

Supplementary Table. Factors influencing rRNA synthesis by pol I^a

Factor ^b	Target ^c	Effect ^d	Refs
Actin-nuclear myosin	Associates with pol I and rDNA	↑	[1,2]
Angiogenin	Accumulates in the nucleolus and binds to DNA	↑	[3]
Basonuclin	Binds rDNA promoter	↑	[4]
Cdc2-cyclin B	Inactivates SL1 and TTF-I in mitosis	↓	[5,6]
Cdk-cyclin complexes (G1-specific)	Activation of UBF	↑	[7,8]
CSB	In a complex that contains pol I, TFIIH and XPG	↑	[9]
DNA-PK	Phosphorylated Ku protein competes with SL1 for binding to the rDNA promoter and prevents PIC formation	↓	[10]
HBV X protein	Increases TBP levels (via Ras)	↑	[11]
HCV core protein	Associates with SL1; hyperphosphorylation of UBF	↑	[12]
IRS-1	Interacts with UBF, and targets the p110 subunit of PI3K to phosphorylate UBF	↑	[13,14]
Large T antigen	Interacts with SL1; induces an increase in UBF phosphorylation	↑	[15]
MAPK (Ras- and ERK-signalling)	ERK activation of UBF and/or TIF-IA (RRN3); Ras signals to elevate TBP expression	↑	[16–18]
mTOR	Activation of TIF-IA (RRN3) and/or UBF (involving p70 S6K); increased TBP levels	↑	[19,20]
Myc/MAD1	Activation or repression of UBF gene expression	↑↓	[21]
ncl-1 or brat	Loss of function mutants of ncl-1 (<i>C. elegans</i>) (or <i>Drosophila</i> homologue brat, for brain tumour) have enlarged nucleoli	↓	[22,23]
Net1 (in yeast RENT complex)	Binds pol I	↑	[24]
NoRC	TTF-I recruits HDAC1 and DNA methyltransferase via a subunit of NoRC	↓	[25,26]
Nopp140	Interacts with pol I and mislocalises pol I	↓	[27]
Nucleolin	Affects the transcription machinery or the rDNA promoter (reduces the level of 40S pre-rRNA in <i>Xenopus</i> oocytes)	↓	[28]
p204 (interferon-inducible)	Interacts with UBF	↓	[29]
p300/CBP	Acetylation of UBF	↑	[30]
p53	Binds primarily to SL1 subunits TBP and TAF ₁₁₀ and prevents the interaction of SL1 with UBF <i>in vitro</i>	↓	[31,32]
P/CAF	Interacts with TTF-I, acetylates TAF ₆₈ in TIF-IB (SL1) and enhances DNA binding of this TAF _i	↑	[33]
PI3K	UBF phosphorylation	↑	[14,34]
RB	Binds UBF and either prevents UBF binding to rDNA or prevents the interaction of UBF with SL1	↓	[35–38]
TAF1 (TAF _{ii250})	Interacts with UBF	↑	[39]
TFIIH	Associates with subpopulations of both pol I and TIF-IB or SL1; required for productive but not abortive rDNA transcription	↑	[40]
TFIIS	Can stimulate elongation by pol I	↑	[41]
Tip60 acetyltransferase subunit	Acetylates UBF	↑	[42]
Topoisomerase I/II	Stimulates elongation by pol I	↑	[43]
Treacle (Treacher Collins syndrome)	Interacts with UBF	↑	[44]
USF1/USF2	Modulate pol I transcription: as an activator (heterodimer) or repressor (homodimer)	↑↓	[45]
WRN (RecQ DNA helicase)/yeast DNA helicases SGS1 and SRS2	WRN interacts with pol I	↑	[46,47]

^aAbbreviations: CBP, CREB (calcium response element binding protein)-binding protein; Cdc, cell-division cycle; Cdk, cyclin-dependent kinase; CSB, Cockayne's syndrome B; DNA-PK, DNA-dependent protein kinase; ERK, extracellular-signal regulated kinase; HBV, hepatitis B virus; HCV, hepatitis C virus; HDAC, histone deacetylase; IRS, insulin receptor substrate; MAPK, mitogen-activated protein kinase; mTOR, mammalian target of rapamycin; NoRC, nucleolar remodelling complex; p70 S6K, ribosomal protein S6 kinase 70 kDa; P/CAF, p300/CBP-associated factor; PIC, pre-initiation complex; PI3K, phosphatidylinositol-3 kinase; pol I, RNA polymerase I; RB, retinoblastoma tumour-suppressor protein; RENT, regulator of nucleolar silencing and telophase exit; RRN3, ribosomal RNA polymerase I complementation group 3; SL1, Selectivity factor 1; TAF_i, TBP-associated factor for pol I transcription; TBP, TATA-box binding protein; TFIIH, transcription factor H for pol II transcription; TIF-IA or B, transcription initiation factor for pol I A (RRN3) or B (SL1); TTF-I, transcription terminator factor I; UBF, upstream binding factor; USF, upstream stimulatory factor; WRN, Werner's syndrome protein; XPG, Xeroderma pigmentosum group G.

^bPrimarily including factors described in the last ~5 years.

^cThe targets might not be known.

^dThe effect might be direct or indirect and increase (↑) and/or decrease (↓) rRNA synthesis by pol I transcription.

References

- 1 Fomproix, N. and Percipalle, P. (2004) An actin–myosin complex on actively transcribing genes. *Exp. Cell. Res.* 294, 140–148
- 2 Philimonenko, V.V. *et al.* (2004) Nuclear actin and myosin I are required for RNA polymerase I transcription. *Nat. Cell Biol.* 6, 1165–1172
- 3 Xu, Z.P. *et al.* (2002) The nuclear function of angiogenin in endothelial cells is related to rRNA production. *Biochem. Biophys. Res. Commun.* 294, 287–292
- 4 Tian, Q. *et al.* (2001) Function of basonuclin in increasing transcription of the ribosomal RNA genes during mouse oogenesis. *Development* 128, 407–416

- 5 Kuhn, A. *et al.* (1998) Mitotic phosphorylation of the TBP-containing factor SL1 represses ribosomal gene transcription. *J. Mol. Biol.* 284, 1–5
- 6 Sirri, V. *et al.* (1999) The mitotically phosphorylated form of the transcription termination factor TTF-1 is associated with the repressed rDNA transcription machinery. *J. Cell. Sci.* 112, 3259–3268
- 7 Voit, R. and Grummt, I. (2001) Phosphorylation of UBF at serine 388 is required for interaction with RNA polymerase I and activation of rDNA transcription. *Proc. Natl. Acad. Sci. U. S. A.* 98, 13631–13636
- 8 Voit, R. *et al.* (1999) Phosphorylation by G1-specific cdk–cyclin complexes activates the nucleolar transcription factor UBF. *EMBO J.* 18, 1891–1899
- 9 Bradsher, J. *et al.* (2002) CSB is a component of RNA pol I transcription. *Mol. Cell* 10, 819–829
- 10 Michaelidis, T.M. and Grummt, I. (2002) Mechanism of inhibition of RNA polymerase I transcription by DNA-dependent protein kinase. *Biol. Chem.* 383., 1683–1690
- 11 Wang, H.D. *et al.* (1998) Regulation of RNA polymerase I-dependent promoters by the hepatitis B virus X protein via activated Ras and TATA-binding protein. *Mol. Cell Biol.* 18, 7086–7094
- 12 Kao, C.F. *et al.* (2004) Activation of RNA polymerase I transcription by hepatitis C virus core protein. *J. Biomed. Sci.* 11, 72–94
- 13 Tu, X. *et al.* (2002) Nuclear translocation of insulin receptor substrate-1 by oncogenes and Igf-I. Effect on ribosomal RNA synthesis. *J. Biol. Chem.* 277, 44357–44365
- 14 Drakas, R. *et al.* (2004) Control of cell size through phosphorylation of upstream binding factor 1 by nuclear phosphatidylinositol 3-kinase. *Proc. Natl. Acad. Sci. U. S. A.* 101, 9272–9276
- 15 Zhai, W. and Comai, L. (1999) A kinase activity associated with simian virus 40 large T antigen phosphorylates upstream binding factor (UBF) and promotes formation of a stable initiation complex between UBF and SL1. *Mol. Cell Biol.* 19, 2791–2802
- 16 Stefanovsky, V.Y. *et al.* (2001) An immediate response of ribosomal transcription to growth factor stimulation in mammals is mediated by ERK phosphorylation of UBF. *Mol. Cell* 8, 1063–1073
- 17 Zhao, J. *et al.* (2003) ERK-dependent phosphorylation of the transcription initiation factor TIF-IA is required for RNA polymerase I transcription and cell growth. *Mol. Cell* 11, 405–413
- 18 Zhong, S. *et al.* (2004) Epidermal growth factor enhances cellular TATA binding protein levels and induces RNA polymerase I- and III-dependent gene activity. *Mol. Cell Biol.* 24, 5119–5129
- 19 Mayer, C. *et al.* (2004) mTOR-dependent activation of the transcription factor TIF-IA links rRNA synthesis to nutrient availability. *Genes Dev.* 18, 423–434
- 20 Hannan, K.M. *et al.* (2003) mTOR-dependent regulation of ribosomal gene transcription requires S6K1 and is mediated by phosphorylation of the carboxy-terminal activation domain of the nucleolar transcription factor UBF. *Mol. Cell Biol.* 23, 8862–8877
- 21 Poortinga, G. *et al.* (2004) MAD1 and c-MYC regulate UBF and rDNA transcription during granulocyte differentiation. *EMBO J.* 23, 3325–3335
- 22 Frank, D.J. and Roth, M.B. (1998) ncl-1 is required for the regulation of cell size and ribosomal RNA synthesis in *Caenorhabditis elegans*. *J. Cell Biol.* 140, 1321–1329
- 23 Frank, D.J. *et al.* (2002) The *Drosophila melanogaster* gene *brain tumor* negatively regulates cell growth and ribosomal RNA synthesis. *Development* 129, 399–407
- 24 Shou, W. *et al.* (2001) Net1 stimulates RNA polymerase I transcription and regulates nucleolar structure independently of controlling mitotic exit. *Mol. Cell* 8, 45–55
- 25 Zhou, Y. *et al.* (2002) The chromatin remodeling complex NoRC targets HDAC1 to the ribosomal gene promoter and represses RNA polymerase I transcription. *EMBO J.* 21, 4632–4640
- 26 Santoro, R. *et al.* (2002) The nucleolar remodeling complex NoRC mediates heterochromatin formation and silencing of ribosomal gene transcription. *Nat. Genet.* 32, 393–396
- 27 Chen, H.K. *et al.* (1999) Human Nopp140, which interacts with RNA polymerase I: implications for rRNA gene transcription and nucleolar structural organization. *Mol. Cell Biol.* 19, 8536–8546
- 28 Roger, B. *et al.* (2002) Repression of RNA polymerase I transcription by nucleolin is independent of the RNA sequence that is transcribed. *J. Biol. Chem.* 277, 10209–10219
- 29 Liu, C.J. *et al.* (1999) The interferon-inducible nucleolar p204 protein binds the ribosomal RNA-specific UBF1 transcription factor and inhibits ribosomal RNA transcription. *EMBO J.* 18, 2845–2854
- 30 Pelletier, G. *et al.* (2000) Competitive recruitment of CBP and Rb-HDAC regulates UBF acetylation and ribosomal transcription. *Mol. Cell* 6, 1059–1066
- 31 Budde, A. and Grummt, I. (1999) p53 represses ribosomal gene transcription. *Oncogene* 18, 1119–1124
- 32 Zhai, W. and Comai, L. (2000) Repression of RNA polymerase I transcription by the tumor suppressor p53. *Mol. Cell Biol.* 20, 5930–5938
- 33 Muth, V. *et al.* (2001) Acetylation of TAF(I)68, a subunit of TIF-IB/SL1, activates RNA polymerase I transcription. *EMBO J.* 20, 1353–1362
- 34 James, M.J. and Zomerdijk, J.C. (2004) Phosphatidylinositol 3-kinase and mTOR signaling pathways regulate RNA polymerase I transcription in response to IGF-1 and nutrients. *J. Biol. Chem.* 279, 8911–8918
- 35 Cavanaugh, A.H. *et al.* (1995) Activity of RNA polymerase I transcription factor UBF blocked by Rb gene product. *Nature* 374, 177–180
- 36 Voit, R. *et al.* (1997) Mechanism of repression of RNA polymerase I transcription by the retinoblastoma protein. *Mol. Cell Biol.* 17, 4230–4237
- 37 Hannan, K.M. *et al.* (2000) Rb and p130 regulate RNA polymerase I transcription: Rb disrupts the interaction between UBF and SL1. *Oncogene* 19, 4988–4999
- 38 Ciarmatori, S. *et al.* (2001) Overlapping functions of the pRb family in the regulation of rRNA synthesis. *Mol. Cell Biol.* 21, 5806–5814
- 39 Lin, C.Y. *et al.* (2002) The cell cycle regulatory factor TAF1 stimulates ribosomal DNA transcription by binding to the activator UBF. *Curr. Biol.* 12, 2142–2146
- 40 Iben, S. *et al.* (2002) TFIIF plays an essential role in RNA polymerase I transcription. *Cell* 109, 297–306
- 41 Schnapp, G. *et al.* (1996) TFIIS binds to mouse RNA polymerase I and stimulates transcript elongation and hydrolytic cleavage of nascent rRNA. *Mol. Gen. Gene.* 252, 412–419

- 42 Halkidou, K. *et al.* (2004) Putative involvement of the histone acetyltransferase Tip60 in ribosomal gene transcription. *Nucleic Acids Res.* 32, 1654–1665
- 43 Brill, S.J. *et al.* (1987) Need for DNA topoisomerase activity as a swivel for DNA replication for transcription of ribosomal RNA. *Nature* 326, 414–416
- 44 Valdez, B.C. *et al.* (2004) The Treacher Collins syndrome (TCOF1) gene product is involved in ribosomal DNA gene transcription by interacting with upstream binding factor. *Proc. Natl. Acad. Sci. U. S. A.* 101, 10709–10714
- 45 Ghosh, A.K. *et al.* (1997) The dual role of helix–loop–helix–zipper protein USF in ribosomal RNA gene transcription in vivo. *Oncogene* 14, 589–594
- 46 Shiratori, M. *et al.* (2002) WRN helicase accelerates the transcription of ribosomal RNA as a component of an RNA polymerase I-associated complex. *Oncogene* 21, 2447–2454
- 47 Lee, S.K. *et al.* (1999) Requirement of yeast SGS1 and SRS2 genes for replication and transcription. *Science* 286, 2339–2342