

**Table 1S.** Up (↑) and down (↓) regulated genes in left ventricles of low protein rats, biological function and references

	GENE	FUNCTION/LOCATION
<b>HYPERTROPHY</b>	↑ elongation factor for RNA polymerase II 2 (Eif2)	pro-hypertrophy (1,2)
	↓ RAB20, member RAS oncogene Family (Rab20)	pro-hypertrophy (3)
	↓ profilin 1 (Pfn1)	pro-hypertrophy (4,5)
	↓ peptidylprolyl isomerase H (Ppih)	pro-hypertrophy (6)
	↑ adenylosuccinate synthase like 1 (Adssl1)	pro-hypertrophy by AngII (7)
	↑ myosin light chain kinase (Mylk)	pro-hypertrophy by AngII (8)
	↑ cAMP responsive element binding protein 5 (Creb5)	pro-hypertrophy (9–11)
	↑ INO80 complex subunit D (Ino80d)	pro-hypertrophy (12,13)
	↓ casein kinase 1, gamma 1 (Csnk1g1)	pro-hypertrophy (14)
↑ CREB binding protein (Crebbp)	pro-hypertrophy (11,15,16)	
<b>FIBROSIS</b>	↑ plasminogen activator, tissue type (Plat)	pro- fibrosis (17)
	↑ procollagen lysine, 2-oxoglutarate 5-dioxygenase 2(Plod2)	pro- fibrosis (18)
	↓ ADAM metallopeptidase domain 33 (Adam33)	anti- fibrosis (19)
	↑ anthrax toxin receptor 1( Antxr1)	anti- fibrosis (20,21)
	↑ ADAM metallopeptidase with thrombospondin type 1 motif, 1 (Adamts1)	anti- fibrosis (22)
	↑ Heparanase (Hpse)	anti- fibrosis (23)
↓ collagen type XXIV alpha 1 chain (Col24a1)	fibrosis indicative (24)	
<b>CARDIAC FUNCTION</b>	↓ protein BEX1-like(LOC100912195) BEX1-like	increases in heart failure (25)
	↑ ankyrin repeat domain 33B (Ankrd33b)	increases in heart failure (26)
	↑ corticotropin releasing hormone receptor 2 (Crhr2)	worse function (27)
	↓ SH3 domain binding glutamate-rich protein (Sh3bgr)	improve function (28)
	↑ proprotein convertase subtilisin/kexin type 6 (Pcsk6)	improve function (29)
<b>ADRENORECEPTORS</b>	↓ adrenoceptor beta 1 (Adrb1)	adrenergic receptor beta1 (30)
	↑ sorting nexin family member 27 (Snx27)	internalization and recycling (31)
	↑ arrestin domain containing 4 (Arrdc4)	internalization and recycling (32)
	↑ kinesin family member 22 (Kif22)	cytoskeleton (33)
	↑ nuclear receptor subfamily 4, group A, member 3(Nr4a3)	regulated by adrenergic signals (34)
<b>INSULIN</b>	↑ inositol hexakisphosphate kinase 3 (Ipk3)	Increases in diabetes mellitus (35)
	↑ Casitas B-lineage lymphoma b (Cblb)	irs1 degradation (36)
	↑ insulin receptor substrate 2 (Irs2)	glucose metabolism (15,37)
	↑ CREB binding protein (Crebbp)	Irs2 inactivation (15,16)
<b>LIPÍDIC METABOLISM</b>	SCAN domain-containing 1(Scand1)	HDL metabolismo regulation (38–41)
	↑ cytochrome P450, family 1, subfamily b, polypeptide 1(Cyp1b1)	lipidic metabolism (42,43)
	↑ lipolysis stimulated lipoprotein receptor(Lsr)	lipidic metabolism (44)
	↑ TLC domain containing 1(Tlcd1)	lipid synthesis and traffic (45–47)
	↓ amyloid beta precursor like protein 1(Aplp1)	Lipid accumulation (9,48,49)
	↑ abhydrolase domain containing 2(Abhd2)	hyperlipidemia marker (50)
<b>CARBOHYDRATE METABOLISM</b>	↑ protein phosphatase 1, regulatory subunit 3C (Ppp1r3c)	glycogen synthesis (51)
	↑ beta-1,3-N-acetylgalactosaminyltransferase 2 (B3galnt2)	oligosaccharide synthesis (52)
	↑ beta-1,4-galactosyltransferase 1 (B4galt1)	carbohydrate synthesis (53)
	↑ ALG2, alpha-1,3/1,6-mannosyltransferase (Alg2)	carbohydrate metabolism (54)
	↑ glutamine-fructose-6-phosphate transaminase 2 (Gfpt2)	glutamine metabolism (54)
	↓ carbohydrate sulfotransferase 12 (Chst12)	carbohydrate metabolism (54)
<b>OXIDATIVE STRESS</b>	↓ thioredoxin 2 (Txn2)	reduces ROS (55)
	↓ reactive oxygen species modulator 1-like(LOC100910944) (Modula ROS)	reduces ROS (56,57)
	↓ glutathione S-transferase theta 1 (Gstt1)	reduces ROS (58)
	↓ glutathione S-transferase alpha 5 (Gsta5)	reduces ROS (59)
	↓ similar to Tpi1 protein(RGD1563601) (sim Tpi1)	reduces ROS (60)
	↓ thioredoxin domain containing 17 (Txndc17)	reduces ROS (61)
	↑ cytochrome P450, family 1, subfamily b, polypeptide 1 (Cyp1b1)	produces ROS (62)
	↑ FAT atypical cadherin 1 (Fat1)	Induced by ROS (63)
↑ anterior gradient 2, protein disulphide isomerase family	Induced by ROS (64)	

	member (Agr2)	
INFLAMMATION	↓adenosine kinase(Adk)	anti-inflammation (65)
	↓ankyrin repeat and SOCS box-containing 18(Asb18)	anti-inflammation (66)
	↑RAD21 cohesin complex component(Rad21)	anti-inflammation (67)
	↑interleukin 2 receptor subunit beta(Ilr2rb)	pro-inflammation (68)
	↑interferon induced with helicase C domain 1(Ifh1)	pro-inflammation (69)
	↓TNF alpha induced protein 6(Tnfaip6)	pro-inflammation (70)
	↑interleukin 18 receptor accessory protein(Ilr18rap)	pro-inflammation (71)
	↑plasminogen activator, tissue type(Plat)	indication of inflammation (17)
	↓CD1d1 molecule(Cd1d1)	indication of inflammation (72)
	↑NLR family, CARD domain containing 5(Nlr5)	indication of inflammation (73)
↑myeloid cell nuclear differentiation antigen(Mnda)	indication of inflammation (74)	
APOPTOSIS	↓similar to RIKEN cDNA B230118H07(RGD1309730) (s RIKEN cDNA)	pro- apoptosis (75)
	↑deoxyribonuclease 1 like 2 (Dnase1l2)	pro- apoptosis (76)
	↓nucleolar protein 12(Nol12)	pro- apoptosis (77)
	↓sphingosine kinase 1(Sphk1)	anti- apoptosis (78)
	↓serpin family B member 7(Serpinb7)	anti- apoptosis (79)
	↑abhydrolase domain containing 2(Abhd2)	anti- apoptosis (50)
	↑CCR4-NOT transcription complex, subunit 1(Cnot1)	anti- apoptosis (80)
↓amyloid beta precursor like protein 1(Aplp1)	indication of apoptosis (81)	
AUTOPHAGY	↓ankyrin repeat and SOCS box-containing 18(Asb18)	pro-autiphagy (82)
	↓biogenesis of lysosomal organelles complex-1, subunit 3(Bloc1s3)	pro-autiphagy (83)
	↑transmembrane protein 41B(Tmem41b)	pro-autiphagy (84)
	↑component of oligomeric golgi complex 2(Cog2)	pro-autiphagy (85)
	↑abhydrolase domain containing 2(Abhd2)	pro-autiphagy (50)
ONCOGENES	↓rabaptin, RAB GTPase binding effector protein 2(Rabep2)	oncogene (54)
	↓RAB20, member RAS oncogene family(Rab20)	oncogene (54)
	↓RAB15, member RAS oncogene family(Rab15)	oncogene (54)
	↓zinc finger and SCAN domain containing 21(Zscan21)	oncogene (54)
	↓RAP1B, member of RAS oncogene family(Rap1b)	oncogene (54)
	↑pogo transposable element with KRAB domain(Pogk)	oncogene (54)
Ca <sup>++</sup> METABOLISM	↓S100 calcium binding protein A16(S100a16)	Ca <sup>++</sup> metabolism (54)
	↓granalcin(Gca)	Ca <sup>++</sup> metabolism (54)
	↑abhydrolase domain containing 2(Abhd2)	Ca <sup>++</sup> metabolism (54)
	↓S100 calcium binding protein A9(S100a9)	Ca <sup>++</sup> metabolism (54)
PROTEIN SYNTHESIS	↓ARP6 actin-related protein 6 homolog(Actr6)	protein synthesis (86)
	↑eukaryotic translation initiation factor 4E binding protein 3(Eif4ebp3)	mRNA translation (54)
	↓ribonucleic acid export 1(Rae1)	protein synthesis (54)
	↑tripartite motif-containing 25(Trim25)	RNA ubiquitination (5)
	↑INO80 complex subunit D(Ino80d)	transcriptional regulation and DNA repair (54)
	↓RNA polymerase II subunit E(Polr2e)	protein synthesis (54)
↑PHD finger protein 8(Phf8)	protein synthesis (87)	
DNA RELATED PROTEINS	↓polynucleotide kinase 3'-phosphatase (Pnkp)	DNA repair (88)
	↓regulator of telomere elongation helicase 1 (Rtel1)	DNA repair (89)
	↑INO80 complex subunit D (Ino80d)	DNA repair (90)
	↓RAD51 associated protein 1 (Rad51ap1)	DNA repair (91)
	↓nucleolar protein 12 (Nol12)	DNA repair (77)
	↓kelch domain containing 8B (Klhdc8b)	DNA stability (92)
	↑deoxyribonuclease 1 like 2 (Dnase1l2)	DNA stability (76)
MEMBRANE COMPOUNDS	↓transmembrane protease, serine 9(Tmprss9)	membrane structure (54)
	↑transmembrane protein 132D(Tmem132d)	membrane structure (54)
	↓transmembrane protein 160(Tmem160)	membrane structure (54)
	↑phosphatidylinositol glycan anchor biosynthesis, class A(Piga)	membrane structure (54)
	↑TLC domain containing 1(Tlcd1)	membrane structure (54)
	↓SH3 domain binding glutamate-rich protein(Sh3bgr)	membrane structure (54)
	↑plakophilin 3(Pkp3)	membrane structure (54)
	↓small cell adhesion glycoprotein(Smagp)	membrane structure (54)
↓adhesion molecule with Ig like domain 2(Amigo2)	membrane structure (54)	
	↓FSDH region gene 1(Frg1)	cytoskeleton (54)
	↑protocadherin alpha 4(Pcdha4)	cytoskeleton (54)

<b>CYTOSKELETON</b>	↑similar to formin-like 2 isoform B(RGD1560248) (s formin-like 2B)	cytoskeleton (54)
	↑tetratricopeptide repeat domain 28(Ttc28)	cytoskeleton (54)
	↓NSL1, MIS12 kinetochore complex component(Nsl1)	cytoskeleton (54)
	epsin 3(Epn3)	cytoskeleton (54)
	↓SH3 domain binding glutamate-rich protein(Sh3bgr)	cytoskeleton
<b>ENZIME METABOLISM</b>	↑cytochrome P450, family 4, subfamily v, polypeptide 3(Cyp4v3)	enzyme metabolism and function (54)
	↑cytochrome P450, family 1, subfamily b, polypeptide 1(Cyp1b1)	enzyme metabolism and function (54)
	↑protein tyrosine kinase 2(Ptk2)	enzyme metabolism and function (54)
	↓biogenesis of lysosomal organelles complex-1, subunit 3(Bloc1s3)	enzyme metabolism and function (54)
	↓potassium voltage-gated channel modifier subfamily G member 2(Kcng2)	ion channel (54)
<b>ION CHANNELS</b>	↑myosin Vb(Myo5b)	ion channel (54)
	↑WNK lysine deficient protein kinase 3(Wnk3)	ion channel (54)
	↑ATPase Na <sup>+</sup> /K <sup>+</sup> transporting subunit beta 1(Atp1b1)	ion channel (54)
	↓hyperpolarization activated cyclic nucleotide-gated potassium channel 4(Hcn4)	ion channel (54)

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