

**Table 1. Targets of let-7c significantly downregulated in DS fetal hearts with a (FC)>|1,2| and p-value<0,05. Number of predictions by different databases are also indicated.**

<b>Gene Symbol</b>	<b>Description</b>	<b>FC</b>	<b>p-value</b>	<b>N. of predictions</b>
E2F6	E2F transcription factor 6	-1,592	0,0328	6
DLSTP1	dihydrolipoamide S-succinyltransferase pseudogene 1	-1,724	0,0138	5
HIF1AN	hypoxia inducible factor 1 alpha subunit inhibitor	-1,575	0,0093	5
SLC25A12	solute carrier family 25 member 12	-1,408	0,0088	5
SLC25A4	solute carrier family 25 member 4	-1,55	0,0263	5
ARMC8	armadillo repeat containing 8	-1,541	0,0463	4
H2AFV	H2A histone family member V	-1,259	0,0039	4
MRS2	MRS2, magnesium transporter	-1,416	0,0054	4
PRDM2	PR/SET domain 2	-1,221	0,0321	4
RBPMS	RNA binding protein with multiple splicing	-1,427	0,0046	4
SORBS2	sorbin and SH3 domain containing 2	-1,451	0,0364	4
ABI2	abl interactor 2	-1,253	0,0137	3
AKAP8	A-kinase anchoring protein 8	-1,361	0,0104	3
ALPK3	alpha kinase 3	-1,406	0,0207	3
AREL1	apoptosis resistant E3 ubiquitin protein ligase 1	-1,429	0,0361	3
ARPC5L	actin related protein 2/3 complex subunit 5 like	-1,351	0,0333	3
ASPH	aspartate beta-hydroxylase	-1,403	0,0468	3
CLK2	CDC like kinase 2	-1,422	0,0385	3
EFEMP1	EGF containing fibulin like extracellular matrix protein 1	-1,453	0,0268	3
GLRX3	glutaredoxin 3	-1,232	0,0384	3
HSPB7	heat shock protein family B (small) member 7	-1,422	0,032	3
KDM5C	lysine demethylase 5C	-1,404	0,043	3
MAX	MYC associated factor X	-1,25	0,0485	3
MECP2	methyl-CpG binding protein 2	-1,22	0,0381	3
NUDT15	nudix hydrolase 15	-1,342	0,0318	3
PANK2	pantothenate kinase 2	-1,361	0,0395	3
PCDH7	protocadherin 7	-1,245	0,0261	3
PDLIM5	PDZ and LIM domain 5	-1,456	0,0265	3
TIMM23	translocase of inner mitochondrial membrane 23	-1,508	0,0382	3
TROVE2	TROVE domain family member 2	-1,248	0,0414	3
UBE2G1	ubiquitin conjugating enzyme E2 G1	-1,299	0,0465	3
WBP4	WW domain binding protein 4	-1,517	0,0508	3
YLPM1	YLP motif containing 1	-1,364	0,0239	3
ZNF219	zinc finger protein 219	-1,453	0,0206	3
APOLD1	apolipoprotein L domain containing 1	-1,511	0,0036	2
BLCAP	bladder cancer associated protein	-1,399	0,0022	2
COX10	COX10, heme A:farnesyltransferase cytochrome c oxidase assembly factor	-1,307	0,0101	2
COX5A	cytochrome c oxidase subunit 5A	-1,263	0,04	2
DIDO1	death inducer-obliterator 1	-1,481	0,0056	2
DLAT	dihydrolipoamide S-acetyltransferase	-1,678	0,0377	2
DNPEP	aspartyl aminopeptidase	-1,287	0,023	2
DPYSL4	dihydropyrimidinase like 4	-2,404	0,0131	2

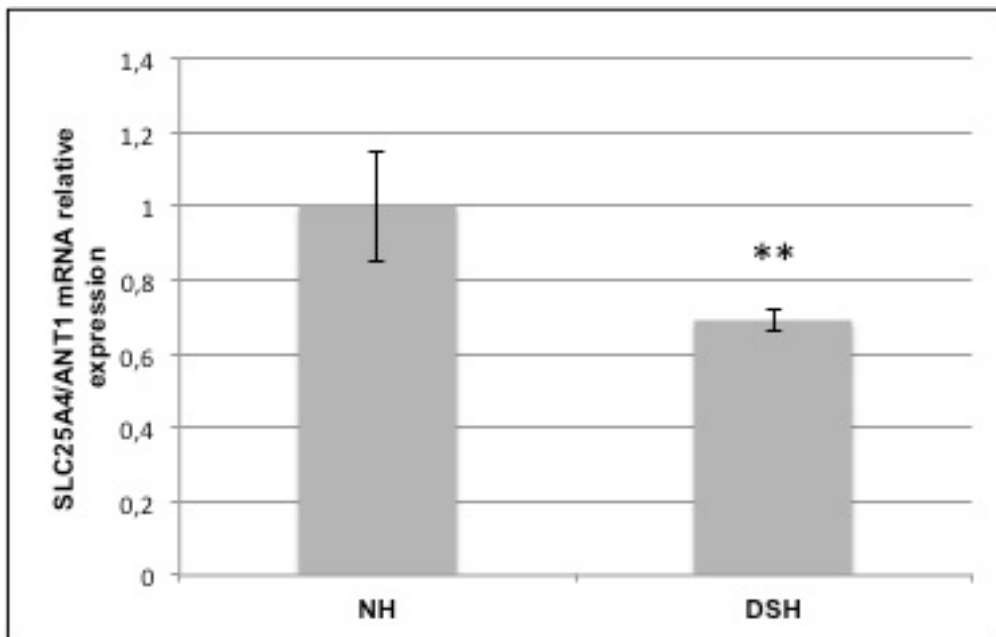
EML5	echinoderm microtubule associated protein like 5	-1,597	0,0522	2
FABP3	fatty acid binding protein 3	-1,692	0,017	2
FKBP4	FK506 binding protein 4	-1,558	0,0549	2
GADD45GIP1	GADD45G interacting protein 1	-1,664	0,0402	2
GHITM	growth hormone inducible transmembrane protein	-1,477	0,0233	2
HERPUD1	homocysteine inducible ER protein with ubiquitin like domain 1	-1,565	0,0331	2
HLA-DRB1	major histocompatibility complex, class II, DR beta 1	-1,634	0,0069	2
KPNB1	karyopherin subunit beta 1	-1,988	0,0012	2
KRT8	keratin 8	-1,629	0,047	2
MAT2A	methionine adenosyltransferase 2A	-1,621	0,0417	2
METAP1	methionyl aminopeptidase 1	-1,381	0,0455	2
MPC1	mitochondrial pyruvate carrier 1	-1,339	0,0129	2
MRPL33	mitochondrial ribosomal protein L33	-1,333	0,0318	2
MTMR9	myotubularin related protein 9	-1,626	0,0287	2
NDST1	N-deacetylase and N-sulfotransferase 1	-1,307	0,0371	2
NDUFS3	NADH:ubiquinone oxidoreductase core subunit S3	-1,314	0,0294	2
NELFB	negative elongation factor complex member B	-1,316	0,0107	2
NMT1	N-myristoyltransferase 1	-1,443	0,0081	2
NOL7	nucleolar protein 7	-1,299	0,0258	2
NQO2	N-ribosyl-dihydropyridinone:quinone reductase 2	-1,348	0,0216	2
PCCB	propionyl-CoA carboxylase beta subunit	-1,335	0,0462	2
PDE4DIP	phosphodiesterase 4D interacting protein	-1,605	0,0172	2
PDHA1	pyruvate dehydrogenase (lipoamide) alpha 1	-1,524	0,0088	2
PDXDC1	pyridoxal dependent decarboxylase domain containing 1	-1,271	0,0363	2
PGS1	phosphatidylglycerophosphate synthase 1	-1,233	0,0387	2
PPFIA4	PTPRF interacting protein alpha 4	-1,629	0,0484	2
RAB27A	RAB27A, member RAS oncogene family	-1,233	0,0186	2
RAB40B	RAB40B, member RAS oncogene family	-1,475	0,0221	2
RASL11B	RAS like family 11 member B	-1,473	0,0287	2
RHBDF1	rhomboid 5 homolog 1	-1,269	0,0159	2
SCHIP1	schwannomin interacting protein 1	-1,267	0,0381	2
SDHC	succinate dehydrogenase complex subunit C	-1,23	0,0456	2
SRSF5	serine and arginine rich splicing factor 5	-1,613	0,0541	2
SUPT20H	SPT20 homolog, SAGA complex component	-1,529	0,0079	2
TMEM161A	transmembrane protein 161A	-1,282	0,0414	2
TMEM43	transmembrane protein 43	-1,252	0,0273	2
TRIP10	thyroid hormone receptor interactor 10	-1,353	0,0476	2
UBN1	ubiquitin 1	-1,357	0,0384	2
UQCC1	ubiquinol-cytochrome c reductase complex assembly factor 1	-1,517	0,0119	2
UQCRFS1	ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1	-1,292	0,0242	2
USP13	ubiquitin specific peptidase 13 (isopeptidase T-3)	-1,431	0,0317	2
ZNF384	zinc finger protein 384	-1,215	0,0322	2
ZNF672	zinc finger protein 672	-1,305	0,0173	2

**Table 2. Targets of miR-155 significantly downregulated in DS fetal hearts with a (FC)>|1,2| and p-value<0,05. Number of predictions by different databases are also indicated.**

<b>Gene Symbol</b>	<b>Description</b>	<b>FC</b>	<b>p-value</b>	<b>N. of predictions</b>
TRIM44	tripartite motif containing 44	-1,664	0,0429	5
WEE1	WEE1 G2 checkpoint kinase	-1,493	0,053	5
ABI2	abl interactor 2	-1,253	0,0137	4
ARMC8	armadillo repeat containing 8	-1,541	0,0463	4
HIPK1	homeodomain interacting protein kinase 1	-1,401	0,052	4
PDLIM5	PDZ and LIM domain 5	-1,456	0,0265	4
EHD1	EH domain containing 1	-1,488	0,0118	3
PCDH7	protocadherin 7	-1,245	0,0261	3
PRDM2	PR/SET domain 2	-1,221	0,0321	3
RANBP10	RAN binding protein 10	-1,311	0,0145	3
RBAK, NT5C	RB associated KRAB zinc finger	-1,524	0,0288	3
WBP4	WW domain binding protein 4	-1,517	0,0508	3
ZNF91	zinc finger protein 91	-1,49	0,0103	3
AATF	apoptosis antagonizing transcription factor	-1,23	0,0168	2
ALPK3	alpha kinase 3	-1,406	0,0207	2
DLAT	dihydrolipoamide S-acetyltransferase	-1,678	0,0377	2
DUSP14	dual specificity phosphatase 14	-1,645	0,0128	2
EEF1D	eukaryotic translation elongation factor 1 delta	-1,321	0,0475	2
EML5	echinoderm microtubule associated protein like 5	-1,597	0,0522	2
HIF1AN	hypoxia inducible factor 1 alpha subunit inhibitor	-1,575	0,0093	2
HSPB7	heat shock protein family B (small) member 7	-1,422	0,032	2
LPIN1	lipin 1	-1,838	0,0317	2
MECP2	methyl-CpG binding protein 2	-1,22	0,0381	2
MNAT1	MNAT1, CDK activating kinase assembly factor	-1,383	0,0308	2
NDUFS3	NADH:ubiquinone oxidoreductase core subunit S3	-1,314	0,0294	2
NGRN	neugrin, neurite outgrowth associated	-1,342	0,0363	2
RNF216	ring finger protein 216	-1,506	0,0185	2
SCHIP1	schwannomin interacting protein 1	-1,267	0,0381	2
SIRT5	sirtuin 5	-1,255	0,029	2
SORBS2	sorbin and SH3 domain containing 2	-1,451	0,0364	2
SUPT20H	SPT20 homolog, SAGA complex component	-1,529	0,0079	2
TAX1BP1	Tax1 binding protein 1	-1,374	0,03	2
YWHAQ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein theta	-1,364	0,0483	2

**Table 3. Targets of miR-99a significantly downregulated in DS fetal hearts with a (FC)>|1,2| and p-value<0,05. Number of predictions by different databases are also indicated.**

Gene Symbol	Description	FC	p-value	N. of predictions
HIPK1	homeodomain interacting protein kinase 1	-1,401	0,05	3
ARPC5L	actin related protein 2/3 complex subunit 5 like	-1,351	0,0333	2
CDC42	cell division cycle 42	-1,416	0,0047	2
ING1	inhibitor of growth family member 1	-1,335	0,0058	2
NMT1	N-myristoyltransferase 1	-1,443	0,0081	2
PCDH7	protocadherin 7	-1,245	0,0261	2
RALGAPB	Ral GTPase activating protein non-catalytic beta subunit	-1,245	0,0414	2
TARDBP	TAR DNA binding protein	-1,3	0,0495	2
TNPO2	transportin 2	-1,325	0,0338	2
UQCC1	ubiquinol-cytochrome c reductase complex assembly factor 1	-1,517	0,0119	2



**Figure 1. *SLC25A4/ANT1* expression in heart tissue by qRT-PCR.**

Real-time PCR of *SLC25A4/ANT1* in trisomic hearts confirmed the downregulation obtained by microarray analysis. Results are expressed as relative mean values  $\pm$  SEM of 3 trisomic samples (DSH), compared with control hearts (NH) set equal to 1.

\*\* p < 0.01. P-value expresses statistical significance for trisomic versus non trisomic sample comparisons.