Supplemental Table 3
Common targets of CUX1 and E2F1 with functions related to cell cycle, DNA repair and DNA replication according to EASE.

Symbol	Gene name	Functions
CALM2	calmodulin 2 (phosphorylase kinase, delta)	Cell Cycle
CCNA2	cyclin A2	Cell Cycle
CDC25A	cell division cycle 25A	Cell Cycle
MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast)	Cell Cycle
MCM3	MCM3 minichromosome maintenance deficient 3	Cell Cycle, DNA Replication
MCM7	MCM7 minichromosome maintenance deficient 7	Cell Cycle, DNA Replication
MLH1	mutL homolog 1, colon cancer, nonpolyposis type 2	Cell Cycle, DNA Repair, DNA Replication
NUMA1	nuclear mitotic apparatus protein 1	Cell Cycle
ORC1L	origin recognition complex, subunit 1-like	Cell Cycle, DNA Replication
PMS1	PMS1 postmeiotic segregation increased 1	Cell Cycle, DNA Repair, DNA Replication
PMS2L5	postmeiotic segregation increased 2-like 5	Cell Cycle, DNA Repair, DNA Replication
POLA	polymerase (DNA directed), alpha	Cell Cycle, DNA Replication
RAD51	RAD51 homolog (RecA homolog, E. coli)	Cell Cycle, DNA Repair
RPA3	replication protein A3, 14kDa	Cell Cycle, DNA Repair, DNA Replication
TP53	tumor protein p53 (Li-Fraumeni syndrome)	Cell Cycle, DNA Repair
DLEU2	deleted in lymphocytic leukemia, 2	Cell Cycle
PRC1	protein regulator of cytokinesis 1	Cell Cycle
SMC4L1	SMC4 structural maintenance of chromosomes 4-like 1	Cell Cycle
DLEU1	deleted in lymphocytic leukemia, 1	Cell Cycle
POLD3	polymerase (DNA-directed), delta 3, accessory subunit	Cell Cycle, DNA Repair, DNA Replication
TOPBP1	topoisomerase (DNA) II binding protein	Cell Cycle
KNSL7	kinesin-like 7	Cell Cycle

Supplemental Table 4
Consensus Binding Sites for p110 CUX1 and E2F1 in Common Targets

Various groups of promoters were examined for the presence of consensus motif for E2F1 sites, which is TTTSSCGC with S = C or G (Tao et al. 1997) and the consensus motif for p110 CUX1, which is ATCRAT with C = A or G (Harada et al. 1995). $E2F^{-1}$ and $p110^{-1}$: the -1 indicates the presence of one mismatch. We analyzed the promoter sequences of non-targets, targets that are unique to CUX1, targets that are unique to E2F1 and targets that are common to E2F1 and CUX1. We performed the same analysis on sub-groups of common targets with functions in cell cycle, DNA replication or DNA repair. The salient points of this analysis are described on page 3.

% of promoters that contain a consensus binding site for E2F and/or p110 CUX1						
Groups of Promoters	n	E2F Site	p110 Site	E2F + p110 Sites	E2F + $p110^{-1}$ Sites	p110 + $E2F^{-1}$ Sites
Non-targets	76	11.8%	17.1%	1.3%	11.8%	15.8%
Unique targets of p110	74	10.8%	*67.6%	5.4%	10.8%	*62.2%
Unique targets of E2F1	79	*34.2%	13.9%	2.5%	*34.2%	12.7%
Common targets to p110 and E2F (all)	81	*29.6%	*40.7%	*12.3%	*28.4%	*39.5%
Common cell cycle targets of p110 and E2F	19	42.1%	36.8%	15.8%	42.1%	36.8%
Common Replication targets of p110 and E2F	5	*80.0%	80.0%	*60.0%	*80.0%	80.0%
Common DNA repair targets of p110 and E2F	6	33.3%	50.0%	16.7%	33.3%	50.0%

E2F site = TTTSSCGC
p110 CUX1 = ATCRAT
$E2F^{-1}$ and $p110^{-1}$: the -1 indicates the presence of one mismatch

Significant differences:

E2F sites:

Unique targets of E2F	Vs	Non-targets and unique targets of p110
Common targets	Vs	Non-targets and unique targets of p110
Common DNA Replication	Vs	Common targets

p110 sites:

Unique targets of p110	Vs	Non-targets, unique targets of E2F1 and common targets
Common targets	Vs	Non-targets and unique targets of E2F1

E2F+p110 sites:

Common targets	Vs	Non-targets and unique targets of E2F1
Common DNA Replication	Vs	Common targets

E2F + $p110^{-1}$ sites:

Unique targets of E2F	Vs	Non-targets and unique targets of p110
Unique targets of p110	Vs	Non-targets and unique targets of p110
Common DNA Replication	Vs	Common targets

E2F-1 + p110 sites:

Unique targets of p110	Vs	Non-targets, unique targets of E2F1 and common targets
Common targets	Vs	Non-targets and unique targets of E2F1

Supplemental Table 5
Average Number of Consensus Binding Sites Per Promoter

Various groups of promoters were examined for the presence of consensus motif for E2F1 sites, which is TTTSSCGC with S = C or G (Tao et al. 1997) and the consensus motif for p110 CUX1, which is ATCRAT with C = A or G (Harada et al. 1995). $E2F^{-1}$ and $p110^{-1}$: the -1 indicates the presence of one mismatch. We analyzed the promoter sequences of non-targets, targets that are unique to CUX1, targets that are unique to E2F1 and targets that are common to E2F1 and CUX1. We performed the same analysis on sub-groups of common targets with functions in cell cycle, DNA replication or DNA repair. The salient points of this analysis are described on page 3.

Average number of consensus binding sites per promoter					
Groups of Promoters	n	E2F Site	p110 Site	$E2F^{-1}$ Sites	$p110^{-1}$ Sites
Non-targets	76	0.1	0.2	3.3	9.3
Unique targets of p110	74	0.1	*1.0	2.7	*13.2
Unique targets of E2F1	79	*0.5	0.2	*4.2	9.6
Common targets of p110 and E2F (all)	81	*0.4	*0.5	*4.3	9.5
Common cell cycle targets of p110 and E2F	19	0.6	0.4	4.3	10.0
Common Replication targets of p110 and E2F	5	1.2	0.8	5.0	12.0
Common DNA repair targets to p110 and E2F	6	0.3	0.5	4.3	10.7

Significant differences:

E2F sites:

Unique targets of E2F Vs Non-targets and unique targets of p110
Common targets Vs Non-targets and unique targets of p110

p110 sites:

Unique targets of p110 Vs Non-targets, unique targets of E2F and common targets
Common targets Vs Non-targets and unique targets of E2F

$E2F1^{-1}$ sites:

Unique targets of E2F Vs Non-targets and unique targets of p110
Common targets Vs Non-targets and unique targets of p110

$p110^{-1}$ sites:

Unique targets of p110 Vs Non-targets, unique targets of E2F and common targets

Salient points from the sequence analysis are the following:

1° When considering the % of promoters that contain a perfect E2F1 binding site, we observed a statistically significant difference between non-targets and targets unique to E2F (11.8% Vs 34.2%). However, the difference was not statistically significant between targets that are unique to E2F1 (34.2%) and those that are common to E2F1 and p110 CUX1 (29.6%). Remarkably, the highest percentage (80%) of promoters with an E2F1 binding site was within the sub-group of common DNA replication targets.

2° When considering the % of promoters that contain perfect binding sites for both E2F1 and p110, we observed statistically significant differences between common targets (12.3%) and non-targets (1.3%) or targets that are unique to E2F1 (2.5%).

3° The frequency of consensus binding sites with one mismatch was clearly too high to be of any predictive value. However, when we examined promoters that contain a perfect site for p110 and an imperfect site (one mismatch) for E2F1, there was a significant difference between the targets unique to E2F1 (12.7%) and the common targets (39.5%).

4° For those promoters in which perfect or imperfect consensus binding sites were identified, the positions of these sites relative to the transcription start site, and relative to each other, was found to be random. Thus, the distance between an E2F site and a p110 site was highly variable, the two sites being close to each other on some promoters, while being distant from each other on other promoters.

5° There was no significant sequence variations among E2F1 binding sites in the following groups of promoters: non-targets, targets unique to E2F1, targets unique to CUX1 and targets common to both.

6° While we observed statistically significant difference in the % of promoters containing one site or the other or both sites (see below), there is a substantial fraction of common targets (42%) that lack perfect binding sites for both factors. Do these promoters contain imperfect binding sites? Yes, but the number of imperfect binding sites, their sequence and their position relative to each other and to the transcription start site was not significantly different than in common targets with binding site(s) for one or two factors.

7° The only difference we observed regarding imperfect binding sites is that E2F1 targets, unique or common, have a greater average number of single-mismatch binding sites (4 sites) than non-targets and targets unique to p110 (3 sites). Similarly, targets unique to p110 have a greater *average number* of single-mismatch p110 sites (13 sites) than common targets (10 sites), targets unique to E2F1 (10 sites) and non-targets (9 sites).