum value of p is achieved at $n = B$, and described as

$$f'(x) = \binom{n_u}{x} / \binom{N}{x} \text{ (for } x \leq n_u), \binom{N - n_u}{x - n_u} / \binom{N}{x} \text{ (for } x > n_u).$$

In the most case, $x \leq n_u$, and the following Property 1 confirms the monotonicity of the minimum p -value, which is required to use the function in LAMP. On the other hand, when $x > n_u$, the property is not satisfied. Therefore, we define a function which is smaller than the minimum p -value to satisfy the monotonicity.

Property 1. For $1 \leq x < N/2$ and $x \leq n_u$, $f'(x) \leq f'(x - 1)$ holds.

Proof. Between x and $x - 1$, the following equation holds:

$$\begin{aligned} \binom{n_u}{x} &= \frac{n_u(n_u - 1) \cdots (n_u - x + 2)(n_u - x + 1)}{x!} \\ &= \frac{n_u - x + 1}{x} \frac{n_u(n_u - 1) \cdots (n_u - x + 2)}{(x - 1)!} \\ &= \frac{n_u - x + 1}{x} \binom{n_u}{x - 1}. \end{aligned}$$

Similarly,

$$\binom{N}{x} = \frac{N - x + 1}{x} \binom{N}{x - 1}.$$

Based on these equations,

$$\begin{aligned}
f'(x) &= \binom{n_u}{x} / \binom{N}{x} \\
&= \left\{ \frac{n_u - x + 1}{x} \binom{n_u}{x-1} \right\} / \left\{ \frac{N - x + 1}{x} \binom{N}{x-1} \right\} \\
&= \left\{ \frac{n_u - x + 1}{x} / \frac{N - x + 1}{x} \right\} \left\{ \binom{n_u}{x-1} / \binom{N}{x-1} \right\} \\
&= \frac{n_u - x + 1}{N - x + 1} f'(x-1)
\end{aligned}$$

From $n_u \leq N$, $(n_u - x + 1)/(N - x + 1) \leq 1$. Hence, $f'(x) \leq f'(x-1)$. \square

For $x > n_u$, the similar calculation of Property 1 shows that $f'(x)$ increases to x monotonically. LAMP requires a monotonically decreasing function to x , and hence $f'(x)$ cannot be used as the minimum p -value directly. Instead of the function, we use

$$f'(x) = 1 / \binom{N}{n_u}$$

as the minimum value since it is smaller than $f'(x)$ and constant, which means that f' is a monotonically decreasing function.

By combining these two formulas, the minimum p -value $f(x)$ that satisfies the monotonicity is defined as

$$f(x) = \binom{n_u}{x} / \binom{N}{x} \text{ (for } x \leq n_u), 1 / \binom{N}{n_u} \text{ (for } x > n_u).$$

Supporting Text 5: Frequent itemset mining algorithm

Overview of the frequent itemset mining algorithms

We here provide an overview of frequent itemset mining algorithms. The frequent itemset mining problem is to list all patterns that appear frequently in a data. One typical application of this problem is to find sets of items (itemsets) that customers are likely to purchase on a given trip to the store. The itemset that satisfies the condition is called a frequent itemset. In this study we used the algorithm to list up sets of motifs that share more than λ target genes.

We here introduce how the frequent itemset mining algorithm efficiently lists up the frequent itemsets. For the listing, the following property is used. Given k -motif combination T that targets x genes. Let t be a motif which is not in T and let us generate T' by adding t to T . The number of target genes of T' is smaller or equal to that of T . From this property, if x becomes less than λ , the number of target genes of any T' is less than λ , and hence it guarantees that T' contains no motif combinations that target λ or more genes.

The frequent itemset mining algorithm generates the motif combinations from lower-arity combinations. It generates all single motifs first, and motifs that target λ or more genes are selected. Let \mathbf{L}_1 be the set of the selected motifs. In LAMP, all motifs in the \mathbf{L}_1 are testable because their bounds of the minimum p -value are less than the candidate p -value. Then, the algorithm generates 2-motif combinations by combining two motifs in \mathbf{L}_1 and selects 2-motifs that target λ or more genes. Since the number of target genes of a 2-motif combination is smaller or equal to both single motifs in the 2-motif, we generate the 2-motif only from the motifs in \mathbf{L}_1 . 2-motif combinations that target λ or more genes are stored in \mathbf{L}_2 .

Let \mathbf{L}_k be the list of k -motif combinations that target λ or more genes. From the list, \mathbf{L}_{k+1} can be generated. The itemset mining algorithm repeats this process until \mathbf{L}_k contains no motif combinations. By combining all \mathbf{L}_k , all itemsets that target λ or more genes are listed without the generation of entire combinations.

Based on this idea, the first algorithm to efficiently list up the frequent itemsets called *Apriori* was introduced by Agrawal and Shrikant [31]. Han *et al.* [32] introduced more efficient algorithm under large memory environment to list up frequent itemsets, called FP-tree. It generates a tree of items in frequent itemsets, and then lists up the frequent items using the tree. Uno *et al.* [33] proposed a memory efficient algorithm, called LCM. We used the Uno's implementation to find frequent sets of motifs.

Supporting Figures

Supporting Fig. S1.

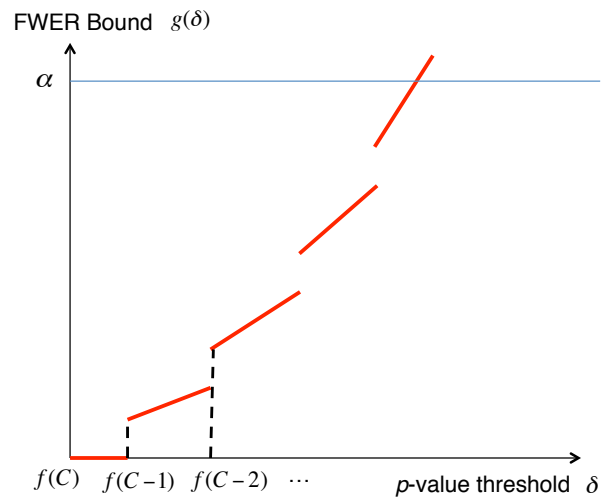


Illustration of the relationship between δ and $g(\delta)$. The red lines form a piece-wise linear function. The gaps are located at $f(\lambda)$, where $\lambda = C, C - 1, \dots, 1$. α is the significance level. The crossing point of the two lines indicates the optimal correction.

Supporting Fig. S2.

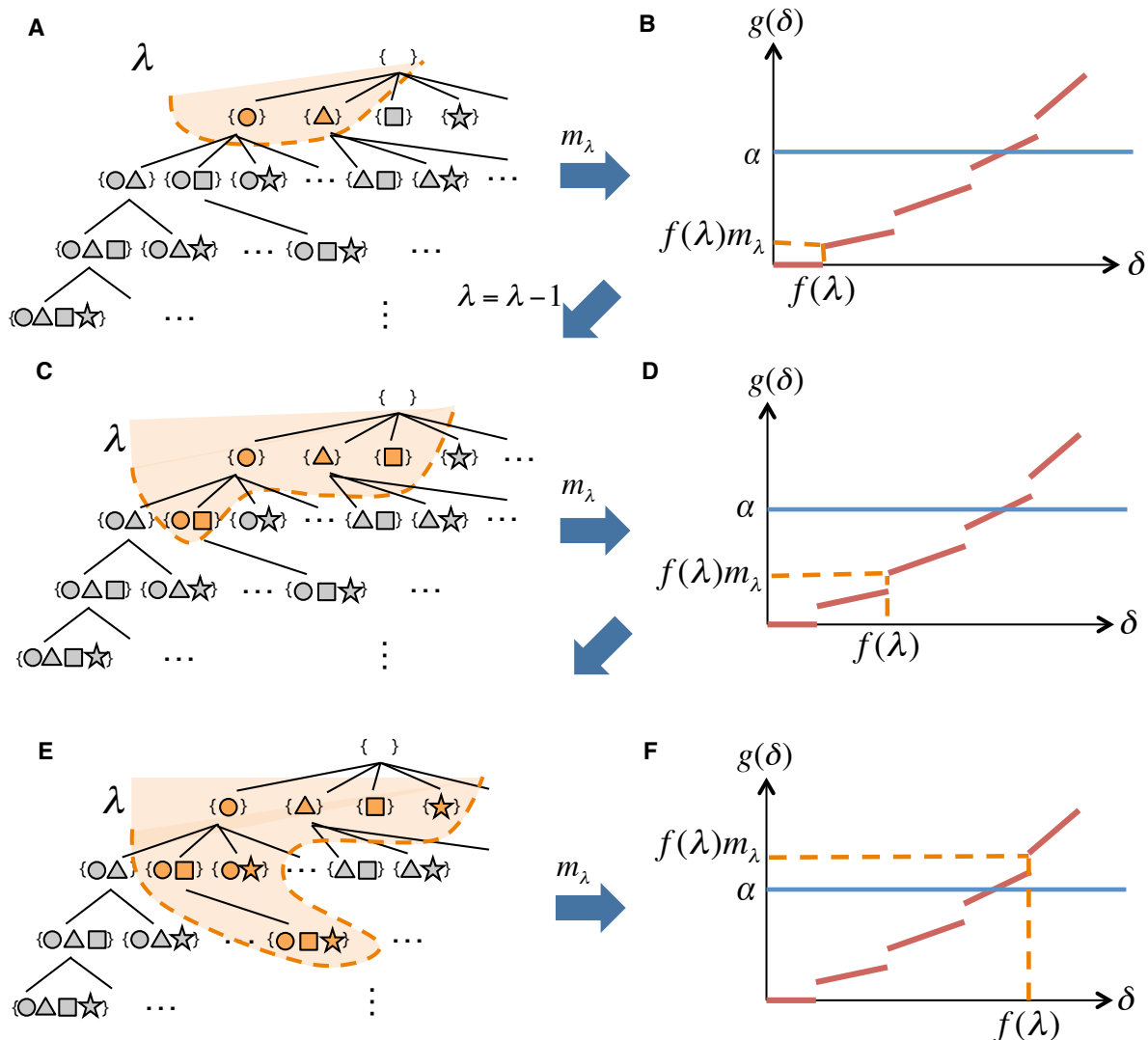


Illustration of the algorithm of the LAMP. (a) Starting from the largest λ , the frequent itemset mining algorithm listed up motif combinations that target λ or more genes. The number of the combinations is m_λ . (b) From m_λ and $f(\lambda)$, the FWER bound $f(\lambda)m_\lambda$ can be calculated. Because the FWER bound is smaller than α in this figure, m_λ is not sufficiently large to be a corrected significance level. (c) By decreasing λ , m_λ becomes large. The motif combinations that target λ or more genes were listed up using a frequent itemset mining algorithm. m_λ is computed from the result. (d) If $f(\lambda)m_\lambda$ is still smaller than α , we change λ for a smaller value and repeat the process. (e)(f) $f(\lambda)m_\lambda$ exceeds α , which indicates that $f(\lambda)$ is too large to control a FWER less than α . From the results, $f(\lambda + 1)$ is the largest value, and $m_{\lambda+1}$ is the optimal Bonferroni factor.

Supporting Table

Supporting Table S1.

List of significant motif combinations.

These tables include the statistically significant motif combinations detected by LAMP and the Bonferroni correction. Both results have the possibility to contain significant combinations that do not have higher-arity effect since motif combinations including a very significant motif may become significant even if there is no synergetic effect. To select the significant combinations caused by higher-arity effect, the combinations whose subsets had smaller p -value than the original one were removed.

Supporting Table S1A. The significant motif combinations in yeast. The yeast gene expression data consist of 173 different stress environments. We computed the combinatorial regulations for each environment. In total 173 experiments were performed. The gene expressions are classified into two groups with three different thresholds: 0.5, 1.0, 1.5 and 2.0. The number of motifs is 102.

Supporting Table S1B. The significant motif combinations in EGF-induced cells. This table contains the significant motif combinations from human breast cancer cells that were induced by EGF. The gene expression profiles were obtained from cells treated with four different doses (0.1, 0.5, 1 and 10 nM) of EGF for seven different time points (5, 10, 15, 30, 45, 60 (except 10 nM) and 90 min). The dataset contains 27 samples. We computed the combinatorial regulations for each sample. A gene was considered up-regulated if its log-fold change expressions, as compared to the control condition, was higher than 0.5, 1.0, 1.5 or 2.0. The number of motifs is 397.

Supporting Table S1C. The significant motif combinations in HRG-induced cells. This table includes all of the statistically significant motif combinations that were induced by HRG. The gene expression profiles were obtained from cells treated with four different doses (0.1, 0.5, 1 and 10 nM) of HRG for seven different time points (5, 10, 15, 30, 45, 60 and 90 min). Thus, this dataset contains 28 samples. We computed the combinatorial regulations for each sample. A gene was considered up-regulated if its log-fold change expressions, as compared to the control condition, was higher than 0.5, 1.0, 1.5 or 2.0. The number of motifs is 397.

The columns in these tables are:

- Sample: Sample name.
- Motif Combination: Significant motif combinations. “-” indicates that no significant result can be found from the sample.
- Arity: Arity of the motif combination
- # of target genes: The number of genes targeted by the motif combination.

- For each threshold:
 - LAMP (m'): The optimized Bonferroni factor used in the LAMP
 - Adjusted p -value: The adjusted p -value used by the LAMP. The red numbers indicate that these are significant (adjusted p -value < 0.05). “-” indicates that the combination cannot be found by this condition. The LAMP does not need to limit the maximum arity.
 - Bonferroni ($\leq S$): p -value adjusted by the Bonferroni correction. The arity limit was varied from 2 to 5. “-” indicates that the combination cannot be found by this condition. For example, if the p -value of a 3-motif combination cannot be found when the arity limit is 2, then the cell is “-”.

redo	MSN2	1	20	-	-	-	-	-	-	0.0076	0.102	>1	>1	>1	-	-	-	-	-	-	-	-	-	-	-					
2.5mM DTT 005 min dtt-1	FHL1	1	81	268	1.96E-12	3.84E-11	1.29E-09	3.24E-08	6.41E-07	358	-	-	-	-	-	490	-	-	-	-	-	-	-	-	644					
2.5mM DTT 015 min dtt-1	-	-	-	258	-	-	-	-	-	492	-	-	-	-	-	492	-	-	-	-	-	-	-	-	492					
2.5mM DTT 030 min dtt-1	YAP7 YAP1 HAP1, YAP1	1 1 2	54 16 2	252	0.0154	0.322	>1	>1	>1	327	0.000306	0.00492	0.166	>1	>1	472	0.000273	0.00304	0.103	>1	>1	-	-	-	472					
2.5mM DTT 045 min dtt-1	HSF1 YAP7 YAP1	1 1 1	67 57 16	274	0.0183	0.351	>1	>1	>1	356	-	-	-	-	-	356	-	-	-	-	-	-	-	-	505					
2.5mM DTT 060 min dtt-1	HSF1 MSN2 STE12 YAP7 YAP1	1 1 1 1 1	59 18 97 58 16	218	3.68E-05	0.000887	0.0299	0.747	>1	354	-	-	-	-	-	354	-	-	-	-	-	-	-	-	487					
2.5mM DTT 090 min dtt-1	STE12	1	104	230	0.0021	0.048	>1	>1	>1	380	0.000453	0.00626	0.211	>1	>1	380	-	-	-	-	-	-	-	-	536					
2.5mM DTT 120 min dtt-1	STE12	1	103	229	0.000562	0.0129	0.434	>1	>1	288	2.32E-05	0.000424	0.0143	0.357	>1	385	-	-	-	-	-	-	-	-	527					
2.5mM DTT 180 min dtt-1	STE12	1	95	216	0.00202	0.0492	>1	>1	>1	280	0.0272	0.51	>1	>1	>1	372	-	-	-	-	-	-	-	-	372					
dtt 000 min dtt	FHL1 SFP1	1 1	85 20	235	1.76E-23	3.94E-22	1.33E-20	3.32E-19	6.58E-18	403	3.06E-31	3.99E-30	1.35E-28	3.37E-27	6.67E-26	553	-	-	-	-	-	-	-	-	553					
dtt 015 min dtt-2	FHL1 SFP1	1 1	86 20	233	5.48E-21	1.24E-19	4.16E-18	1.04E-16	2.06E-15	398	2.59E-07	3.42E-06	0.000115	0.00288	0.0571	549	-	-	-	-	-	-	-	-	-					
dtt 030 min dtt-2	FHL1 YAP1 SFP1	1 1 1	87 17 20	301	2.00E-20	3.50E-19	1.18E-17	2.95E-16	5.84E-15	553	-	-	-	-	-	701	-	-	-	-	-	-	-	-	701					
dtt 060 min dtt-2	CAD1, YAP7 YAP7 YAP1	2 1 1	12 65 17	303	0.000437	0.00762	0.257	>1	>1	553	0.0428	0.406	>1	>1	>1	553	-	-	-	-	-	-	-	-	553					
dtt 120 min dtt-2	STE12 RPN4 TYE7 STE12, DIG1	1 1 1 2	104 63 34 58	236	5.98E-07	1.33E-05	0.000449	0.0112	0.222	401	-	-	-	-	-	548	-	-	-	-	-	-	-	-	694					
dtt 240 min dtt-2	SKN7 HSF1 HAP4 MSN2 RLM1	1 1 1 1 1	73 70 26 21 9	195	0.00177	0.0476	>1	>1	>1	301	-	-	-	-	-	399	-	-	-	-	-	-	-	-	550					
dtt 480 min dtt-2	SWI6 SWI4 TEC1 NRG1 SKN7 SOK2 RLM1	1 1 1 1 1 1 1	88 66 34 54 73 41 9	303	7.06E-11	1.22E-09	4.12E-08	1.03E-06	2.04E-05	398	0.000379	0.00501	0.169	>1	>1	548	-	-	-	-	-	-	-	-	548					
1.5 mM diamide (5 min)	HSF1 YAP7 MSN4 MSN2 YAP1 SKN7, NRG1 STB5 CIN5	1 1 1 1 1 2 1 1	70 64 25 21 17 8 15 52	299	1.17E-20	2.05E-19	6.90E-18	1.73E-16	3.42E-15	399	3.87E-13	5.09E-12	1.72E-10	4.29E-09	8.50E-08	548	0.00503	0.0482	>1	>1	>1	-	-	-	548					
1.5 mM diamide (10 min)	HSF1 YAP7 HAP4 RPN4 MSN4 MSN2 YAP1 STB5	1 1 1 1 1 1 1 1	70 64 27 61 25 21 17 15	195	3.34E-12	9.01E-11	3.03E-09	7.59E-08	1.50E-06	304	3.59E-22	6.21E-21	2.09E-19	5.23E-18	1.04E-16	401	1.11E-12	1.45E-11	4.89E-10	1.22E-08	2.42E-07	0.127	0.000262	0.00343	0.116	>1	>1	0.000239		
1.5 mM diamide (20 min)	HSF1 RPN4 YAP7 MSN4 MSN2 STB5 YAP1 SNT2	1 1 1 1 1 1 1 1	70 61 64 25 21 14 17 18	195	7.60E-12	2.05E-10	6.90E-09	1.73E-07	3.42E-06	304	2.13E-15	3.68E-14	1.24E-12	3.10E-11	6.14E-10	402	6.43E-16	8.41E-15	2.83E-13	7.08E-12	1.40E-10	-	-	-	402	5.89E-10	7.70E-09	2.59E-07	6.49E-06	0.000129
1.5 mM diamide (30 min)	RPN4 YAP7 HSF1 MSN4 MSN2 STB5	1 1 1 1 1 1	62 65 70 25 21 15	195	3.71E-09	1.00E-07	3.37E-06	8.43E-05	0.00167	306	3.40E-11	5.83E-10	1.96E-08	4.91E-07	9.74E-06	402	-	-	-	-	-	-	-	-	402	-	-	-	-	-
1.5 mM diamide (40 min)	HSF1 RPN4 YAP7 MSN4 MSN2 AFI2 STB5	1 1 1 1 1 1 1	70 61 65 25 21 58 15	195	3.27E-10	8.81E-09	2.97E-07	7.42E-06	0.000147	300	2.85E-12	5.00E-11	1.68E-09	4.21E-08	8.34E-07	399	1.03E-09	1.35E-08	4.56E-07	1.14E-05	0.000226	-	-	-	399	0.000274	0.0036	0.121	>1	>1
1.5 mM diamide (50 min)	HSF1 RPN4 YAP7 MSN4 MSN2 STB5	1 1 1 1 1 1	69 61 65 25 21 14	195	5.35E-12	1.44E-10	4.86E-09	1.21E-07	2.41E-06	305	1.34E-10	2.30E-09	7.75E-08	1.94E-06	3.84E-05	402	6.29E-08	8.22E-07	2.77E-05	0.000692	0.0137	-	-	-	402	0.00646	0.0844	>1	>1	>1
1.5 mM diamide (60 min)	HSF1 RPN4	1 1	70 61	194	2.06E-14	5.56E-13	1.87E-11	4.69E-10	9.29E-09	303	9.40E-14	1.63E-12	5.49E-11	1.37E-09	2.72E-08	401	8.52E-09	1.12E-07	3.76E-06	9.40E-05	0.00186	-	-	-	401	2.59E-06	3.39E-05	0.00114	0.0285	0.566

phase 8 h ypd-1	BAS1	1	21	0.0129	0.426	> 1	> 1	> 1	0.000246	0.0052	0.175	> 1	> 1	1.48E-08	2.37E-07	8.00E-06	0.0002	0.00396	7.59E-11	8.42E-10	2.83E-08	7.09E-07	1.41E-05	
	NRG1	1	48	0.0271	0.895	> 1	> 1	> 1																
YPD stationary phase 12 h	HAP4	1	27	142 9.25E-05	0.00342	0.115	> 1	> 1	191 2.90E-08	7.97E-07	2.68E-05	0.000671	0.0133	297 1.53E-10	2.70E-09	9.09E-08	2.27E-06	4.51E-05	297 2.87E-13	5.07E-12	1.71E-10	4.27E-09	8.46E-08	
	MSN2	1	21	0.0152	0.563	> 1	> 1	> 1	0.0357	0.98	> 1	> 1	> 1	0.00868	0.153	> 1	> 1	> 1						
	MSN4	1	25																0.00053	0.00937	0.316	> 1	> 1	
YPD stationary phase 1 d ypd-1	HAP4	1	27	191 3.71E-06	0.000102	0.00344	0.086	> 1	230 2.42E-09	5.54E-08	1.87E-06	4.67E-05	0.000925	299 5.10E-12	8.96E-11	3.02E-09	7.55E-08	1.50E-06	395 4.30E-11	5.72E-10	1.93E-08	4.82E-07	9.56E-06	
	SKN7	1	73	0.000659	0.0181	0.611	> 1	> 1	0.0223	0.509	> 1	> 1	> 1	0.0316	0.555	> 1	> 1	> 1						
	GLN3	1	33	0.018	0.494	> 1	> 1	> 1																
	MSN2	1	21						0.0005	0.0114	0.385	> 1	> 1	0.000333	0.00585	0.197	> 1	> 1	0.0134	0.179	> 1	> 1	> 1	
	UME6	1	93						0.00779	0.178	> 1	> 1	> 1	0.00595	0.105	> 1	> 1	> 1	0.0446	0.593	> 1	> 1	> 1	
	SKO1	1	6						0.0464	> 1	> 1	> 1	> 1											
	MSN4	1	25											0.00232	0.0408	> 1	> 1	> 1	0.0051	0.0678	> 1	> 1	> 1	
	HAP1	1	45																0.0148	0.197	> 1	> 1	> 1	
YPD stationary phase 2 d ypd-1	HAP4	1	27	161 1.62E-06	5.27E-05	0.00178	0.0444	0.88	228 5.55E-08	1.28E-06	4.31E-05	0.00108	0.0214	295 2.91E-06	5.18E-05	0.00175	0.0437	0.885	391 0.0242	0.325	> 1	> 1	> 1	
	SKN7	1	72	0.00106	0.0345	> 1	> 1	> 1	0.000988	0.0228	0.767	> 1	> 1											
	HSF1	1	70	0.0108	0.354	> 1	> 1	> 1	0.000142	0.00328	0.111	> 1	> 1						0.0311	0.418	> 1	> 1	> 1	
	SOK2	1	41	0.0211	0.688	> 1	> 1	> 1																
	MSN4	1	25						0.00553	0.127	> 1	> 1	> 1	0.00741	0.132	> 1	> 1	> 1	0.013	0.174	> 1	> 1	> 1	
	MSN2	1	21						0.0219	0.504	> 1	> 1	> 1	0.00989	0.176	> 1	> 1	> 1	0.00295	0.0397	> 1	> 1	> 1	
	SUT1	1	15						0.0243	0.559	> 1	> 1	> 1											
	UME6	1	91																0.0375	0.504	> 1	> 1	> 1	
YPD stationary phase 3 d ypd-1	HAP4	1	27	164 0.000163	0.00522	0.176	> 1	> 1	226 6.30E-06	0.000147	0.00494	0.123	> 1	295 1.88E-06	3.35E-05	0.00113	0.0282	0.56	295					
	MSN2	1	21	0.000703	0.0225	0.759	> 1	> 1												0.00757	0.135	> 1	> 1	> 1
	HSF1	1	70	0.0102	0.327	> 1	> 1	> 1	5.46E-05	0.00127	0.0428	> 1	> 1	0.00103	0.0184	0.618	> 1	> 1	0.0079	0.141	> 1	> 1	> 1	
	SUT1	1	15	0.0255	0.818	> 1	> 1	> 1	0.00907	0.211	> 1	> 1	> 1											
	SOK2	1	40	0.0303	0.971	> 1	> 1	> 1	0.0145	0.336	> 1	> 1	> 1	0.0306	0.545	> 1	> 1	> 1						
	SKN7	1	72						0.0371	0.861	> 1	> 1	> 1											
	MSN4	1	24											0.0177	0.316	> 1	> 1	> 1	0.0027	0.0481	> 1	> 1	> 1	
YPD stationary phase 5 d ypd-1	GAL4	1	13	163 0.00148	0.0476	> 1	> 1	> 1	183 0.0251	0.72	> 1	> 1	> 1	293										
	HAP4	1	27	0.0308	0.994	> 1	> 1	> 1	2.25E-05	0.000645	0.0217	0.544	> 1	0.0293	0.525	> 1	> 1	> 1	0.0102	0.182	> 1	> 1	> 1	
	SUT1	1	15						0.0168	0.481	> 1	> 1	> 1	0.0267	0.479	> 1	> 1	> 1	0.00611	0.11	> 1	> 1	> 1	
	HAP3	1	13	0.00148	0.0476	> 1	> 1	> 1	0.0251	0.72	> 1	> 1	> 1											
	UME6	1	92											0.0225	0.404	> 1	> 1	> 1	0.025	0.449	> 1	> 1	> 1	
	PHD1	1	33																0.00953	0.171	> 1	> 1	> 1	
YPD stationary phase 7 d ypd-1	GAL4	1	14	163 0.00039	0.0126	0.424	> 1	> 1	231					290										
	SOK2	1	40	0.00153	0.0494	> 1	> 1	> 1																
	HAP4	1	26	0.0109	0.352	> 1	> 1	> 1	0.00192	0.0436	> 1	> 1	> 1											
	PHD1	1	32						0.0106	0.242	> 1	> 1	> 1	0.0078	0.141	> 1	> 1	> 1						
	UME6	1	93																					
YPD stationary	UME6	1	80	173					204 0.0373	0.96	> 1	> 1	> 1	254 0.00196	0.0405	> 1	> 1	> 1	345 0.0119	0.182	> 1	> 1	> 1	
	SOK2	1	35																	0.0341	0.519	> 1	> 1	> 1
YPD stationary phase 22 d	YAP7	1	62	164 0.00361	0.116	> 1	> 1	> 1	229 0.0467	> 1	> 1	> 1	> 1	297										
	MSN4	1	24	0.0271	0.868	> 1	> 1	> 1																
	UME6	1	92	0.0467	> 1	> 1	> 1	> 1	0.0029	0.0665	> 1	> 1	> 1	0.00242	0.0429	> 1	> 1	> 1	0.00303	0.0536	> 1	> 1	> 1	
YPD stationary phase 28 d	YAP7	1	62	162 0.018	0.583	> 1	> 1	> 1	228 0.00511	0.118	> 1	> 1	> 1	292										
	UME6	1	90						0.000638	0.0147	0.495	> 1	> 1	0.000867	0.0156	0.525	> 1	> 1	0.000673	0.0121	0.408	> 1	> 1	
	SUT1	1	15																0.0313	0.562	> 1	> 1	> 1	
DBY7286 37degree heat - 20 min	HSF1	1	68	234 1.02E-13	2.28E-12	7.69E-11	1.92E-09	3.81E-08	303 2.39E-18	4.15E-17	1.40E-15	3.49E-14	6.93E-13	401 1.01E-15	1.32E-14	4.44E-13	1.11E-11	2.20E-10	401 6.63E-13	8.68E-12	2.92E-10	7.31E-09	1.45E-07	
	RPN4	1	64	9.53E-10	2.14E-08	7.21E-07	1.80E-05	0.000357	0.000183	0.00317	0.107	> 1	> 1											
	MSN2	1	21	4.12E-06	9.24E-05	0.00311	0.0779	> 1	1.73E-06	3.00E-05	0.00101	0.0253	0.5	0.00691	0.0906	> 1	> 1	> 1						
	MSN4	1	24	0.000514	0.0115	0.389	> 1	> 1												0.0099	0.13	> 1	> 1	> 1
	NRG1	1	57	0.019	0.426	> 1	> 1	> 1																
	UME6	1	93	0.0316	0.71	> 1	> 1	> 1																
DBYmsn2-4 37degree heat - 20 min	HSF1	1	70	233 2.22E-14	5.00E-13	1.68E-11	4.21E-10	8.35E-09	398 6.38E-25	8.43E-24	2.84E-22	7.10E-21	1.41E-19	398 6.52E-25	8.60E-24	2.90E-22	7.25E-21	1.44E-19	548 2.98E-23	2.86E-22	9.62E-21	2.41E-19	4.77E-18	
	RPN4	1	63	7.63E-14	1.72E-12	5.80E-11	1.45E-09	2.87E-08	1.93E-09	2.55E-08	8.59E-07	2.15E-05	0.000426											
	MOT3	1	13						0.00289	0.0382	> 1	> 1	> 1	6.31E-06	8.33E-05	0.00281	0.0702	> 1						
	RLM1	1	9						0.00572	0.0755	> 1	> 1	> 1											
	AFT2_GCN4	2	3						0.0299	0.395	> 1	> 1	> 1											
	UME6	1	94											0.0305	0.402	> 1	> 1	> 1						
DBYmsn2/4 (real strain) + 37degrees	RPN4	1	64	240 1.33E-11	2.91E-10	9.80E-09	2.45E-07	4.86E-06	405 2.61E-05	0.000338	0.0114	0.285	> 1	556										
	HSF1	1	70	1.49E-08	3.26E-07	1.10E-05	0.000275	0.00545	1.29E-13	1.67E-12	5.64E-11	1.41E-09	2.79E-08	4.57E-12	4.32E-11	1.46E-09	3.64E-08	7.21E-07	5.56	1.11E-07	1.05E-06	3.54E-05	0.000885	0.0175
	CBF1_PHO2	2	4																	0.0213	0.202	> 1	> 1	> 1
DBYyap1 37degree heat - 20 min (redo)	HSF1	1	69	234 2.02E-13	4.53E-12	1.53E-10	3.82E-09	7.57E-08	401 1.08E-17	1.41E-16	4.75E-15	1.19E-13	2.35E-12	401 5.48E-15	7.18E-14	2.42E-12	6.05E-11	1.20E-09	401 1.21E-12	1.59E-11	5.34E-10	1.34E-08	2.65E-07	
	RPN4	1	64	7.39E-08	1.66E-06	5.59E-05	0.0014	0.0277																
	MSN2	1	21	2.01E-06	4.51E-05	0.00152	0.038	0.753	4.16E-07	5.45E-06	0.000183	0.00459	0.091	0.000248	0.00325	0.11	> 1	> 1	0.00544	0.0713	> 1	> 1		

B. EGF (human breast cancer cell)

Condition	Motif Combination	Arity	# of target genes	Adjusted p-value (exp > 0.5)					Adjusted p-value (exp > 1.0)					Adjusted p-value (exp > 1.5)					Adjusted p-value (exp > 2.0)								
				LAMP		Bonferroni			LAMP		Bonferroni			LAMP		Bonferroni			LAMP		Bonferroni						
				m'	Arity limit 2	3	4	5	m'	Arity limit 2	3	4	5	m'	Arity limit 2	3	4	5	m'	Arity limit 2	3	4	5				
m=79,003 10,428,793 1,029,883,108 8.12E+10					m=79,003 10,428,793 1,029,883,108 8.12E+10					m=79,003 10,428,793 1,029,883,108 8.12E+10					m=79,003 10,428,793 1,029,883,108 8.12E+10												
0.1nM 5min	TATA	1	957	1459869	0.00389	2.10E-04	0.0278	>1	>1	3750336	0.000511	1.08E-05	0.00142	0.14	>1	5238103	2.26E-06	3.41E-08	4.51E-06	0.000445	0.0351	7247034	0.000123	1.34E-06	0.000176	0.0174	>1
	MEIS1, LMO2, COM, AR	3	14		0.03	-	0.214	>1	>1		-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-
	GATA6	1	160		0.49	0.0265	>1	>1	>1		-	-	-	-	-		0.0237	0.000357	0.0472	>1	>1		-	-	-	-	-
	CTGYNNCTYTAA, TGACATY	2	12		-	-	-	-	-	1.03	0.0217	>1	>1	>1			-	-	-	-	-		-	-	-	-	-
	MEF2, AACTTT	2	198		-	-	-	-	-	-	-	-	-	-		1.59	0.024	>1	>1	>1		-	-	-	-	-	-
	RSRFC4, IK1	2	26		-	-	-	-	-	-	-	-	-	-		1.77	0.0266	>1	>1	>1		0.376	0.0041	0.541	>1	>1	
0.1nM 10min	TATA	1	957	1459869	-	-	-	-	-	3750336	-	-	-	-	-	5238103	0.175	0.00264	0.349	>1	>1	7247034	-	-	-	-	-
0.1nM 15min	TATA	1	957	1459869	-	-	-	-	-	3750336	1.1	0.0232	>1	>1	>1	5238103	-	-	-	-	-	7247034	-	-	-	-	-
0.1nM 30min	CTGCAGY, LEF1, VDR, MAZ	4	28	1459869	0.0177	-	-	>1	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-
	TATA	1	957		0.877	0.0475	>1	>1	>1		0.000437	9.21E-06	0.00122	0.12	>1		0.0041	6.19E-05	0.00816	0.806	>1		0.284	0.00309	0.409	>1	>1
	AACTTT, CART1	2	71		-	-	-	-	-		0.000791	1.67E-05	0.0022	0.217	>1		0.326	0.00492	0.649	>1	>1		-	-	-	-	-
	CP2, CTGCAGY, LEF1, MAZ, STAT5A	5	9		-	-	-	-	-		0.00157	-	-	>1			-	-	-	-	-		-	-	-	-	-
	CP2, CTGCAGY, LEF1, MAZ, AACTTT	5	18		-	-	-	-	-		0.0127	-	-	>1			-	-	-	-	-		-	-	-	-	-
	CP2, CTGCAGY, AACTTT, LEF1, CTTTAAAR	5	10		-	-	-	-	-		0.0144	-	-	>1			-	-	-	-	-		-	-	-	-	-
	OCT, NFAT	2	115		-	-	-	-	-		0.0804	0.00169	0.223	>1	>1		-	-	-	-	-		-	-	-	-	-
	AAAYRNCTG, CART1	2	18		-	-	-	-	-		-	-	-	-	-		1	0.0151	>1	>1	>1		-	-	-	-	-
	AAAYRNCTG, NKX61	2	19		-	-	-	-	-		-	-	-	-	-		1.81	0.0272	>1	>1	>1		-	-	-	-	-
	MEF2, GATA6	2	38		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-		3.13	0.0341	>1	>1	>1
0.1nM 45min	-	-	-	1969633	-	-	-	-	-	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-
0.1nM 60min	NFAT, AACTTT	2	425	1969633	0.423	0.017	>1	>1	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-
	TATA	1	957		0.619	0.0248	>1	>1	>1		0.395	0.00832	>1	>1	>1		0.109	0.00165	0.218	>1	>1		-	-	-	-	-
0.1nM 90min	SRF, FREAC3	2	16	1969633	0.954	0.0383	>1	>1	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-
0.5nM 5min	AACTTT, CART1	2	71	1459869	-	-	-	-	-	3750336	0.421	0.00887	>1	>1	>1	5238103	-	-	-	-	-	7247034	-	-	-	-	-
	E12, AACTTT	2	401		-	-	-	-	-		1.7	0.0358	>1	>1	>1		-	-	-	-	-		-	-	-	-	-
	TATA	1	957		-	-	-	-	-		-	-	-	-	-		0.0603	0.000909	0.12	>1	>1		0.348	0.00379	0.501	>1	>1
	CTGCAGY, OCT1, PAX4, MSX1, AACTTT	5	6		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-		0.0398	-	-	-	>1
0.5nM 10min	NFAT, AACTTT	2	425	1459869	0.409	0.0221	>1	>1	>1	3750336	0.0802	0.00169	0.223	>1	>1	5238103	-	-	-	-	-	7247034	-	-	-	-	-
	TATA	1	957		-	-	-	-	-		0.00066	1.39E-05	0.00184	0.181	>1		0.0595	0.000898	0.119	>1	>1		1.83	0.02	>1	>1	>1
	WWTAAAGGC, NF1	2	27		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-		0.125	0.00136	0.18	>1	>1
0.5nM 15min	TATA	1	957	1969633	0.194	0.00776	>1	>1	>1	3750336	0.00139	2.93E-05	0.00387	0.382	>1	5238103	0.00112	1.69E-05	0.00224	0.221	>1	7247034	0.134	0.00146	0.192	>1	>1
	GATA6, CREB, GR, EVI1, CTTTAAAR, LEF1, OCT1, NFAT, FOXO4, CEBP	8	8		-	-	-	-	-		0.0137	-	-	-	-		-	-	-	-	-		-	-	-	-	-
	GATA6, FOXO4	2	63		-	-	-	-	-		0.904	0.019	>1	>1	>1		-	-	-	-	-		-	-	-	-	-
	MEF2, E12, TGACATY, OCT1, AP1	5	13		-	-	-	-	-		-	-	-	-	-		0.0198	-	-	-	>1		-	-	-	-	-
	GATA6, PIT1	2	11		-	-	-	-	-		-	-	-	-	-		2.84	0.0428	>1	>1	>1		-	-	-	-	-
0.5nM 30min	NFAT, AACTTT	2	425	1459869	0.042	0.00227	0.3	>1	>1	2700718	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-
	TATA	1	957		0.155	0.00838	>1	>1	>1		0.00211	6.18E-05	0.00816	0.805	>1		-	-	-	-	-		-	-	-	-	-
	NFAT, AREB6	2	288		0.156	0.00847	>1	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-
	E12	1	1491		0.65	0.0352	>1	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-
0.5nM 45min	FOXO4, SRF	2	100	1969633	0.000403	1.62E-05	0.00213	0.211	>1	3750336	0.0223	0.00047	0.062	>1	>1	5238103	-	-	-	-	-	7247034	-	-	-	-	-
	YY1, SRF, AACTTT	3	23		0.00534	-	0.0283	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-
	HFH8, E4F1, CREB	3	11		0.00646	-	0.0342	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-
	SRF, HNF3	2	54		0.0455	0.00183	0.241	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-
	SRF, FREAC2	2	65		0.08	0.00321	0.424	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-
	NFAT, AACTTT	2	425		0.278	0.0112	>1	>1	>1		0.00138	2.90E-05	0.00383	0.378	>1		-	-	-	-	-		-	-	-	-	-
	SRF, ATF, AACTTT	3	16		-	-	-	-	-		0.00113	-	0.00314	0.31	>1		-	-	-	-	-		-	-	-	-	-
	YY1, SRF, NFKB, AACTTT	4	9		-	-	-	-	-		0.00127	-	-	0.348	>1		-	-	-	-	-		-	-	-	-	-
	TATA	1	957		0.00405	8.53E-05	0.0113	>1	>1		0.00405	8.53E-05	0.0113	>1	>1		0.000145	2.19E-06	0.000289	0.0286	>1		-	-	-	-	-
	GATA6	1	160		0.0504	0.00106	0.14	>1	>1		0.0504	0.00106	0.14	>1	>1		-	-	-	-	-		-	-	-	-	-
	NFAT, CART1	2	62		0.744	0.0157	>1	>1	>1		0.744	0.0157	>1	>1	>1		-	-	-	-	-		-	-	-	-	-
	NF1, E2F	2	57		-	-	-	-	-		0.836	0.0176	>1	>1	>1		-	-	-	-	-		-	-	-	-	-
0.5nM 60min	CTGCAGY, LEF1, CREB, AREB6, AACTTT	5	15	1969633	0.000776	-	-	-	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-
	LEF1, E12, CREB, AACTTT	4	35		0.008	-	-	>1	>1		-	-	-	-	-		-	-	-	-	-						

0.5nM 90min	LEF1, CTGCAGY, TATA, VDR, MAZ	5	9	1969633	-	-	-	-	-	3750336	0.0457	-	-	-	-	>1	5238103	-	-	-	-	-	7247034	-	-	-	-	-	-
	MYC, TATA, CREB, CREBP1, FOXO4	5	7		-	-	-	-	-		-	-	-	-	-	-	-	0.00345	-	-	-	-	>1	-	-	-	-	-	-
	E12, AACCTT, LEF1, TATA, OCT1, NFAT, CREB	7	8		-	-	-	-	-		-	-	-	-	-	-	-	0.0264	-	-	-	-	-	-	-	-	-	-	-
1.0nM 5min	TATA	1	957	1459869	-	-	-	-	-	3750336	0.0181	0.00038	0.0502	>1	>1	5238103	0.000195	2.94E-06	0.000388	0.0384	>1	7247034	0.026	0.000283	0.0374	>1	>1		
	AACCTT, CART1	2	71		-	-	-	-	-		-	-	-	-	-		0.102	0.00154	0.204	>1	>1		0.323	0.00352	0.465	>1	>1		
	NFAT, CART1	2	62		-	-	-	-	-		-	-	-	-	-		2.33	0.0351	>1	>1	>1		-	-	-	-	-	-	
1.0nM 10min	YY1, LEF1, NF1, NFAT	4	26	1459869	0.015	-	-	>1	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-	-	
	CRX, AACCTT	2	69		0.0268	0.00145	0.192	>1	>1		0.216	0.00455	0.601	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	E12, AACCTT	2	401		0.0577	0.00312	0.412	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	NFAT, AACCTT	2	425		0.0613	0.00332	0.438	>1	>1		2.01	0.0424	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	AREB6, AACCTT	2	274		0.483	0.0262	>1	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	TATA	1	957		-	-	-	-	-		0.411	0.00865	>1	>1	>1		0.0522	0.000787	0.104	>1	>1		-	-	-	-	-	-	
	AACCTT, CART1	2	71		-	-	-	-	-		1.77	0.0373	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	FOXO4, TAAYNRNNTCC	2	44		-	-	-	-	-		-	-	-	-	-		1.7	0.0257	>1	>1	>1		-	-	-	-	-	-	
	1.0nM 15min	NFAT, AACCTT	2	425	1459869	0.00601	0.000325	0.0429	>1	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-	-
TATA	1	957		0.282	0.0153	>1	>1	>1		0.0149	0.000313	0.0413	>1	>1		0.0245	0.00037	0.0488	>1	>1		0.101	0.0011	0.145	>1	>1			
FOXO3, HNF3	2	51		0.595	0.0322	>1	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-		
HFH8, GATA6, CTGYNNCTYTAA, AACCTT	2	10		-	-	-	-	-		-	-	-	-	-		2.25	0.0339	>1	>1	>1		-	-	-	-	-	-		
2	19		-	-	-	-	-	-		-	-	-	-	-		-	-	-	-	-		3.67	0.04	>1	>1	>1			
1.0nM 30min	NFAT, AREB6, AACCTT	3	138	1459869	0.0206	-	0.147	>1	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-	-	
	TATA	1	957		0.0757	0.00409	0.54	>1	>1		0.0319	0.000672	0.0887	>1	>1		0.00233	3.52E-05	0.00465	0.459	>1		-	-	-	-	-	-	
	ATF6, CTTTAAR	2	16		0.217	0.0117	>1	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	ATF6, SP1	2	40		0.723	0.0391	>1	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	LEF1, CDPCR3HD, OCT1, MSX1, AACCTT	5	8		-	-	-	-	-		0.0401	-	-	-	>1		-	-	-	-	-		0.0087	-	-	-	-	>1	
	YNGTINNNATT, AACCTT	2	100		-	-	-	-	-		0.383	0.00807	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	NFAT, AACCTT	2	425		-	-	-	-	-		0.411	0.00867	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	OCT, NFAT	2	115		-	-	-	-	-		0.873	0.0184	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	LEF1, NFAT	2	497		-	-	-	-	-		1.35	0.0285	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
SREBP1, MSX1	2	27		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-		4.29	0.0468	>1	>1	>1			
1.0nM 45min	HFH4, NFAT, E4F1, AACCTT	4	11	1459869	0.0173	-	-	>1	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-	-	
	CTGCAGY, LEF1, AREB6, AACCTT	4	51		0.0175	-	-	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	YY1, NF1, NFAT, AACCTT	4	23		0.0251	-	-	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	TATA, OCT1, CREB, NFAT, AACCTT	5	15		0.0445	-	-	-	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	YY1, CHX10, NFAT, AACCTT	4	17		0.045	-	-	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	SRF, HNF3	2	54		0.0918	0.00497	0.656	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
	AACCTT, CART1	2	71		0.708	0.0383	>1	>1	>1		0.00375	7.89E-05	0.0104	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	MEIS1, LEF1, NFAT, NKX62	4	23		-	-	-	-	-		0.00895	-	-	-	>1	>1		-	-	-	-		-	-	-	-	-	-	
	TATA, OCT1, NFAT, AACCTT	4	74		-	-	-	-	-		0.0105	-	-	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	MEIS1, NFAT, AACCTT	3	97		-	-	-	-	-		0.0209	-	0.0581	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	NFAT, CART1	2	62		-	-	-	-	-		0.0259	0.000545	0.0719	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	IRF7, PPAR	2	8		-	-	-	-	-		0.0307	0.000647	0.0854	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	MEF2, CIZ	2	32		-	-	-	-	-		0.28	0.00591	0.78	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	IK3, AACCTT	2	57		-	-	-	-	-		0.726	0.0153	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	HFH4, CREB	2	23		-	-	-	-	-		1.32	0.0278	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	AACCTT, PPAR	2	55		-	-	-	-	-		1.94	0.0408	>1	>1	>1		-	-	-	-	-		-	-	-	-	-	-	
	TATA	1	957		-	-	-	-	-		-	-	-	-	-		0.0791	0.00119	0.157	>1	>1		-	-	-	-	-	-	
	NFAT, AACCTT, LEF1, CHX10, LHX3, STAT5A, STAT5B	7	6		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-		0.0184	-	-	-	-	-	
	1.0nM 60min	MAZ, E12, CREB, ATF4	4	15	1969633	0.0007	-	-	0.366	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	-	-
		CTGCAGY, LEF1, PAX4, AREB6, AACCTT	5	29		0.0304	-	-	-	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-
MEIS1, NFAT, FREAC2		3	64		0.0312	-	0.165	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
NFAT, STAT5A, AACCTT		3	106		0.0486	-	0.257	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
LEF1, NFAT		2	497		1.13	0.0453	>1	>1	>1		-	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
LEF1, TATA, NFAT, NFKB, AACCTT		5	20		-	-	-	-	-		0.00725	-	-	-	>1		-	-	-	-	-		-	-	-	-	-	-	
EVH1, MEF2, LEF1, TATA, SREBP1, NFAT, FOXO4		7	10		-	-	-	-	-		0.0207	-	-	-	-		-	-	-	-	-		-	-	-	-	-	-	
PTF1BETA, LEF1, NFAT, CREB, AACCTT		5	8		-	-	-	-	-		0.024	-	-	-	>1		-	-	-	-	-		-	-	-	-	-	-	
MEF2, LEF1, POU6F1, FOXO4, AR		5	8		-	-	-	-	-		0.024	-	-	-	>1		-	-	-	-	-		-	-	-	-	-	-	

0min	NFAT, AACTTT	2	425	6.54E-05	3.54E-06	0.000467	0.0461	>1		0.593	0.0173	>1	>1	>1													
	OCT, OCT1, NFAT	3	90	0.00161	-	0.0115	>1	>1		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	E12, AACTTT	2	401	0.00311	0.000168	0.0222	>1	>1		0.17	0.00498	0.657	>1	>1													
	E12, OCT, LEF1, OCT1	4	44	0.0113	-	-	>1	>1		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	E12, FOXO4, SOX5	3	45	0.0226	-	0.162	>1	>1		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	ETS2, FOXO4	2	208	0.276	0.015	-	>1	>1		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	SRF, SRF	2	29	0.442	0.0239	>1	>1	>1		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	TFIIA	1	180	0.662	0.0358	>1	>1	>1		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	FOXO4, PITX2	2	160	0.83	0.0449	>1	>1	>1		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	NFAT, CART1	2	62	-	-	-	-	-		0.121	0.00355	0.468	>1	>1													
	AACTTT, CART1	2	71	-	-	-	-	-		0.561	0.0164	>1	>1	>1													
	OCT1, MEIS1, LEF1, E12, NFAT, AP1	6	17	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	FOXO4, CTCTAAR, MEIS1, E12, RSRFC4, NFAT	6	11	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-				
																								0.0102			
																								0.0394			
	10.0nM 45min	TATA	1	957	2700718	3.96E-05	1.16E-06	0.000153	0.0151	>1	3750336	2.37E-08	5.00E-10	6.60E-08	6.52E-06	0.000514	5238103	0.00023	3.47E-06	0.000458	0.0452	>1	7247034	0.0497	0.000542	0.0716	>1
	MAZ, AACTTT, CREB, CREBP1, AREB6	5	12		0.0126	-	-	-	>1																		
	ATF1, MAZ, AACTTT	3	24		0.0158	-	0.0611	>1	>1																		
	HNF3ALPHA, OCT	2	24		1.63	0.0476	>1	>1	>1																		
	PAX3, CREBP1	2	30		-	-	-	-	-	0.751	0.0158	>1	>1	>1													
	OCT, NFAT	2	115		-	-	-	-	-	1.33	0.028	>1	>1	>1													
	CREB, FOXO4, HFH3, CREBP1	4	8		-	-	-	-	-	-	-	-	-	-		0.0451	-	-	-	>1	>1						
	CREBP1, AACTTT	2	96		-	-	-	-	-	-	-	-	-	-		0.57	0.0086	>1	>1	>1							
	FOXO4, TAAYNRRNTCC	2	44		-	-	-	-	-	-	-	-	-	-		1.35	0.0204	>1	>1	>1							
	ATF, CREBP1	2	105		-	-	-	-	-	-	-	-	-	-		2.65	0.04	>1	>1	>1							
10.0nM 90min	CREB, FOXO4, E4F1, CREBP1	4	39	1969633	0.00995	-	-	>1	>1	3750336	-	-	-	-	-	5238103	-	-	-	-	-	7247034	-	-	-	-	
	NFAT, AACTTT	2	425		0.022	0.000883	0.117	>1	>1		0.349	0.00736	0.971	>1	>1												
	AACTTT, CART1	2	71		0.311	0.0125	>1	>1	>1		1.01	0.0212	>1	>1	>1												
	NF1	1	596		0.948	0.038	>1	>1	>1		-	-	-	-	-												
	CTGCAGY, LEF1, CREB, AREB6, AACTTT	5	15		-	-	-	-	-		0.0165	-	-	-	>1												
	TATA	1	957		-	-	-	-	-		0.0627	0.00132	0.174	>1	>1		0.783	0.0118	>1	>1	>1		0.863	0.00941	>1	>1	
	HFH4, CREB	2	23		-	-	-	-	-		0.813	0.0171	>1	>1	>1		-	-	-	-	-		-	-	-		
	NFAT, CART1	2	62		-	-	-	-	-		1.69	0.0356	>1	>1	>1		-	-	-	-	-		-	-	-		
	AACTTT, LEF1, FREAC2, CTGCAGY, CREB, MAZ	6	10		-	-	-	-	-		-	-	-	-	-		0.0308	-	-	-	-		-	-	-		

C. HRG (human breast cancer cell)

condition	Motif Combination	Arity	# of target genes	Adjusted p-value (exp > 0.5)						Adjusted p-value (exp > 1.0)						Adjusted p-value (exp > 1.5)						Adjusted p-value (exp > 2.0)					
				LAMP			Bonferroni			LAMP			Bonferroni			LAMP			Bonferroni			LAMP			Bonferroni		
				m'	Arity limit 2	3	4	5	m'	Arity limit 2	3	4	5	m'	Arity limit 2	3	4	5	m'	Arity limit 2	3	4	5	m'	Arity limit 2	3	4
0.1nM 5min	-	-	-	1174108	-	-	-	-	-	-	2874627	-	-	-	-	-	5542428	-	-	-	-	-	7635557	-	-	-	-
0.1nM 10min	<i>MAZ, E12, SP1</i> <i>E12, YATTNATC</i> <i>ERR1, AP4</i>	3 2 2	227 83 162	552135	0.00197	0.0372	>1	>1	>1	2099869	-	-	-	-	-	-	3982295	-	0.262	0.00519	0.686	>1	>1	-	-	-	-
0.1nM 15min	<i>MAZ</i> <i>MAZ, E12</i> <i>MAZ, AP4</i> <i>ZIC1, E47</i> <i>AP4</i> <i>LEF1, CTGCAGY, E12, PAX4, MAZ</i> <i>OP2, CTGCAGY, E12</i> <i>E12, MAZ, NFAT, FOXO4</i>	1 2 2 2 1 5 3 4	1474 478 388 19 1016 38 28 87	552135	0.111	0.0159	>1	>1	>1	1557482	-	-	-	-	-	-	3982295	-	2.17	0.043	>1	>1	>1	-	-	-	-
0.1nM 30min	<i>MAZ, E12</i> <i>ELK1, MYOD, ATF</i>	2 3	478 11	699536	0.108	0.0122	>1	>1	>1	2099869	0.00328	0.000123	0.0163	>1	>1	3982295	-	-	-	-	-	-	-	-	-	-	-
0.1nM 45min	<i>SP1</i> <i>MAZ, E12</i> <i>SRF, PAX3</i>	1 2 2	1915 478 12	699536	0.0193	0.00218	0.288	>1	>1	2099869	-	-	-	-	-	-	3982295	-	-	-	-	-	-	-	-	-	-
0.1nM 60min	<i>MAZ, E12</i> <i>PAX4</i> <i>ELK1, MYOD, ATF</i> <i>MAZ</i> <i>E12, PAX4</i> <i>AP4</i> <i>RFX1</i> <i>TATA, NFKB</i>	2 1 3 1 2 1 1 2	478 1182 11 1474 428 1016 296 75	552135	0.00616	0.000882	0.116	>1	>1	1557482	-	-	-	-	-	-	3982295	0.00692	0.000137	0.0181	>1	>1	-	-	-	-	-
0.1nM 90min	<i>E12, PAX4</i> <i>MAZ</i> <i>ZIC1, E47</i>	2 1 2	428 1474 19	552135	0.0224	0.0032	0.422	>1	>1	1557482	-	-	-	-	-	-	3982295	0.242	0.00481	0.635	>1	>1	-	-	-	-	-
0.5nM 5min	<i>MAZ</i> <i>AP4</i>	1 1	1474 1016	699536	0.0432	0.00488	0.644	>1	>1	2099869	-	-	-	-	-	-	3982295	-	-	-	-	-	-	-	-	-	-
0.5nM 10min	<i>MAZ</i> <i>SP1</i> <i>MAZ, E12</i>	1 1 2	1474 1915 478	552135	0.0425	0.00608	0.802	>1	>1	1557482	-	-	-	-	-	-	3982295	-	-	-	-	-	-	-	-	-	-
0.5nM 15min	-	-	-	552135	-	-	-	-	-	2099869	-	-	-	-	-	-	3982295	-	-	-	-	-	-	-	-	-	-
0.5nM 30min	<i>MAZ</i> <i>ELK1, MYOD, ATF</i> <i>OCT, USF, OCT1, NFKB, AACTTT</i> <i>SRF, PAX3</i>	1 3 5 2	1474 11 8 12	699536	0.000982	0.000111	0.0146	>1	>1	2099869	0.000921	3.47E-05	0.00457	0.452	>1	3982295	-	-	-	-	-	-	-	-	-	-	-
0.5nM 45min	<i>PAX4</i> <i>MAZ</i> <i>ETS2</i> <i>SP1</i> <i>AP4</i> <i>SRF, PAX3</i>	1 1 1 1 1 2	1182 1474 757 1915 1016 12	699536	0.00359	0.000406	0.0536	>1	>1	2099869	-	-	-	-	-	-	3982295	-	-	-	-	-	-	-	-	-	-
0.5nM 60min	<i>SP1</i> <i>MAZ</i> <i>SRF, PAX3</i>	1 1 2	1915 1474 12	699536	0.00278	0.000314	0.0414	>1	>1	2099869	-	-	-	-	-	-	3982295	-	-	-	-	-	-	-	-	-	-
0.5nM 90min	<i>E12</i> <i>MAZ, E12</i> <i>E12, PAX4</i> <i>MAZ, MYOD</i> <i>MAZ, AP4</i> <i>TATA</i>	1 2 2 2 2 1	1512 478 428 303 388 968	552135	3.17E-05	4.54E-06	0.000599	0.0592	>1	1557482	-	-	-	-	-	-	3982295	-	-	-	-	-	-	-	-	-	-
1.0nM 5min	<i>MAZ, E12</i>	2	478	442874	0.00753	0.00134	0.177	>1	>1	1557482	-	-	-	-	-	-	2874627	-	-	-	-	-	-	-	-	-	-
1.0nM 10min	-	-	-	442874	-	-	-	-	-	1557482	-	-	-	-	-	-	2874627	-	-	-	-	-	-	-	-	-	-
1.0nM 15min	<i>ZIC1, E47</i> <i>MAZ</i> <i>E12, MYOD, E47</i> <i>E12, AP4</i> <i>MAZ, AP4</i> <i>ETS2, E12</i> <i>MAZ, SRF, T3R</i> <i>YATTNATC, YCATTTAA</i> <i>TATA, NFAT, YATTNATC, AACTTT</i> <i>NFAT, YATTNATC, YCATTTAA</i> <i>OCT, TATA</i>	2 1 3 2 2 2 3 2 4 3 2	19 1474 136 362 388 232 11 55 26 26 91	359149	0.00486	0.00107	0.141	>1	>1	1174108	-	-	-	-	-	-	2874627	-	-	-	-	-	-	-	-	-	-
1.0nM 30min	<i>MAZ, E12</i>	2	478	442874	0.00187	0.000333	0.0439	>1	>1	1557482	0.000854	4.33E-05	0.00572	0.565	>1	2874627	0.704	0.0193	>1	>1	>1	-	-	-	-	-	

