

Text S2 Relevant references for transcription factors (TFs) that correspond to implicated motifs and are active in ES cells.

### **TFs associated with Ezh2-positive CpG islands**

#### NRSF

- Chen ZF, Paquette AJ, Anderson DJ. NRSF/REST is required *in vivo* for repression of multiple neuronal target genes during embryogenesis. *Nat Genet*. 1998 Oct;20(2):136-42.
- Naruse Y, Aoki T, Kojima T, Mori N. Neural restrictive silencer factor recruits mSin3 and histone deacetylase complex to repress neuron-specific target genes. *Proc Natl Acad Sci U S A*. 1999 Nov 23;96(24):13691-6.
- Huang Y, Myers SJ, Dingledine R. Transcriptional repression by REST: recruitment of Sin3A and histone deacetylase to neuronal genes. *Nat Neurosci*. 1999 Oct;2(10):867-72.
- Lunyak VV, Burgess R, Prefontaine GG, Nelson C, Sze SH, Chenoweth J, Schwartz P, Pevzner PA, Glass C, Mandel G, Rosenfeld MG. Corepressor-dependent silencing of chromosomal regions encoding neuronal genes. *Science*. 2002 Nov 29;298(5599):1747-52. Epub 2002 Oct 24. Erratum in: *Science*. 2003 Mar 14;299(5613):1663.
- Su X, Kameoka S, Lentz S, Majumder S. Activation of REST/NRSF target genes in neural stem cells is sufficient to cause neuronal differentiation. *Mol Cell Biol*. 2004 Sep;24(18):8018-25.
- Murai K, Naruse Y, Shaul Y, Agata Y, Mori N. Direct interaction of NRSF with TBP: chromatin reorganization and core promoter repression for neuron-specific gene transcription. *Nucleic Acids Res*. 2004 Jun 14;32(10):3180-9.
- Singh SK, Kagalwala MN, Parker-Thornburg J, Adams H, Majumder S. REST maintains self-renewal and pluripotency of embryonic stem cells. *Nature*. 2008 May 8;453(7192):223-7. Epub 2008 Mar 23.

#### Cux1

- Mailly F, Bérubé G, Harada R, Mao PL, Phillips S, Nepveu A. The human cut homeodomain protein can repress gene expression by two distinct mechanisms: active repression and competition for binding site occupancy. *Mol Cell Biol*. 1996 Oct;16(10):5346-57.
- Lizarraga G, Lichtler A, Upholt WB, Kosher RA. Studies on the role of Cux1 in regulation of the onset of joint formation in the developing limb. *Dev Biol*. 2002 Mar 1;243(1):44-54.
- Truscott M, Harada R, Vadnais C, Robert F, Nepveu A. p110 CUX1 cooperates with E2F transcription factors in the transcriptional activation of cell cycle-regulated genes. *Mol Cell Biol*. 2008 May;28(10):3127-38. Epub 2008 Mar 17.
- Harada R, Vadnais C, Sansregret L, Leduy L, Bérubé G, Robert F, Nepveu A. Genomewide location analysis and expression studies reveal a role for p110 CUX1 in the activation of DNA replication genes. *Nucleic Acids Res*. 2008 Jan;36(1):189-202. Epub 2007 Nov 14.

## TFs associated with Ezh2-negative CpG islands

### Ets family (Ets1, Ets2)

- Bhat, N. K.; Thompson, C. B.; Lindsten, T.; June, C. H.; Fujiwara, S.; Koizumi, S.; Fisher, R. J.; Papas, T. S. Reciprocal expression of human ETS1 and ETS2 genes during T-cell activation: regulatory role for the protooncogene ETS1. *Proc. Natl. Acad. Sci.* 1990 87: 3723-3727.
- Ohtani, N.; Zebedee, Z.; Huot, T. J. G.; Stinson, J. A.; Sugimoto, M.; Ohashi, Y.; Sharrocks, A. D.; Peters, G.; Hara, E. Opposing effects of Ets and Id proteins on p16(INK4A) expression during cellular senescence. *Nature* 2001 409: 1067-1070.
- Wen, F.; Tynan, J. A.; Cecena, G.; Williams, R.; Munera, J.; Mavrothalassitis, G.; Oshima, R. G. Ets2 is required for trophoblast stem cell self-renewal. *Dev. Biol.* 2007 312: 284-299.
- Oikawa, T., and Yamada, T. Molecular biology of the Ets family of transcription factors. *Gene* 2001 303, 11-34.
- Sumanas, S., and Lin, S. Ets1-related protein is a key regulator of vasculogenesis in zebrafish. *PLoS Biol.* 2006 4, e10. 10.1371
- Hollenhorst, P. C.; Shah, A. A.; Hopkins, C.; Graves, B. J. Genome-wide analyses reveal properties of redundant and specific

### Gabpa (NRF2)

- LaMarco, K., Thompson, C. C., Byers, B. P., Walton, E. M. & McKnight, S. L. Identification of Ets and notch-related subunits in GA binding protein. *Science* 1991 253, 789-792.
- Gugneja, S.; Virbasius, J. V.; Scarpulla, R. C. Four structurally distinct, non-DNA-binding subunits of human nuclear respiratory factor 2 share a conserved transcriptional activation domain. *Mol. Cell. Biol.* 1995 15: 102-111.
- Ristevski S, O'Leary DA, Thornell AP, Owen MJ, Kola I, Hertzog PJ. The Ets transcription factor GABPalpha is essential for early embryogenesis. *Mol. Cell Biol.* 2004 24, 5844-5849
- Resendes, K. K. & Rosmarin, A. G. Interaction between GABPalpha pointed domain and p300 mediates retinoic acid induced transcriptional activation of CD18 in myeloid cells. *Mol. Cell Biol.* 2006 26, 3060-3070
- Yang ZF, Mott S, Rosmarin AG. The Ets transcription factor GABP is required for cell-cycle progression. *Nature Cell Biology* 2007 9, 339-346.

### YY1 (closely related to Rex1)

- Park, K.; Atchison, M. L. Isolation of a candidate repressor/activator, NF-E1 (YY-1, delta), that binds to the immunoglobulin kappa 3-prime enhancer and the immunoglobulin heavy-chain micro-E1 site. *Proc. Natl. Acad. Sci.* 1991 88: 9804-9808.
- Hariharan N., Kelley D.E. and Perry R.P., Delta, a transcription factor that binds to downstream elements in several polymerase II promoters, is a functionally versatile zinc finger protein, *Proc. Natl. Acad. Sci. USA* 1991 88 pp. 9799-9803
- Wilkinson, F. H., Park, K. & Atchison, M. L. Polycomb recruitment to DNA in vivo by the YY1 REPO domain. *Proc. Natl. Acad. Sci.* 2006 103, 19296-19301
- Cunningham, J. T.; Rodgers, J. T.; Arlow, D. H.; Vazquez, F.; Mootha, V. K.; Puigserver, P. mTOR controls mitochondrial oxidative function through a YY1-PGC-1-alpha transcriptional complex. *Nature* 2007 450: 736-740.
- Kim J., Chu J., Shen X., Wang J., Orkin S. An extended transcriptional network for pluripotency of embryonic stem cells. *Cell* 2008 132, 1049-1061.

### NFY family

- Li Q, Herrler M, Landsberger N, Kaludov N, Ogryzko VV, Nakatani Y, Wolffe AP. Xenopus NF-Y pre-sets chromatin to potentiate p300 and acetylation-responsive transcription from the Xenopus hsp70 promoter in vivo. *EMBO J* 1998 17(21): 6300-15.
- Faniello MC, Bevilacqua MA, Condorelli G, de Crombrugghe B, Maity SN, Avvedimento VE, Cimino F, Costanzo F. (1999). The B subunit of the CAAT-binding factor NFY binds the central segment of the Co-activator p300. *J Biol Chem* 274(12): 7623-6.
- Mantovani, R., 1999. The molecular biology of the CCAAT-binding factor NFY. *Gene* 239, 15–27.
- Gilthorpe J, Vandromme M, Brend T, Gutman A, Summerbell D, Totty N, Rigby PW. Spatially specific expression of Hoxb4 is dependent on the ubiquitous transcription factor NFY. *Development* 2002 129(16): 3887-99.
- Frontini M, Imbriano C, diSilvio A, Bell B, Bogni A, Romier C, Moras D, Tora L, Davidson I, Mantovani R. NF-Y recruitment of TFIID, multiple interactions with histone fold TAF(II)s. *J Biol Chem* 2002 277(8): 5841-8.
- Udayakumar TS, Belakavadi M, Choi KH, Pandey PK, Fondell JD. Regulation of Aurora-A kinase gene expression via GABP recruitment of TRAP220/MED1. *J Biol Chem* 2006 281(21): 14691-9.
- Donati G, Gatta R, Dolfini D, Fossati A, Ceribelli M, Mantovani R. An NF-Y-dependent switch of positive and negative histone methyl marks on CCAAT promoters. *PLoS ONE* 2008 3(4): e2066.

### Atf family

- Hai, T.; Liu, F.; Coukos, W. J.; Green, M. R. Transcription factor ATF cDNA clones: an extensive family of leucine zipper proteins able to selectively form DNA-binding heterodimers. *Genes Dev.* 1989 3: 2083-2090.
- Liu, F. & Green, M. A specific member of the ATF transcription factor family can mediate transcription activation by the adenovirus E1A protein. *Cell* 1990 61, 1217–1224.
- Li M, Baumeister P, Roy B, Phan T, Foti D, Luo S, Lee AS. ATF6 as a transcription activator of the endoplasmic reticulum stress element: thapsigargin stress-induced changes and synergistic interactions with NF-Y and YY1. *Mol Cell Biol* 2000. 20(14): 5096-106.
- Kawasaki, H., L. Schiltz, Chiu R, Itakura K, Taira K, Nakatani Y, Yokoyama KK. ATF-2 has intrinsic histone acetyltransferase activity which is modulated by phosphorylation. *Nature* 2000 405(6783):195-200.
- Yoshida, H., Matsui, T., Yamamoto, A., Okada, T. and Mori, K. XBP1 mRNA is induced by ATF6 and spliced by IRE1 in response to ER stress to produce a highly active transcription factor. *Cell* 2001 107, pp. 881–891.

### Myc family

- Gomez-Roman, N., C. Grandori, Eisenman RN, White RJ. Direct activation of RNA polymerase III transcription by c-Myc. *Nature* 2003 421(6920): 290-4.
- Grandori, C., N. Gomez-Roman, Felton-Edkins ZA, Ngouenet C, Galloway DA, Eisenman RN, White RJ. c-Myc binds to human ribosomal DNA and stimulates transcription of rRNA genes by RNA polymerase I. *Nat Cell Biol* 2005. 7(3): 311-8.
- Lin JM, Collins PJ, Trinklein ND, Fu Y, Xi H, Myers RM, Weng Z. Transcription factor binding and modified histones in human bidirectional promoters. *Genome Res.* 2007 Jun;17(6):818-27.
- Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult

fibroblast cultures by defined factors. *Cell*. 2006 Aug 25;126(4):663-76. Epub 2006 Aug 10.  
Kim J, Chu J, Shen X, Wang J, Orkin SH. 2008 An extended transcriptional network for  
pluripotency of embryonic stem cells. *Cell* 2008 132(6): 1049-61.