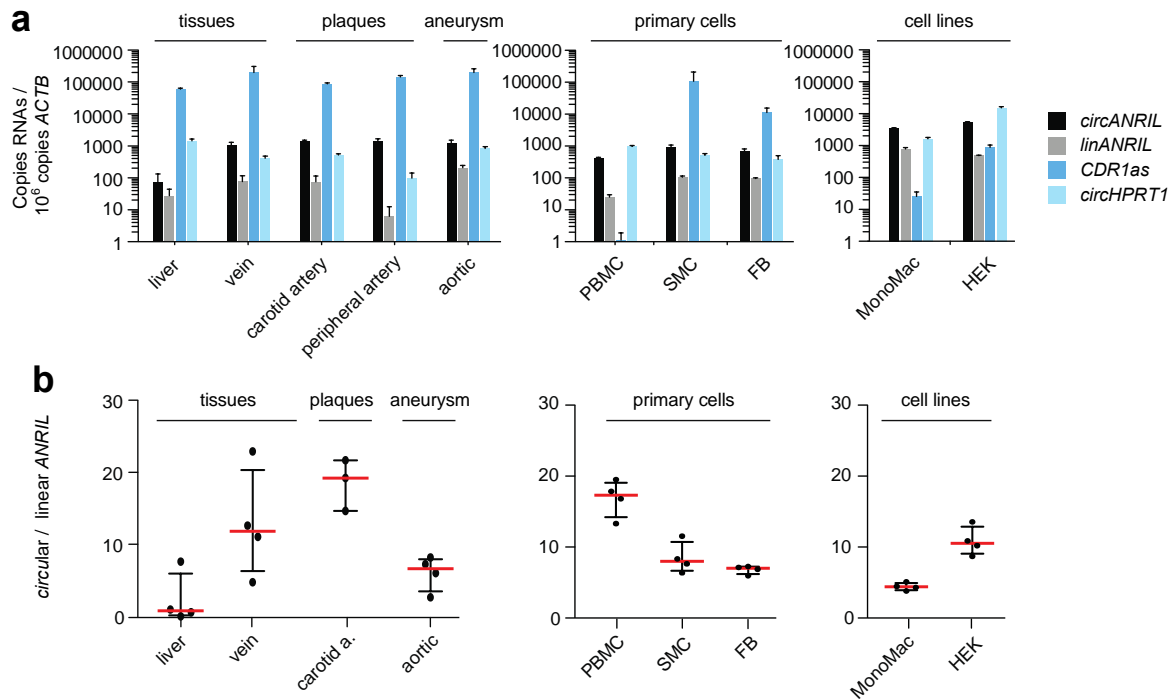
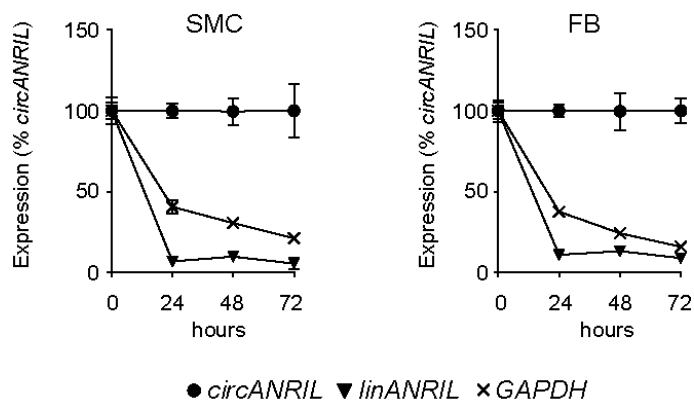


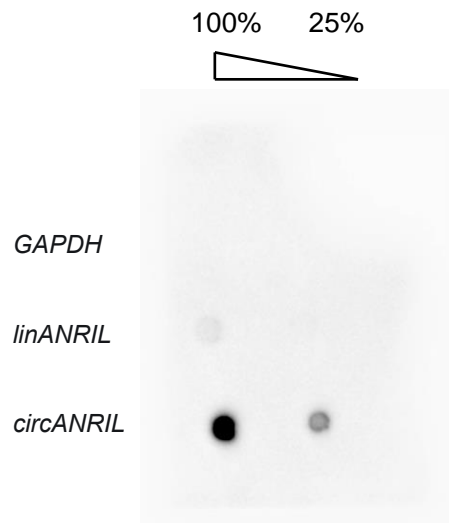
**Supplementary Figure 1.** Investigation of *circANRIL* transcript structure in human cell lines and primary cells. Annotated *ANRIL* exons and location of outward-facing PCR primers in exon 6. *CircANRIL* isoforms identified in human embryonic kidney cell line (HEK-293), human monocytic cell line (MonoMac), primary smooth muscle cells (SMC), and adventitial fibroblasts (FB). No exon scrambling except for back-splicing events was detected in *circANRIL* isoforms. abun. – abundance; ++ - at least two sequences, +++ - most abundant isoforms. *CircANRIL* consisting of exons 5, 6, 7, where exon 7 is back-spliced to exon 5, was the most abundant isoform detected in all investigated cells and was selected for functional studies.



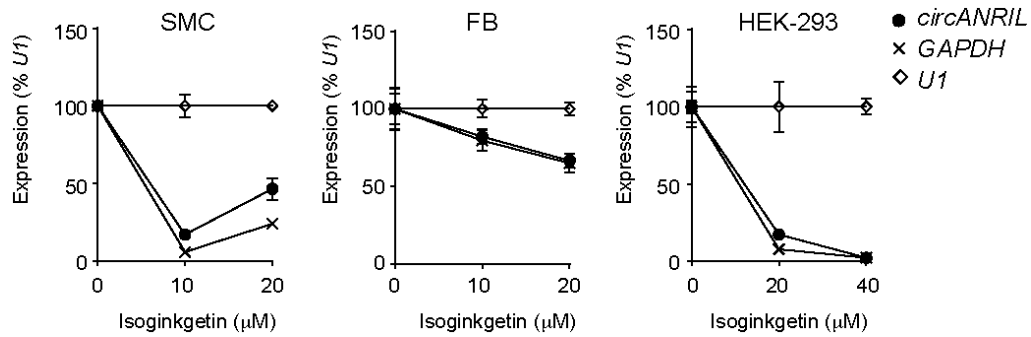
**Supplementary Figure 2.** RNA abundance of different circular RNAs in tissues and cells. **(a)** Copies of *circANRIL*, circular *CDR1as*, *circHPRT1*, and of linear *ANRIL* (*linANRIL*) RNA in human tissues, primary vascular cells, and cell lines normalized to  $10^6$  copies of housekeeping gene *ACTB*. Slight differences of *circANRIL* expression levels compared to Fig. 1b are explained by the use of a new batch of reverse-transcribed cDNAs. Peripheral blood mononuclear cells (PBMC), smooth muscle cells (SMC), adventitial fibroblasts (FB), human monocytic cell line MonoMac, human embryonic kidney cell line HEK-293. **(b)** Ratio of circular/linear *ANRIL* in tissues (left panel), primary cells (middle panel), and cell lines (right panel). Ratios were not calculated for plaques of peripheral arteries, for ECs, and for the THP1 cell line due to absence or very low expression of *linANRIL* in these samples. Red lines indicate median of ratios. Interquartile ranges are shown.



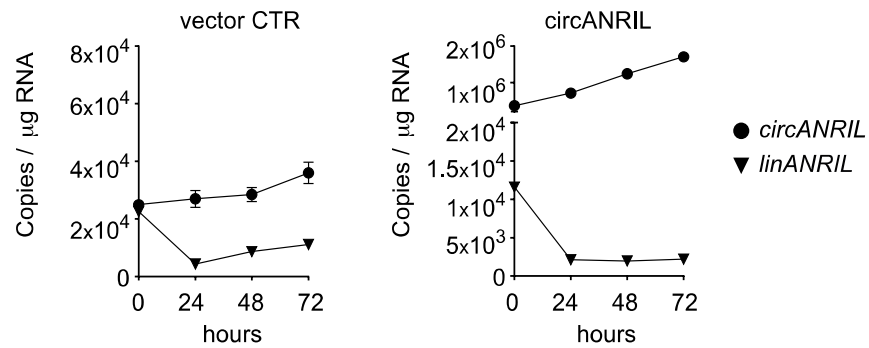
**Supplementary Figure 3.** *CircANRIL* is more stable than *linANRIL* in human primary cells. Half-lives of *circANRIL*, *linANRIL*, and of house-keeping *GAPDH* mRNA were determined in smooth muscle cells (SMC) and adventitial fibroblasts (FB) by qPCR analysis following inhibition of transcription with 50ng/ml actinomycin D. Analyses were performed in triplicates in RNA of 3 biological replicates. Data are given as mean  $\pm$  s.e.m.



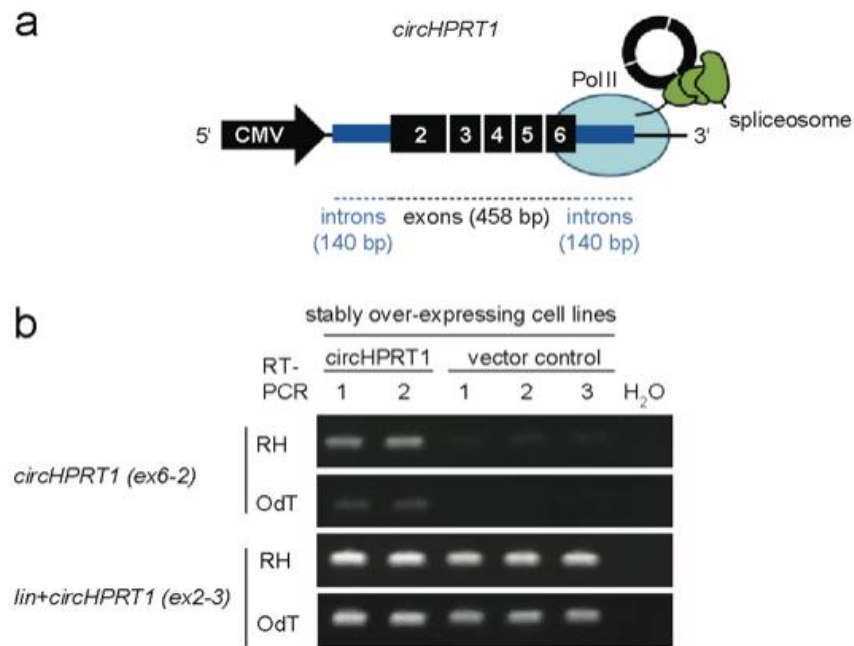
**Supplementary Figure 4.** Dot blot analysis of DIG-labeled probe that was subsequently used for *in situ* hybridization in Fig. 1c. RNAs for *GAPDH*, *linANRIL*, and *circANRIL* were spotted on a nylon membrane (*GAPDH*, *circANRIL* (line 1 5 fmol each) *linANRIL* (line 1 0,5 fmol resembling observed expression differences in Supplementary Fig. 2b)) and hybridized with the DIG-labeled probe.



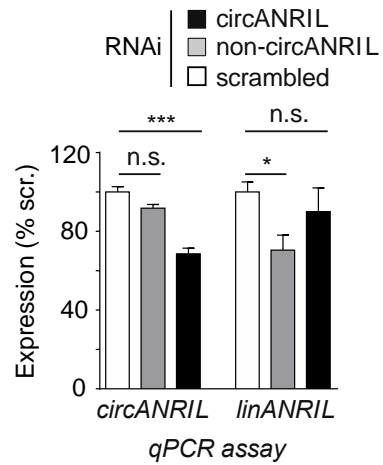
**Supplementary Figure 5.** Spliceosome-dependent generation of *circANRIL*. Reduced generation of *circANRIL* after incubation of smooth muscle cells (SMC), adventitial fibroblasts (FB) and HEK-293 cells with isoginkgetin, a general splicing inhibitor. Data were derived from quadruplicate measurements per condition. *U1* is not spliced and was used as reference RNA. *GAPDH* mRNA generation is known to be spliceosome-dependent.



**Supplementary Figure 6.** *CircANRIL* is more stable than *linANRIL* in HEK-293 cells. Half-lives of *circANRIL* and of *linANRIL* were determined by qPCR analysis after inhibition of transcription with 50ng/ml actinomycin D in HEK-293 (left panel) or in HEK-293 cells overexpressing *circular* or *linear ANRIL*, respectively (right panel). Analyses were performed in triplicates in RNA of 3 biological replicates. Data are given as mean  $\pm$  s.e.m.

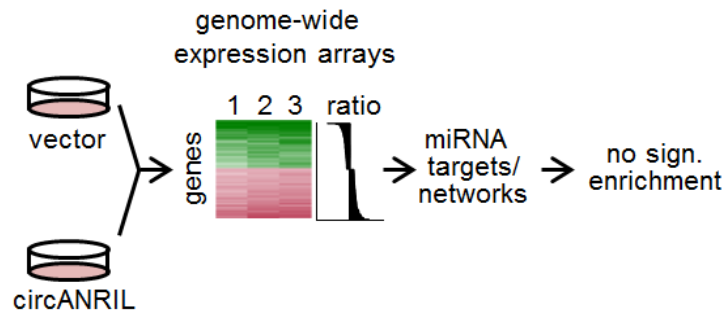


**Supplementary Figure 7.** Overexpression of *circHPRT1*. **(a)** Schematic of vector construct for expression of circular *HPRT1*. **(b)** Validation of *circHPRT1* overexpression by qPCR from random hexamer-primed (RH) or from oligo(d)T-primed (OdT) cDNA preparations. Results of biological replicates are shown on the agarose gel. Primer pair ex6-2 amplifies *HPRT1* RNA only after RNA circularization by back-splicing, primer pair ex2-3 recognizes both linear and circular *HPRT1* RNA.

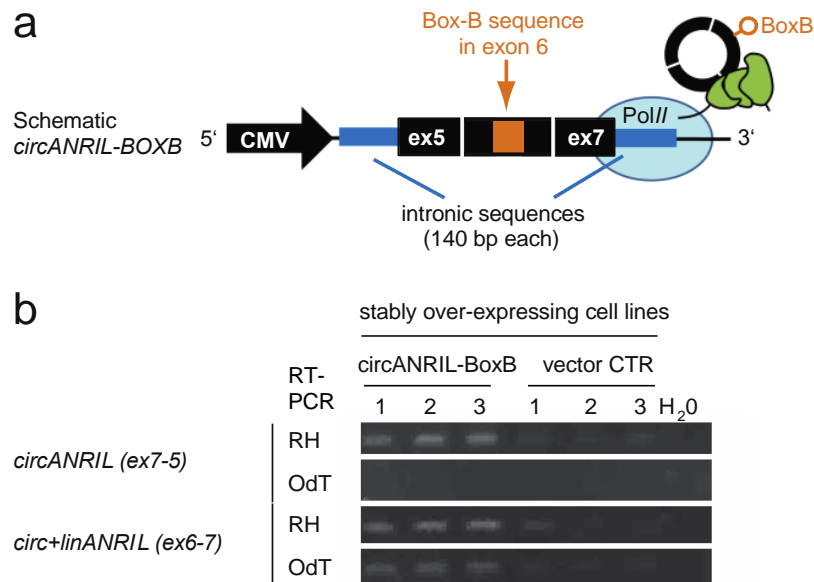


**Supplementary Figure 8.** Validation of linear or circular *ANRIL* siRNA-mediated down-regulation related to Fig. 2. qPCR Analysis was performed in quadruplicate measurements per condition. \*  $p < 0.05$ ; \*\*\*  $p < 0.001$ . Data are given mean  $\pm$  s.e.m.

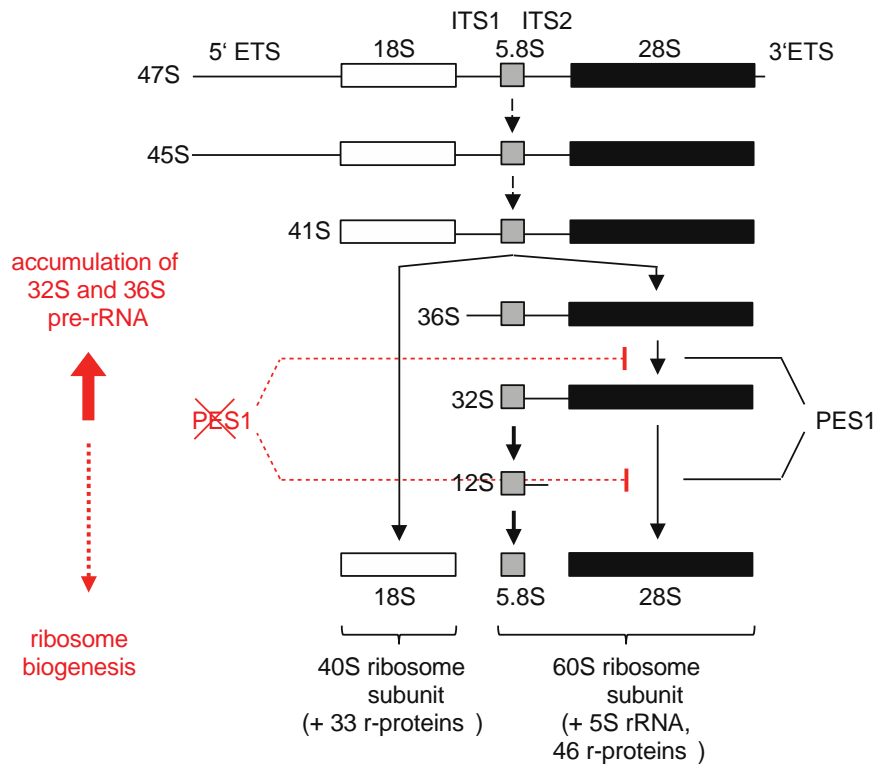




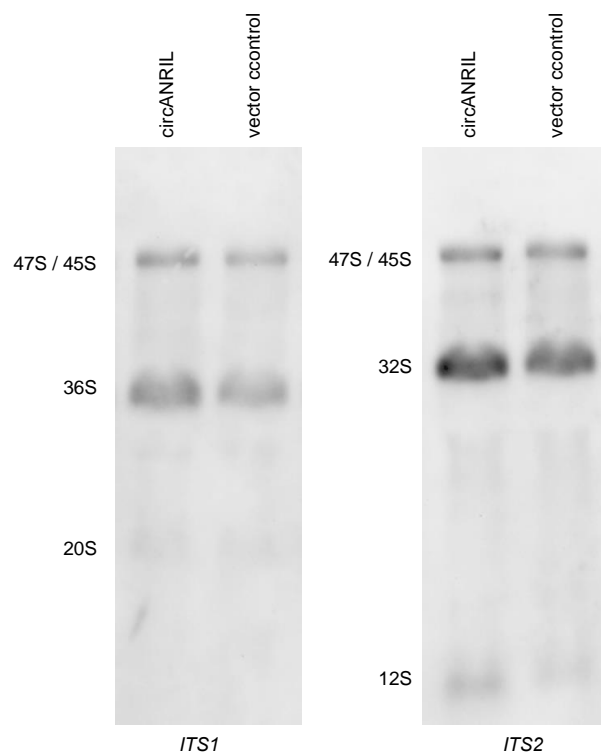
**Supplementary Figure 9.** Schematic of genome-wide expression analysis in *circANRIL* overexpressing (n=3) and vector control cells (n=3). Illumina HumanHT-12 v4 BeadChips were used for expression analyses. No significant regulation of miRNA-target gene networks was observed using the Ingenuity algorithm ([www.ingenuity.com](http://www.ingenuity.com)). Gene expression data have been deposited at Gene Expression Omnibus (GSE65392).



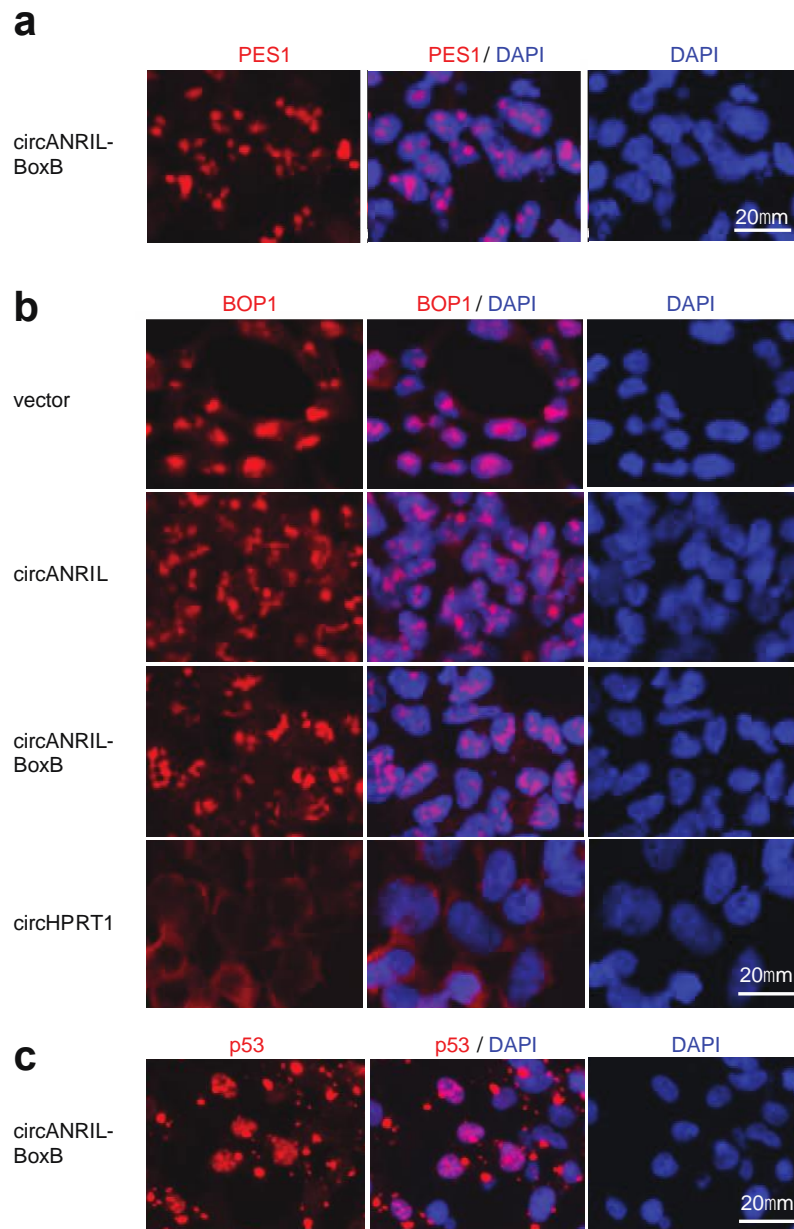
**Supplementary Figure 10.** Validation of *circANRIL* RNA containing BoxB RNA hairpin sequences. **(a)** Schematic of vector construct of *circANRIL* containing BoxB (*circANRIL-BoxB*). **(b)** Validation of *circANRIL-BoxB* overexpression by qPCR of random hexamer-primed (RH) or of oligo(d)T-primed (OdT) cDNA (3 biological replicates). Primer pair ex7-5 results in a PCR product only after RNA circularization by back-splicing, primer pair ex6-7 recognizes both linear and circular *ANRIL* RNA.



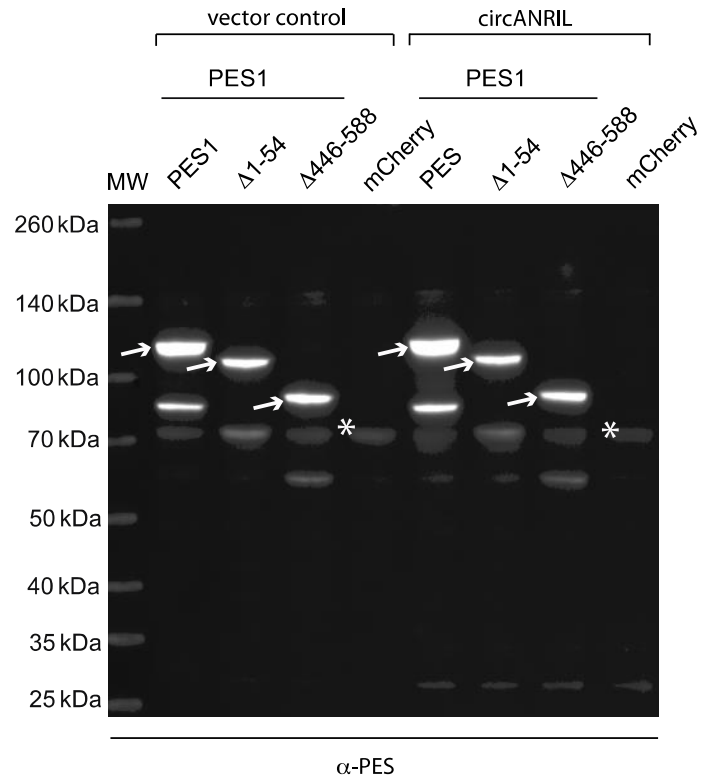
**Supplementary Figure 11.** Schematic of ribosomal RNA (rRNA) maturation and PES1 function. PES1 is required for 36S and 32S pre-rRNA processing to mature 5.8S and 28S rRNA. Impaired PES1 functions leads to accumulation of pre-rRNAs and reduced 60S ribosome biogenesis. ETS- external transcribed spacer; ITS- internal transcribed spacer.



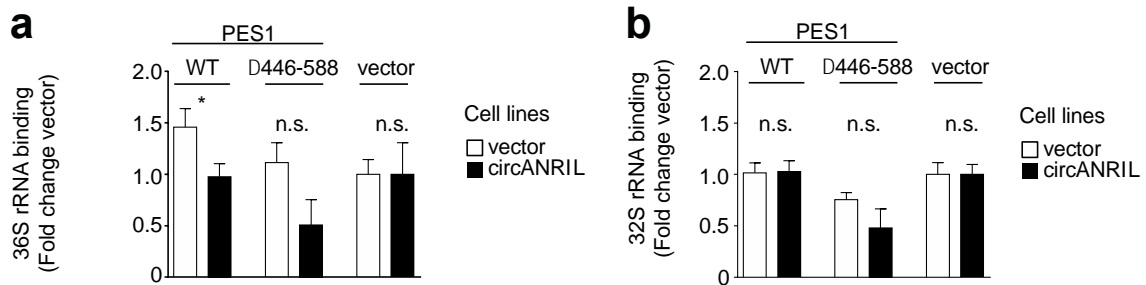
**Supplementary Figure 12.** Northern blotting in *circANRIL* overexpressing and vector control HEK-293 cell lines. *ITS1* and *ITS2* were used to detect pre-rRNA processing and pre-rRNA abundance in controls of following *circANRIL* RNA overexpression in HEK-293 cells.



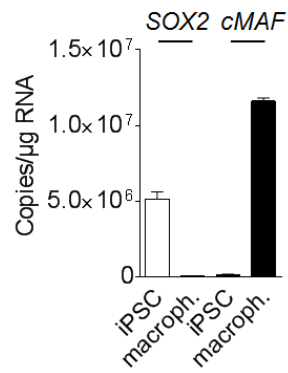
**Supplementary Figure 13.** Immunofluorescent stainings of PES1, BOP1, and p53 in *circANRIL* overexpressing and in control HEK-293 cells. **(a)** PES1 immunofluorescent staining in *circANRIL*-BoxB overexpressing cells corresponding to Fig. 6c. **(b)** BOP1 immunofluorescent staining in *circANRIL* overexpressing HEK-293 cells revealed altered nucleolar morphology. *circHPRT1* overexpression does not trigger nucleolar alterations. **(c)** p53 immunofluorescent staining in *circANRIL*-BoxB overexpressing HEK-293 cells corresponding to Fig. 6f.



**Supplementary Figure 14.** Western Blot using PES1-specific antibody of protein extracts used for immunoprecipitation (IP) in Fig. 7e. The following constructs were expressed in HEK-293 cells: full length PES1 (PES1), the N-terminal deletion mutant lacking amino acids 1-54 ( $\Delta$ 1-54), the C-terminal deletion mutant lacking amino acids 446-588 ( $\Delta$ 446-588) or empty vector expressing mCherry alone. An asterisk indicates endogenous untagged PES1 protein.



**Supplementary Figure 15.** Immunoprecipitation (IP) of PES1 isoforms and quantification of associated pre-rRNA by qPCR **(a)** 36S pre-rRNA binding to full length PES1 (PES1-WT) is significantly reduced when *circANRIL* is overexpressed. **(b)** 32S pre-rRNA binding to PES1 is not reduced by *circANRIL* overexpression. IP was performed in a pool of 3 biological replicates, qPCR measurements were performed in quadruplicates.



**Supplementary Figure 16.** Quantification of iPSC marker *SOX2* and macrophage differentiation marker *cMAF* in iPSC and iPSC-derived macrophages (macroph.) related to Fig. 8. Analysis was performed in quadruplicate measurements per condition. Data are given mean  $\pm$  s.e.m.



**a**

Figure 2b, source data

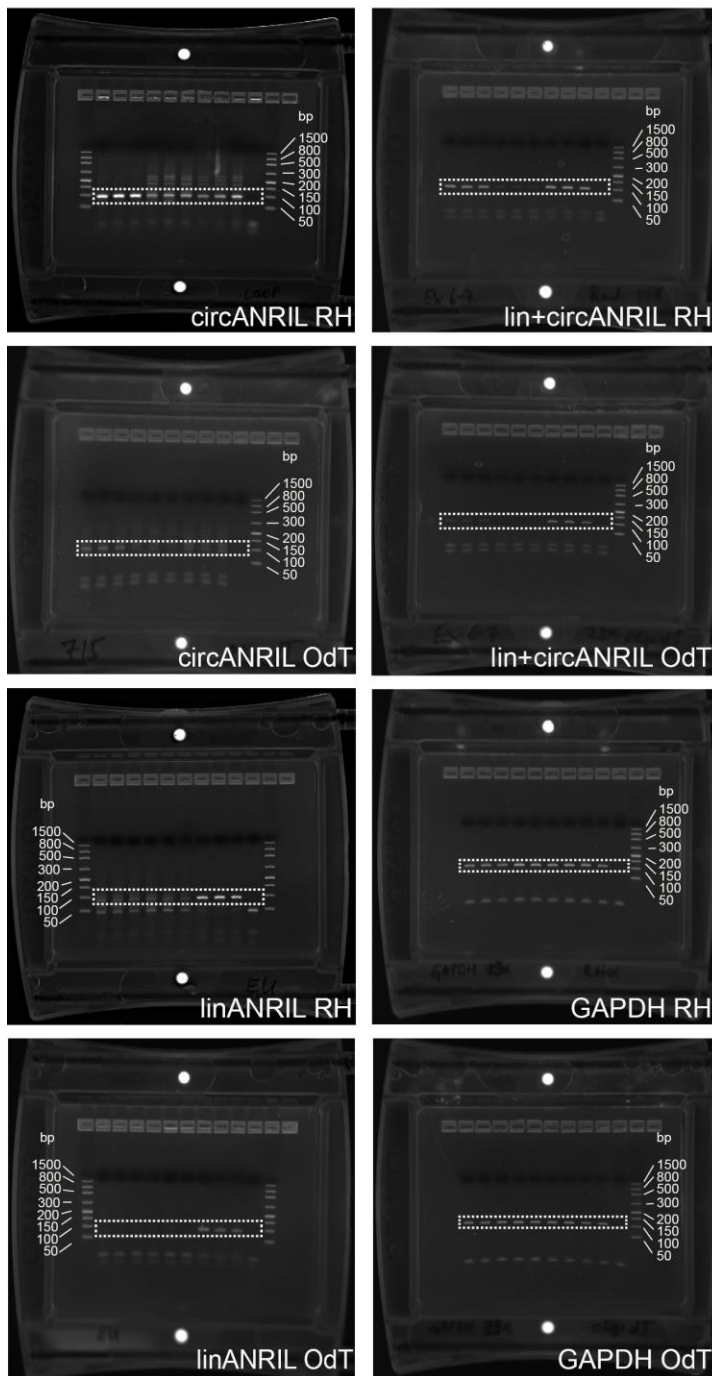
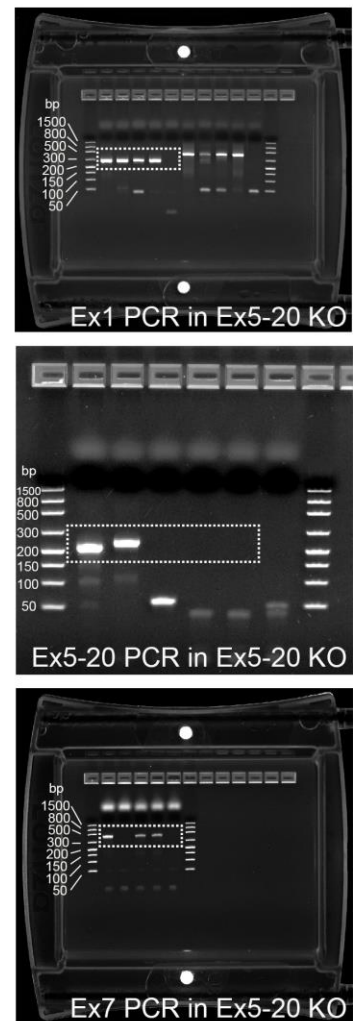
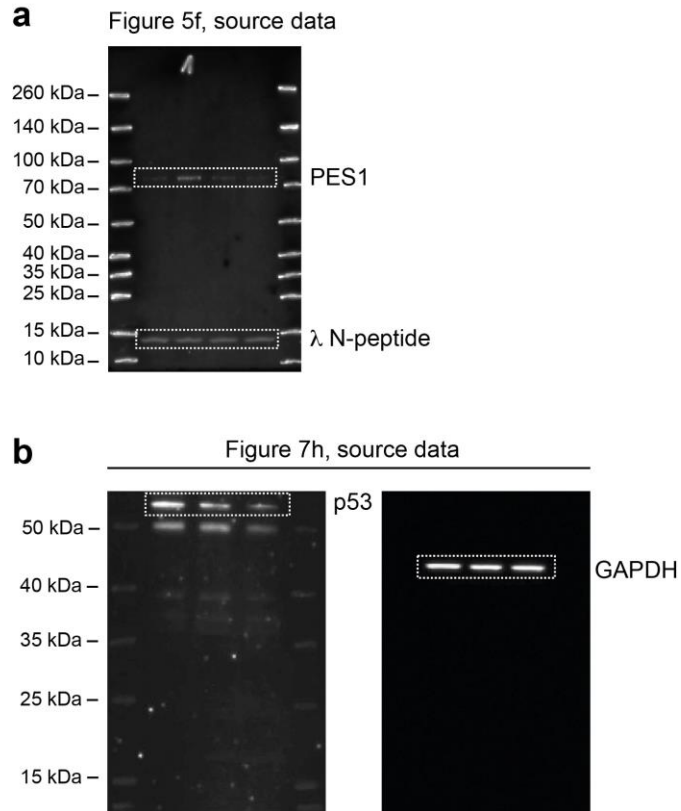
**b**

Figure 3b, source data



**Supplementary Figure 17.** Uncropped scans of DNA agarose gels used in Figures 2b and 3b. Regions that were selected for assembling the figures are indicated with dotted squares. Molecular size marker in base pairs (bp).



**Supplementary Figure 18.** Uncropped scans of Western blots used in Figures 5f and 7h. Regions that were selected for assembling the figures are indicated with dotted squares. The GAPDH blot was stripped and re-probed. Molecular weight marker in kilodaltons (kDa).

## SUPPLEMENTARY TABLES

**Supplementary Table 1.** Plasmid sequences for circular RNA and BoxB overexpression.

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>*circANRIL(ex5-6-7)*, 689 bp without restriction sites, 409 bp exonic sequence

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GAAATTCGCGGCCGC CAATGTATTTCTCTGCTTCATACACTATCCAAGGTGATAAAAAGTGTTTATGAAGAG  
GGATTAGGAAATATCTGCTGTGTTTAGGTCATAGTCCAACCAAAGGATTAATTAACATTTGCCTCTTTTT  
TCTCCTACATCCAGTGTCCCTTTTGTATGAGAAGAATAAGCCTCATTCTGATTCAACAGCAGAGATCAAAG  
AAAAGACTTCTGTTTTCTGGCCACCAGATATATGTTATCTGTGCTTAAAGAAATGAAAAACACACATCAA  
AGGAGAAATTTCTTGAAAGAGAGGGTTCAAGCATCACTGTTAGGTGTGCTGGAATCCTTTCCCGAGTCA  
GTACTGCTTTCTAGAAAAACC GGGGAGATCTATTTGGAATGTATCTAACTCCAAAGAAACCATCAGAG  
GTAACAGTAGAGACGGGGTTTACCATGTTGGCCAGACTGGTCTTGAAC TCCCGACCTCGTGATTGCGCC  
GCCTCGGCC TCCCAAAGTGTGGGATTACAGGTGTGAGACACCACGCCCGGCGGATAGAGAGAATTTTGA  
CAGGTGAGGAGGTATTCCAATGCAAAAAGAATAATAGGAGCAAAAGCACAGTGGTGAGAAAATTGGAGGGGA  
ACTGTGAAAATTGCCACATAGATTAGAGGCAGGAAAATAAAGGACGGCTAAGTTTATATAGTGAACAGTG  
AGCAAGCTTGAATTC

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>*circANRIL-BoxB*, 928 bp without restriction sites, 648 bp exonic sequence incl. BoxB

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GAAATTCGCGGCCGC CAATGTATTTCTCTGCTTCATACACTATCCAAGGTGATAAAAAGTGTTTATGAAGAG  
GGATTAGGAAATATCTGCTGTGTTTAGGTCATAGTCCAACCAAAGGATTAATTAACATTTGCCTCTTTTT  
TCTCCTACATCCAGTGTCCCTTTTGTATGAGAAGAATAAGCCTCATTCTGATTCAACAGCAGAGATCAAAG  
AAAAGACTTCTGTTTTCTGGCCACCAGATATATGTTATCTGTGCTTAAAGAAATGAAAAACACACATCAA  
AGGAGAAATTTCTTGAAAGAGAGGGTTCAAGCATCACTGTTAGGTGTGCTGGAATCCTTTCCATGGCAC  
CATGTGGAATTC TCCGAAAGCTTTTCGCGACTCGAGACTAGTTCTAGATGATCACCCGAGGGGCCCTGAA  
GAAGGGCCCTCGACTAAGTCCAAC TACTAACTGGGGCCCTGAAGAAGGGCCCATATAGGGCCCTGAAGA  
AGGGCCCTATCGAGGATATTTCTCGACTAAGTCCAAC TACTAACTGGGGCCCTGAAGAAGGGCCCATAT  
AGGGCCCTGAAGAAGGGCCCTCCGAGT CAGTACTGCTTTCTAGAAAGAAAACC GGGGAGATCTATTTGGAA  
TGTATCTAACTCCAAAGAAACCATCAGAGGTAACAGTAGAGACGGGGTTTACCATGTTGGCCAGACTGG  
TCTTGAAC TCCCGACCTCGTGATTGCGCCCGCTCGGCC TCCCAAAGTGTGGGATTACAGGTGTGAGACA  
CCACGCCCGCGGATAGAGAGAATTTTGACAGGTGAGGAGGTATTCCAATGCAAAAAGAATAATAGGAGCA  
AAAGCACAGTGGTGAGAAAATTGGAGGGGA ACTGTGAAAATTGCCACATAGATTAGAGGCAGGAAAATAAA  
GGACGGCTAAGTTTATATAGTGAACAGTGAGCAAGCTTGAATTC

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>*BoxB*, 170 bp without restriction sites

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AAGCTTGGGCCCTGAAGAAGGGCCCTCGACTAAGTCCAAC TACTAACTGGGGCCCTGAAGAAGGGCCCA  
TATAGGGCCCTGAAGAAGGGCCCTATCGAGGATATTTCTCGACTAAGTCCAAC TACTAACTGGGGCCCT  
GAAGAAGGGCCCATATAGGGCCCTGAAGAAGGGCCCTCGAC AAGCTT

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>*circHPRT1(ex2-3-4-5-6)*, 738 bp without restriction sites, 458 bp exonic sequence

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GAAATTCGCGGCCGC ACCTACAAAGTTAACAGTTACTAATATCATCTTACACCTAAATTTCTCTGATAGAC  
TAAGGTTATTTTTTAACATCTTAATCCAATCAAATGTTTGTATCCTGTAATGCTCTCATTGAAACAGCTA  
TATTTCTTTTTCAGATTAGTGATGATGAACCAGGTTATGACCTTGATTTATTTTGCATACCTAATCATT  
TGCTGAGGATTTGGAAAGGGTGTTTATTCTCATGGACTAATTTATGGACAGGACTGAACGCTCTTGCTCGA  
GATGTGATGAAGGAGATGGGAGGCCATCACATTGTAGCCCTCTGTGTGCTCAAGGGGGGCTATAAAATCT  
TTGCTGACCTGCTGGATTACATCAAAGCACTGAATAGAAAAGTGTGATAGATCCATTCCATGACTGTAGA  
TTTTATCAGACTGAAGAGCTATTGTAATGACCAGTCAACAGGGGACATAAAAAGTAAATGGTGGAGATGAT  
CTCTCAACTTTAACTGGAAAAGATGCTTTGATTGTGGAAGATATAAATGACACTGGCAAAAACAATGCAGA  
CTTTGCTTTTCCCTGGT CAGGCAGTATAATCCAAGATGGTCAAGGTCGCAAGGTATGTATGACATTTTGA  
CACAGAATATTTTCTCATTGAAGGGGGATTAAGTGATTGCTTCTTTTAAAGGATAAATGTTTTCAACT  
GTCATTTTATCTTCGAAAAGTAATGTAATCTCATATAAGACTTAAGATATAA AAGCTTGAATTC

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DNA sequences for overexpression of circular RNA were cloned into the bicistronic pBI-CMV2 vector (Clontech). GAATTC (dark blue)- EcoRI restriction site, GCGGCCGC (grey) – NotI restriction site, AAGCTT (light blue)- HindIII restriction site, ACGTGGACGT- exonic sequence, exon-exon boundary, ACGT- intronic sequence, ACGT- BoxB sequence.

**Supplementary Table 2.** Sequence validation of ANRIL genomic knockout in HEK-293 cells. Related to Figure 3.

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*>9p21 heterozygous knockout cell line, 202 bp PCR product*

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GGCAGGAGGATCTGGGGCATATGTTTAAATCAGGCATTGGCATCTGTACTAGAATTGAAAGGTGGAAC  
TTATTGTGTTCTATTTATTGAGTATAGGTATACCATATACTATAAGTATAGGTATAGTATACCATACCT  
TAGAGGTTGCTCAAAAAGAAACACAAAATATATCCTCTTTTAAGGATCCTGATGCTTTGCTC

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*>9p21 homozygous knockout cell line, 226 bp PCR product*

---

GGCAGGAGGATCTGGGGCATATGTTTAAATCAGGCATTGGCATCTGTACTAGAATTGAAAGGTGGAAC  
TTATTGTGTTCTATTTATTGAGTATAGGTATACCATATACTATAAGTATAGGTATAGTATACCATACCT  
TGGCAAGGGTGTGGGTAGATGGGTAGAGGTTGCTCAAAAAGAAACACAAAATATATCCTCTTTTAAGGA  
TCCTGATGCTTTGCTC

---

DNA sequences from HEK-293 cell lines with heterozygous or homozygous knockout of 9p21 region. ACGTACGT - genomic sequence, ACGTACGT - primers (see also Supplementary Table 7).

**Supplementary Table 3.** *circANRIL*-bound proteins identified by label-free mass-spectrometric quantification (LFQ).

<b>Proteins</b>	<b>MS/MS Count</b>	<b>LFQ circANRIL+BoxB (log intensity)</b>	<b>LFQ circANRIL (log intensity)</b>	<b>Difference -log(p)* (Δlog)</b>	
NOP14	145	29.07	26.86	2.21	2.09
PES1	117	28.03	25.99	2.04	1.38
SDAD1	27	28.10	26.52	1.58	1.61
LYAR	372	26.95	25.66	1.29	1.67
EIF1AX;EIF1AY	19	27.85	26.67	1.18	2.36
NOLC1	338	30.32	29.18	1.14	2.85
FRG1;FRG1B	57	28.07	26.94	1.12	1.44
DDX54	203	26.13	25.08	1.05	1.48
BMS1	159	26.85	25.92	0.93	2.00
SURF6	219	26.89	26.01	0.88	1.41
ARL6IP4	218	32.07	31.19	0.88	2.95
RFC1	68	31.50	30.63	0.87	2.74
NAT10	356	30.25	29.40	0.86	1.36
NOM1	121	28.78	27.95	0.83	2.16
SLC16A1	35	28.30	27.48	0.82	1.33
MAZ	52	28.43	27.63	0.81	2.88
AKAP17A	232	28.44	27.66	0.78	1.53
UBTF	172	29.59	28.85	0.74	2.16
SF3B2	82	28.67	27.96	0.71	2.30
RPL22	94	30.25	29.67	0.58	2.92
HSPA8	339	30.42	29.90	0.53	2.93
THRAP3	290	30.19	29.68	0.51	1.51
RRP1	143	29.63	29.13	0.50	2.18
RPL36A	84	30.66	30.18	0.48	1.43
PRPF38B	131	29.11	28.65	0.47	2.26
ESF1	112	28.19	27.73	0.46	2.34
PRPF40A	320	30.94	30.49	0.45	1.89
PGAM5	170	30.90	30.46	0.43	1.76
RPL19	241	32.77	32.35	0.42	1.82
PRPF3	164	29.44	29.07	0.37	2.29
ZNF512	88	28.24	27.88	0.36	1.37
RPL13	301	32.50	32.23	0.26	2.09
NOP14	145	29.07	26.86	2.21	2.09
HADHB	24	28,12	25,93	2.04	1.38

\* proteins with significant binding ( $p < 0.05$ ; e.g.  $(-\log(p) > 1.3)$  are given.

**Supplementary Table 4** *De novo* translated proteins in *circANRIL* overexpressing compared to vector control (CTR) HEK-293 cells.

<b>Gene name</b>	<b>Protein name</b>	<b>Ratio 48h/24h (circANRIL/CTR)</b>
SNRPD1	Small nuclear ribonucleoprotein Sm D1	-1.56
EPPK1	Epiplakin	-1.41
EIF1;EIF1B	Eukaryotic translation initiation factor 1;Eukaryotic translation initiation factor 1b	-1.41
CARM1	Histone-arginine methyltransferase CARM1	-1.40
HSPA4L	Heat shock 70 kDa protein 4L	-1.37
TBCE	Tubulin-specific chaperone E	-1.35
CNOT1	CCR4-NOT transcription complex subunit 1	-1.34
KPNA2	Importin subunit alpha-1	-1.33
AIMP1	Aminoacyl tRNA synthase complex-interacting multifunctional protein 1;Endothelial monocyte-activating polypeptide 2	-1.32
BOP1;KM-PA-2	Ribosome biogenesis protein BOP1	-1.32
PSIP1	PC4 and SFRS1-interacting protein	-1.32
GCLM	Glutamate--cysteine ligase regulatory subunit	-1.28
HEATR1	HEAT repeat-containing protein 1	-1.28
TRMT112	tRNA methyltransferase 112 homolog	-1.27
THOC2	THO complex subunit 2	-1.26
CBX5	Chromobox protein homolog 5	-1.26
PPIH	Peptidyl-prolyl cis-trans isomerase H;Peptidyl-prolyl cis-trans isomerase	-1.26
IMPDH1	Inosine-5-monophosphate dehydrogenase 1;Inosine-5-monophosphate dehydrogenase	-1.26
TIAL1	Nucleolysin TIAR	-1.26
EIF4G2	Eukaryotic translation initiation factor 4 gamma 2	-1.26
NOP56	Nucleolar protein 56	-1.25
KRR1	KRR1 small subunit processome component homolog	-1.23
DKC1	H/ACA ribonucleoprotein complex subunit 4	-1.22
HSPA14	Heat shock 70 kDa protein 14	-1.22
EIF5	Eukaryotic translation initiation factor 5	-1.21
ARPC1A	Actin-related protein 2/3 complex subunit 1A	-1.21
MRPL38	39S ribosomal protein L38, mitochondrial	-1.21
H2AFY2	Core histone macro-H2A.2	-1.20
TOP2A	DNA topoisomerase 2-alpha	-1.20
VPS29	Vacuolar protein sorting-associated protein 29	-1.20
CDV3	Protein CDV3 homolog	-1.20
SCAF4	Splicing factor, arginine/serine-rich 15	-1.19
CFL2	Cofilin-2	-1.19
NUP93	Nuclear pore complex protein Nup93	-1.19
PPIF	Peptidyl-prolyl cis-trans isomerase F, mitochondrial	-1.19
RPL35	60S ribosomal protein L35	-1.19
SKIV2L2	Superkiller viralicidic activity 2-like 2	-1.19
DNAJC8	DnaJ homolog subfamily C member 8	-1.19

UGDH	UDP-glucose 6-dehydrogenase	-1.18
HUWE1	E3 ubiquitin-protein ligase HUWE1	-1.18
EEF1A2	Elongation factor 1-alpha 2	-1.18
TOP1	DNA topoisomerase 1	-1.18
EMD	Emerin	-1.18
	Methionine aminopeptidase 2;Methionine	
METAP2	aminopeptidase	-1.18
DIABLO	Diablo homolog, mitochondrial	-1.17
WBP11	WW domain-binding protein 11	-1.17
	Actin, alpha skeletal muscle;Actin, alpha cardiac	
ACTA1;ACTC1;	muscle 1;Actin, gamma-enteric smooth muscle;Actin,	-1.17
ACTG2;ACTA2	aortic smooth muscle	
RFC5	Replication factor C subunit 5	-1.17
KPNA1	Importin subunit alpha-5	-1.17
RRP1B	Ribosomal RNA processing protein 1 homolog B	-1.16
	Protein kinase C and casein kinase substrate in neurons	
PACSIN2	protein 2	-1.16
PPA2	Inorganic pyrophosphatase 2, mitochondrial	-1.16
DDX23	Probable ATP-dependent RNA helicase DDX23	-1.16
DRG1	Developmentally-regulated GTP-binding protein 1	-1.16
PPP1R2;PPP1R2	Protein phosphatase inhibitor 2;Putative protein	-1.16
P3	phosphatase inhibitor 2-like protein 3	
CBX3	Chromobox protein homolog 3	-1.16
TPR	Nucleoprotein TPR	-1.16
	Eukaryotic translation initiation factor 2 subunit	
	3;Putative eukaryotic translation initiation factor 2	-1.15
EIF2S3;EIF2S3L	subunit 3-like protein	
RRP12	RRP12-like protein	-1.15
EIF3K	Eukaryotic translation initiation factor 3 subunit K	-1.15
PLEC	Plectin	-1.15
NUP205	Nuclear pore complex protein Nup205	-1.15
SCFD1	Sec1 family domain-containing protein 1	-1.15
SNRPA1	U2 small nuclear ribonucleoprotein A	-1.15
AKAP12	A-kinase anchor protein 12	-1.15
	Basic leucine zipper and W2 domain-containing protein	
BZW2	2	-1.15
EIF4G1	Eukaryotic translation initiation factor 4 gamma 1	-1.15
PRPF6	Pre-mRNA-processing factor 6	-1.14
	Basic leucine zipper and W2 domain-containing protein	
BZW1	1	-1.14
MST4	Serine/threonine-protein kinase MST4	-1.14
	NHP2-like protein 1;NHP2-like protein 1, N-terminally	
NHP2L1	processed	-1.14
RPL29	60S ribosomal protein L29	-1.14
GDI1	Rab GDP dissociation inhibitor alpha	-1.13
HSP90AB1	Heat shock protein HSP 90-beta	-1.13
SNRPD2	Small nuclear ribonucleoprotein Sm D2	-1.13
DFFA	DNA fragmentation factor subunit alpha	-1.13



NUTF2	Nuclear transport factor 2	-1.13
SUPT5H	Transcription elongation factor SPT5	-1.13
ENO2	Gamma-enolase;Enolase	-1.13
	Glutamine--fructose-6-phosphate aminotransferase	-1.13
GFPT1	[isomerizing] 1	-1.13
RPL30	60S ribosomal protein L30	-1.13
MTPN	Myotrophin	-1.13
EIF3D	Eukaryotic translation initiation factor 3 subunit D	-1.13
UBQLN2	Ubiquilin-2	-1.12
RBM39	RNA-binding protein 39	-1.12
VCL	Vinculin	-1.12
DIS3	Exosome complex exonuclease RRP44	-1.12
IPO9	Importin-9	-1.12
SRRT	Serrate RNA effector molecule homolog	-1.12
COPE	Coatomer subunit epsilon	-1.12
U2AF2	Splicing factor U2AF 65 kDa subunit	-1.12
MLEC	Malectin	-1.12
RPS20	40S ribosomal protein S20	-1.12
	Ribose-phosphate pyrophosphokinase 1;Ribose-	-1.12
PRPS1	phosphate pyrophosphokinase	-1.12
SNRNP70	U1 small nuclear ribonucleoprotein 70 kDa	-1.12
MTA2;DKFZp68		-1.12
6F2281	Metastasis-associated protein MTA2	-1.12
GFM1	Elongation factor G, mitochondrial	-1.12
	Mitochondrial import receptor subunit TOM22	-1.12
TOMM22	homolog	-1.12
	Lamina-associated polypeptide 2, isoform	-1.12
TMPO	alpha;Thymopoietin;Thymopentin	-1.12
PSME3	Proteasome activator complex subunit 3	-1.11
RRS1	Ribosome biogenesis regulatory protein homolog	-1.11
	Deoxyuridine 5-triphosphate nucleotidohydrolase,	-1.11
DUT	mitochondrial	-1.11
UCHL5	Ubiquitin carboxyl-terminal hydrolase isozyme L5	-1.11
	Barrier-to-autointegration factor;Barrier-to-	1.10
BANF1	autointegration factor, N-terminally processed	1.10
CLTB	Clathrin light chain B	1.10
VPS35	Vacuolar protein sorting-associated protein 35	1.10
	Malate dehydrogenase, cytoplasmic;Malate	1.10
MDH1	dehydrogenase	1.10
TSN	Translin	1.11
DNM2	Dynamin-2	1.11
SKP1	S-phase kinase-associated protein 1	1.11
TTLL12	Tubulin--tyrosine ligase-like protein 12	1.11
	Platelet-activating factor acetylhydrolase IB subunit	1.11
PAFAH1B3	gamma	1.11
PSMB5	Proteasome subunit beta type-5	1.11
ANXA7	Annexin A7;Annexin	1.11
HNRNPUL1	Heterogeneous nuclear ribonucleoprotein U-like protein	1.11

	1	
EDC4	Enhancer of mRNA-decapping protein 4	1.11
HIST1H1C	Histone H1.2	1.11
PFKP	6-phosphofructokinase type C	1.11
G6PD	Glucose-6-phosphate 1-dehydrogenase	1.11
HSPA1A	Heat shock 70 kDa protein 1A/1B	1.11
	BH3-interacting domain death agonist;BH3-interacting domain death agonist p15;BH3-interacting domain death agonist p13;BH3-interacting domain death agonist p11	1.12
BID		
FUBP3	Far upstream element-binding protein 3	1.12
ACAT2	Acetyl-CoA acetyltransferase, cytosolic	1.12
FKBP3	Peptidyl-prolyl cis-trans isomerase FKBP3	1.12
RPL19	60S ribosomal protein L19	1.12
	NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial	1.12
NDUFS3		
MAPK1	Mitogen-activated protein kinase 1	1.12
CHORDC1	Cysteine and histidine-rich domain-containing protein 1	1.12
GLOD4	Glyoxalase domain-containing protein 4	1.12
PIIB	Peptidyl-prolyl cis-trans isomerase B	1.12
DDX1	ATP-dependent RNA helicase DDX1	1.12
RAB2A;RAB2B	Ras-related protein Rab-2A;Ras-related protein Rab-2B	1.12
NNT	NAD(P) transhydrogenase, mitochondrial	1.13
HAT1	Histone acetyltransferase type B catalytic subunit	1.13
APRT	Adenine phosphoribosyltransferase	1.13
ASNA1	ATPase ASNA1	1.13
TKT	Transketolase	1.14
CLUH	Clustered mitochondria protein homolog	1.14
	Band 4.1-like protein 3;Band 4.1-like protein 3, N-terminally processed	1.14
EPB41L3		
	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	1.14
ECH1		
PDLIM1	PDZ and LIM domain protein 1	1.14
PHF6	PHD finger protein 6	1.14
SNRPB2	U2 small nuclear ribonucleoprotein B	1.14
	Mini-chromosome maintenance complex-binding protein	1.14
MCMBP		
IARS	Isoleucine--tRNA ligase, cytoplasmic	1.15
THOC3	THO complex subunit 3	1.15
GSTM3	Glutathione S-transferase Mu 3	1.15
CBR1	Carbonyl reductase [NADPH] 1	1.15
	NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial	1.15
NDUFS2		
TCERG1	Transcription elongation regulator 1	1.15
PHPT1	14 kDa phosphohistidine phosphatase	1.15
RCN2	Reticulocalbin-2	1.15
NASP	Nuclear autoantigenic sperm protein	1.16
ECI1;DCI	Enoyl-CoA delta isomerase 1, mitochondrial	1.16

GPD2	Glycerol-3-phosphate dehydrogenase, mitochondrial	1.16
MCM2	DNA replication licensing factor MCM2	1.16
ALDH9A1	4-trimethylaminobutyraldehyde dehydrogenase	1.16
PCBP2;PCBP3	Poly(rC)-binding protein 2;Poly(rC)-binding protein 3	1.16
PSMB6	Proteasome subunit beta type-6	1.17
SEC24C	Protein transport protein Sec24C	1.17
DCTN1	Dynactin subunit 1	1.17
	UDP-N-acetylhexosamine pyrophosphorylase;UDP-N-acetylglucosamine pyrophosphorylase;UDP-N-acetylglucosamine pyrophosphorylase	1.17
UAP1	acetylglucosamine pyrophosphorylase	
APMAP	Adipocyte plasma membrane-associated protein	1.17
	Aspartate aminotransferase, cytoplasmic;Aspartate aminotransferase	1.17
GOT1		
MCM5	DNA replication licensing factor MCM5	1.17
MCM3	DNA replication licensing factor MCM3	1.18
ACO2	Aconitate hydratase, mitochondrial	1.18
	Transforming protein RhoA;Rho-related GTP-binding protein RhoC	1.19
RHOA;RHOC		
MRTO4	mRNA turnover protein 4 homolog	1.19
	Mitochondrial import receptor subunit TOM40 homolog	1.19
TOMM40		
ATP6V1B2	V-type proton ATPase subunit B, brain isoform	1.20
ANXA6	Annexin A6;Annexin	1.20
COPS2	COP9 signalosome complex subunit 2	1.20
MRI1	Methylthioribose-1-phosphate isomerase	1.20
DPYSL2	Dihydropyrimidinase-related protein 2	1.21
BCAP31	B-cell receptor-associated protein 31	1.21
PGP	Phosphoglycolate phosphatase	1.21
KIAA1279	KIF1-binding protein	1.21
PSME1	Proteasome activator complex subunit 1	1.23
CPVL	Probable serine carboxypeptidase CPVL	1.23
IDE	Insulin-degrading enzyme	1.23
GPS1	COP9 signalosome complex subunit 1	1.23
PGD	6-phosphogluconate dehydrogenase, decarboxylating	1.24
IDH1	Isocitrate dehydrogenase [NADP] cytoplasmic	1.24
PRDX2	Peroxiredoxin-2	1.25
	Beta-hexosaminidase subunit beta;Beta-hexosaminidase subunit beta chain B;Beta-hexosaminidase subunit beta chain A	1.25
HEXB		
RFC2	Replication factor C subunit 2	1.27
CAPNS1	Calpain small subunit 1	1.28
NEFL	Neurofilament light polypeptide	1.28
	Glutamate dehydrogenase 1, mitochondrial;Glutamate dehydrogenase;Glutamate dehydrogenase 2, mitochondrial	1.29
GLUD1;GLUD2		
TPP2	Tripeptidyl-peptidase 2	1.30
APEH	Acylamino-acid-releasing enzyme	1.30
MRPS22	28S ribosomal protein S22, mitochondrial	1.30

BPNT1	3(2),5-bisphosphate nucleotidase 1	1.32
CUL4B	Cullin-4B	1.36
COMT	Catechol O-methyltransferase	1.43
BLVRA	Biliverdin reductase A	1.68

*De novo* translated proteins with expression changes +/- 10% within 24 h in *circANRIL* overexpressing relative to control cells (n=197) are listed.

**Supplementary Table 5** Upstream regulator analysis of differentially *de novo* translated proteins in *circANRIL* overexpressing and vector control HEK-293 cells.

<b>Transcription regulator</b>	<b>p-value</b>
HNF4A	$2.43 \times 10^{-8}$
MYC	$3.19 \times 10^{-8}$
TP53	$3.45 \times 10^{-7}$
NFE2L2	$8.14 \times 10^{-7}$
KDM5B	$4.84 \times 10^{-6}$
E2F1	$1.15 \times 10^{-5}$
E2F4	$8.11 \times 10^{-5}$
MYCN	$1.67 \times 10^{-4}$

*De novo* translated proteins with expression changes +/- 10% within 24 h in *circANRIL* overexpressing relative to control cells (n=197) were included in the analysis.

**Supplementary Table 6** Upstream regulator analysis of differentially regulated genes in *circANRIL* overexpressing and vector control HEK-293 cells.

<b>Transcription regulator</b>	<b>p-value</b>
TP53	$8.53 \times 10^{-16}$
MYC	$8.27 \times 10^{-09}$
NUPR1	$2.67 \times 10^{-08}$
TP63	$1.35 \times 10^{-07}$
E2F1	$5.23 \times 10^{-07}$
HNF4A	$6.11 \times 10^{-07}$
HIF1A	$9.38 \times 10^{-07}$
EPAS1	$1.40 \times 10^{-05}$

Genes with expression fold changes of  $< 0.5$  and  $> 2$  in *circANRIL* overexpressing cell lines (n=3; n= 1809) compared to vector control cell lines (n=3) were included in the analysis.

**Supplementary Table 7** Sequence alignment of *circANRIL* and precursor S45S5 rRNA (NM\_046235) using the BLASTn algorithm.

<b>Motif</b>	<b>Sequence alignment</b>				<b>bp (circANRIL)</b>
M1	circANRIL	81	CAGATATATGTTATCTGTGCTT	102	81-102
	RNA45S5	12545	CAGACATTTGGTGTATGTGCTT	12566	
M2	circANRIL	144	AAGAGAGGGTTCAAG	158	144-158
	RNA45S5	8319	AAGAGAGAGTTCAAG	8333	
M3	circANRIL	276	GAGACGGGGTTTTACCATGTTGGCCAGAC	304	276-304
	RNA45S5	6509	GAGAGGGGGTTGCCTCAGGCCGGCCAGAC	6481	
M4	circANRIL	332	CGCCCGCCTCGGCCTCCCAAAGTGCTGGGA	361	332-361
	RNA45S5	1713	CGCCGGCCGCGCGTCCCAACCCGCTGGGA	1684	
M5	circANRIL	381	CGCCGGCGGATAGAGA	397	381-397
	RNA45S5	6965	CGCCGGCTGAGAGAGA	6981	

**Supplementary Table 8.** Plasmid sequences for PES1 wildtype (PES1-WT), PES1 $\Delta$ 1-54 and PES1 $\Delta$ 446-588 overexpression.

*>PES1-WT, 1790 bp exonic sequence*

GCATCCGTCGCCACCATGGGAGGCCCTTGAGAAGAAGAAGTATGAACGAGGCTCGGCCACCAACTACATCA  
CCCCGAAACAAAGCCCCGGAAGAAGCTCCAGCTGAGCTTGGCTGACTTTAGGCGGCTGTGCATTTCTGAAGGG  
CATTTATCCCCATGAACCCAAACACAAGAAGAAGGTTAAACAAGGGTTCACAGCAGCCCCGAACGTTTTTAC  
CTTATCAAAGACATCAGGTTTTCTCCTCCACGAACCCATTGTCAACAAGTTCGGTGAATACAAGGTGTTTCG  
TCCGGAAGCTCCGGAAGGCTTATGGGAAGAGCGAGTGGAACTGTAGAGCGTTTAAAGGACAATAAGCC  
CAACTACAAACTCGACCACATCATCAAGGAACGGTATCCCACGTTTCATCGATGCCCTGCGGGACCTGGAC  
GATGCCCTCTCCATGTGCTTCCGTGTTTTCCACCTTCCCGCGACTGGCAAGTGCCACGTGCAGACCATT  
AGCTGTGCCGCCGGCTCACTGTGGAGTTCATGCACTACATTTATCGCTGCCCGTGCCCTGCGCAAGGCTTT  
CCTGTCCATCAAAGGCATTTACTACCAGGCCGAGGTACTGGGGCAGCCCATCGTGTGGATCACTCCCTAT  
GCCTTCTCCCATGACCACCCGACAGACGTGGACTACAGGGTCATGGCCACCTTCACCGAGTTCTACACCA  
CGCTGCTGGGCTTTGTCAACTTCCGCCCTTACCAGTTGCTCAACCTCCACTATCCCCGAAGCTCGAGGG  
TCAGGCCCAAGCAGAGGCAAAGGCCGGTGGGGCACCTACGCGTTGGACTCCGAGAGTTGTATGGAGAAA  
CTGGCAGCCCTCAGTGCCAGCCTGGCCCCGCTGGTGGTGCCTGCCACAGAGGAGGAGGCCGAGGTGGATG  
AGTTTCCCACCGATGGGGAGATGTCAGCGCAGGAGGAAGACCGCAGGAAGGAGCTGGAGGCCGAGGAGAA  
GCACAAGAAGCTTTTTGAGGGCCTGAAGTCTTCTTCCGAGAGGTGCCCGTGAGGCCCTGACCTGACGTC  
ATCATCAGGAGTTTTGGTGGGGAAGTGTCTGGGACAAATCTTTGTGCATTTGGGGCCACCTATGACGTC  
CAGACTCCCGCATCACCCATCAGATTGTCTGACCCGGCTGGGCAGCAGACCTCAGTCAATTGGCAGGTGCTA  
CGTGCAGCCCCAGTGGGTGTTTACTCAGTGAACGCCAGGCTCCTTCTCCCCGTGGCAGAGTACTTCTCT  
GGGGTGCAGCTGCCCCACACCTTTCACCTTGTGACCGAGAAGGAAGGAGATTACGTTCCACCTGAGA  
AGCTGAAGCTGCTGGCTGTCAGCGGGGAGAGGACCCAGGAACTGAATGAGTCAGAAGAGGAGGAGGA  
AGAGGACGACAACAACGAAGGTGATGGTGAAGAGGGAGAAAATGAGGAGGAGGAGGAAGATGCAGAG  
GCTGGTTTCAGAAAAGGAGGAAGAGGCCCGGCTGGCAGCCCTGGAAGAGCAGAGGATGGAGGGGAAGAAGC  
CCAGGGTGAAGGAGGACCTTGAAGCTGGAGGATAAGCAGCGGCTGGCCCAGGAGGAGGAGAGTGGAGG  
CAAGCGCTGGCCATTATGATGATGAAGAAGCGGAGAAAGTACCTGTACCAGAAGATCATGTTTGGCAAG  
AGGCGAAAATCCGAGAGGCCAACAAGCTGGCGGAGAACGGAAAGCCACGATGAGGCGGTGAGGCTG  
AGAAGAAGGCCAAGAAGGCAAGGCCGAGGGGGGCCACCGTCTGACCGGCCG

*>PES1 $\Delta$ 1-54, 1605 bp exonic sequence*

GCATCCGTCGCCACCATGAACAAGGGTTCACAGCAGCCCCGAACGTTTTTACCTTATCAAAGACATCAGGT  
TTCTCCTCCACGAACCCATTGTCAACAAGTTCGGTGAATACAAGGTGTTTCGTCGGAAGCTCCGGAAGGC  
TTATGGGAAGAGCGAGTGGAACTGTAGAGCGTTTAAAGGACAATAAGCCCAACTACAAACTCGACCAC  
ATCATCAAGGAACGGTATCCCACGTTTCATCGATGCCCTGCGGGACCTGGACGATGCCCTCTCCATGTGCT  
TCCTGTTTTCCACCTTCCCGCGACTGGCAAGTGCCACGTGCAGACCATTACGCTGTGCCGCCGGCTCAC  
TGTGGAGTTTCATGCATACATTTATCGCTGCCCGTGCCCTGCGCAAGGCTTCTCCTGTCCATCAAAGGCA  
TACTACCAGGCCAGGTACTGGGGCAGCCATCGTGTGGATCACTCCCTATGCCCTTCTCCCATGACCACC  
CGACAGACGTGGACTACAGGGTTCATGGCCACCTTACCAGTTCTACACCACGCTGCTGGGCTTTGTCAA  
CTTCCGCCCTTACCAGTTGCTCAACCTCCACTATCCCCGAAGCTCGAGGGTCAAGGCCAAGCAGAGGCA  
AAGGCCGGTGGAGGCCACTACGCGTTGGACTCCGAGAGTTGTATGGAGAACTGGCAGCCCTCAGTGCCA  
GCCTGGCCCCGCTGGTGGTGCCTGCCACAGAGGAGGAGGCCGAGGTGGATGAGTTTCCCACCGATGGGGA  
GATGTCAGCGCAGGAGGAAGACCGCAGGAAGGAGCTGGAGGCCGAGGAGAAGCACAAGAAGCTTTTTGAG  
GGCTGAAGTTCTTCCGAGAGGTTGCCCGTGAGGCCCTGGCCTTTCATCATCAGGAGTTTTTGGT  
GGGAAGTGTCTGGGACAAATCTTTGTGCATTTGGGGCCACCTATGACGTCACAGACTCCCGCATCACCCA  
TCAGATTGTGACCGGCTGGGCAGCAGACCTCAGTCAATTGGCAGGTGCTACGTGCAGCCCCAGTGGGTG  
TTTGACTCAGTGAACGCCAGGCTCCTTCTCCCCGTGGCAGAGTACTTCTCTGGGGTGCAGCTGCCCCAC  
ACCTTTCACCTTTGTGACCGAGAAGGAAGGAGATTACGTTCCACCTGAGAAGCTGAAGCTGCTGGCTCT  
GCAGCGGGGAGAGGACCCAGGAACTGAATGAGTCAGAAGAGGAGGAGGAAGAGGACGACAACAACGAA  
GGTGAATGGTGAAGAGGGAGAAAATGAGGAGGAGGAGGAAGATGCAGAGGCTGGTTTCAGAAAAGGAGG  
AAGAGGCCCGGCTGGCAGCCCTGGAAGAGCAGAGGATGGAGGGGAAGAAGCCAGGGTGAATGGCAGGCAC  
CTTGAAGCTGGAGGATAAGCAGCGGCTGGCCCAGGAGGAGGAGTGGAGGCCAAGCGCTGGCCATTATG  
ATGATGAAGAAGCGGAGAAAGTACCTGTACCAGAAGATCATGTTTGGCAAGAGGCGAAAATCCGAGAGG  
CCAACAAGCTGGCGGAGAACGGAAAGCCACGATGAGGCGGTGAGGCTGAGAAAGAAGGCCAAGAAGGC  
AAGGCCGAGGGGGGCCACCGTCTGACCGGCCG



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>PES1 $\Delta$ 446-588, 1335 bp exonic sequence

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GGATCCGTCGCCACCATGGGAGGCCCTTGAGAAGAAGAAGTATGAACGAGGCTCGGCCACCAACTACATCAC  
CCGGAACAAAGCCCGGAAGAAGCTCCAGCTGAGCTTGGCTGACTTTAGGCGGCTGTGCATTCTGAAGGGCA  
TTTATCCCCATGAACCCAAACACAAGAAGAAGGTTAACAAAGGGTTCTACAGCAGCCCGAACGTTTTACCTT  
ATCAAAGACATCAGGTTTCTCCTCCACGAACCCATTGTCAACAAGTTCCGTGAATACAAGGTGTTTCGTCCG  
GAAGTCCCGAAGGCTTATGGGAAGAGCGAGTGGAACTGTAGAGCGTTTAAAGGACAATAAGCCCAACT  
ACAACTCGACCACATCATCAAGGAACGGTATCCCACGTTTCATCGATGCCCTGCGGGACCTGGACGATGCC  
CTCTCCATGTGCTTCCGTGTTTTCCACCTTCCCGCGACTGGCAAGTGCCACGTGCAGACCATTCAGCTGTG  
CCGCCGGCTCACTGTGGAGTTCATGCACTACATTATCGCTGCCCGTGCCCTGCGCAAGGTCTTCTGTCCA  
TCAAAGGCATTTACTACCAGGCCGAGGTACTGGGGCAGCCCATCGTGTGGATCACTCCCTATGCCTTCTCC  
CATGACCACCCGACAGACGTGGACTACAGGGTTCATGGCCACCTTCACCGAGTTCACACCACGCTGCTGGG  
CTTTGTCAACTTCCGCCTTTACCAGTTGCTCAACCTCCACTATCCCCCGAAGCTCGAGGGTCAGGCCCAAG  
CAGAGGCAAAGGCCGGTGAAGGCACCTACGCGTTGGACTCCGAGAGTTGTATGGAGAACTGGCAGCCCTC  
AGTGCCAGCCTGGCCCGCTGGTGGTGCCTGCCACAGAGGAGGAGCCGAGGTGGATGAGTTTCCACCGA  
TGGGGAGATGTCAGCGCAGGAGGAAGACCGCAGGAAGGAGCTGGAGGCGCAGGAGAAGCACAAGAAGCTTT  
TTGAGGGCCTGAAGTTCTTCTTGAACCGAGAGGTGCCCGTGAGGCCCTGGCCTTCATCATCAGGAGTTTT  
GGTGGGAAGTGTCTGGGACAAATCTTTGTGCATTGGGGCCACCTATGACGTCACAGACTCCCGCATCAC  
CCATCAGATTGTGACCGGCCCTGGGCAGCAGACCTCAGTCATTGGCAGGTGCTACGTGCAGCCCCAGTGGG  
TGTTTGACTCAGTGAACGCCAGGCTCCTTCTCCCGTGGCAGAGTACTTCTCTGGGGTGCAGCTGCCCCCA  
CACCTTTCACCCTTTGTGACCGAGAAGGAAGGAGATTACGTTCCACCTGAGAAGCTGAAGCTGCTGGCTCT  
GGGGGGGCCACCGGTCTGAGCGGCCG

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DNA sequences for overexpression of PES1 wildtype (PES1-WT) and truncated PES1 (PES1 $\square$ 1-54 and PES1 $\square$ 446-588, respectively) were cloned in the pmCherry-N1 vector (Clontech). GGATCC (dark blue)- BamHI restriction site, ACCGGT (grey) – AgeI restriction site, GCGGCCGC (light blue)- NotI restriction site, ACGTACGT - exonic sequence, ACGTACGT- tag-linking sequence.

**Supplementary Table 9** Primers and probes for PCR and qPCR.

Transcript/ NM number	Primer/ probe	Sequence
<i>circANRIL (ex7-5)</i>	5'-primer	5'-GCTGGGATTACAGGTGTGAGACACC-3'
	3'-primer	5'-GAATCAGAATGAGGCTTATTCTTCTCATC-3'
	probe	5'-F-CCCGGCGGATAGAGAGAATTTTGACAGTGTC-3'T
<i>lin+circANRIL (ex6-7)</i>	5'-primer	5'-GGGAGATCTATTTGGAATGTATCTAACTCC-3'
	3'-primer	5'-GAGAGTTCAAGACCAGTCTGGCC-3'
	probe	5'-F-CCATCAGAGGTAACAGTAGAGACGGGGTTTCACC-3'T
<i>circHPRT1 (ex6-2)</i> NM_000194	5'-primer	5'-GGTCAGGCAGTATAATCCAAAGATGG-3'
	3'-primer	5'-CAAATCCTCAGCATAATGATTAGGTATGC-3'
	probe	5'-F-CAAGGTCGCAAGATTAGTGATGATGAACCAGG-3'T
<i>lin+circHPRT1 (ex2-3)</i> NM_000194	5'-primer	5'-GGAAAGGGTGTTTATTCCTCATGG-3'
	3'-primer	5'-GGCCTCCCATCTCCTTCATCA-3'
	probe	5'-F-TGGACAGGACTGAACGTCTTGCTCGAGAT-3'T
<i>PES1</i> NM_014303	5'-primer	5'-GAGTTCATGCACTACATTATCGCTGC-3'
	3'-primer	5'-CTGCCCCAGTACCTCGGCC-3'
	probe	5'-F-TGCCCTGCGCAAGGTCTTCCTGTC-3'T
<i>SOX2</i> NM_003106	5'-primer	5'-CCAGCGCATGGACAGTTACG-3'
	3'-primer	5'-CTGGTCCTGCATCATGCTGTAG-3'
	probe	5'-F-TGAACGGCTGGAGCAACGGCA-3'T
<i>cMAF</i> NM_005360	5'-primer	5'-CAGCGACAACCCGTCCTCTC-3'
	3'-primer	5'-GGCTTCCAAAATGTGGCGTAT-3'
	probe	5'-F-TAACTGAGCCCACTCGCAAGTTGGAGC-3'T

probes: 5'F-= 5'FAMRA-; -3'T = -3'TAMRA

**Supplementary Table 10** gRNA sequences and PCR primers for validation.

<b>Name</b>	<b>gRNA/ primer</b>	<b>Sequence</b>
gRNA 5' <i>ANRIL</i> exon 5	gRNA	5'-GCAGAGAAATACATTGAATA-3'
gRNA 3' <i>ANRIL</i> exon 20	gRNA	5'-GTTAGTTTGGTTGAGGTAAG-3'
Ex1 PCR	5'-primer	5'-CGCGGATTCTGGTGCTGCTC-3'
	3'-primer	5'-GTCCAGATGTCGCGTCAGAGG-3'
Ex7 PCR	5'-primer	5'-CAGACTGGTCTTGA ACTCTCGACCTC-3'
	3'-primer	5'-GCATTCAGGCCAAGGAAGAGAAG-3'
Ex5-20 PCR	5'-primer	5'-GGCAGGAGGATCTGGGGCATATG-3'
	3'-primer	5'-GAGCAAAGCATCAGGATCCTTAAAAG-3'

**Supplementary Table 11** Antibodies for Western blotting (WB), native gel electrophoresis (NG), RNA-immunoprecipitation (RIP), immunofluorescent (IF) stainings and secondary antibodies.

<b>Antibody</b>	<b>Supplier</b>	<b>Catalogue number</b>	<b>Primary/secondary antibody</b>	<b>Host</b>	<b>Mono-/poly-clonal</b>	<b>WB</b>	<b>NG</b>	<b>RIP</b>	<b>IF</b>
GAPDH	Fitzgerald	10R-G109a	p	mouse	m	+			
LAMIN B2	Santa Cruz	sc-377379	p	mouse	m	+			
PES1	Abcam	ab72539	p	rabbit	p	+	+		+
PES1	Santa Cruz	sc-166300	p	mouse	m	+			
TP53 (p53)	Abcam	ab26	p	mouse	m	+			
AGO2	Thermo Scientific	MA5-14861	p	rabbit	m			+	
BOP1	Santa Cruz	sc-390672	p	mouse	m	+	+	+	+
BRIX1	Santa Cruz	sc-373680	p	mouse	m			+	
NOLC1	Santa Cruz	sc-374033	p	mouse	m			+	
NOP14	Abnova	H00008602-B01P	p	mouse	p			+	
PES1	Santa Cruz	sc-166300	p	mouse	m			+	
TP53 (p53)	Abcam	ab90363	p	mouse	m				+
Peroxidase labelled anti-mouse	Vektor Laboratories	PI-2000	s	horse	p	+			
Peroxidase labelled anti-rabbit	Vektor Laboratories	PI-1000	s	goat	p	+			
Alexa Fluor 568 anti-rabbit	Life Technologies	A-11036	s	goat	p				+
Alexa Fluor 568 anti-mouse	Life Technologies	A-11031	s	goat	p				+