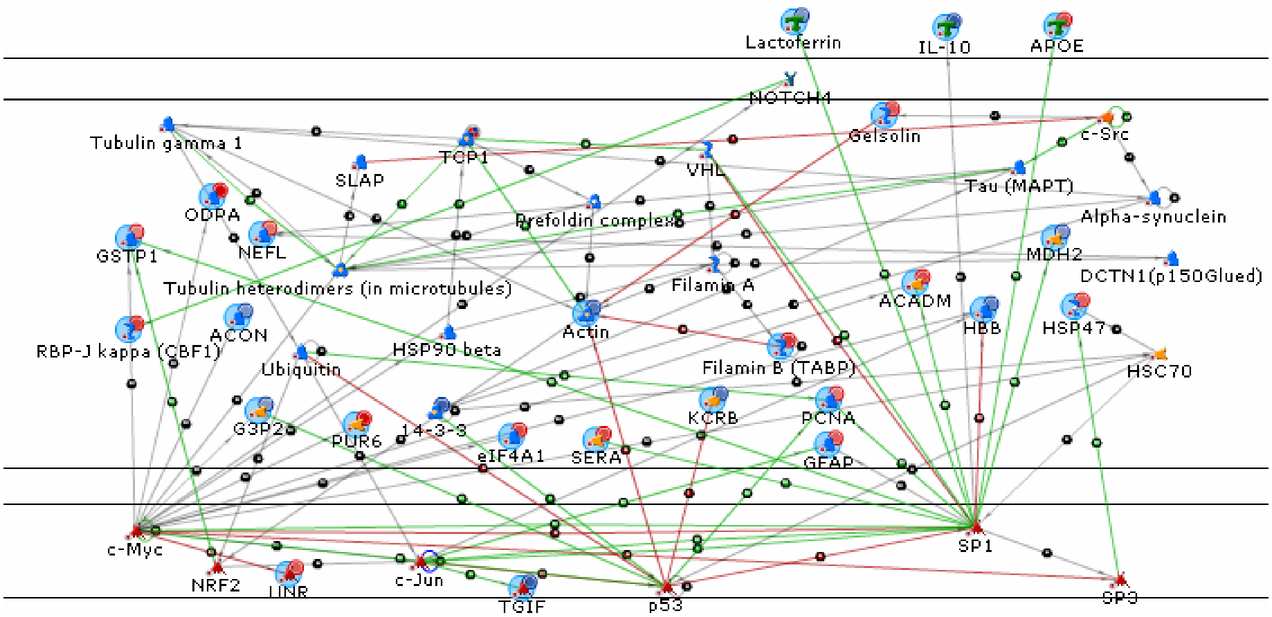
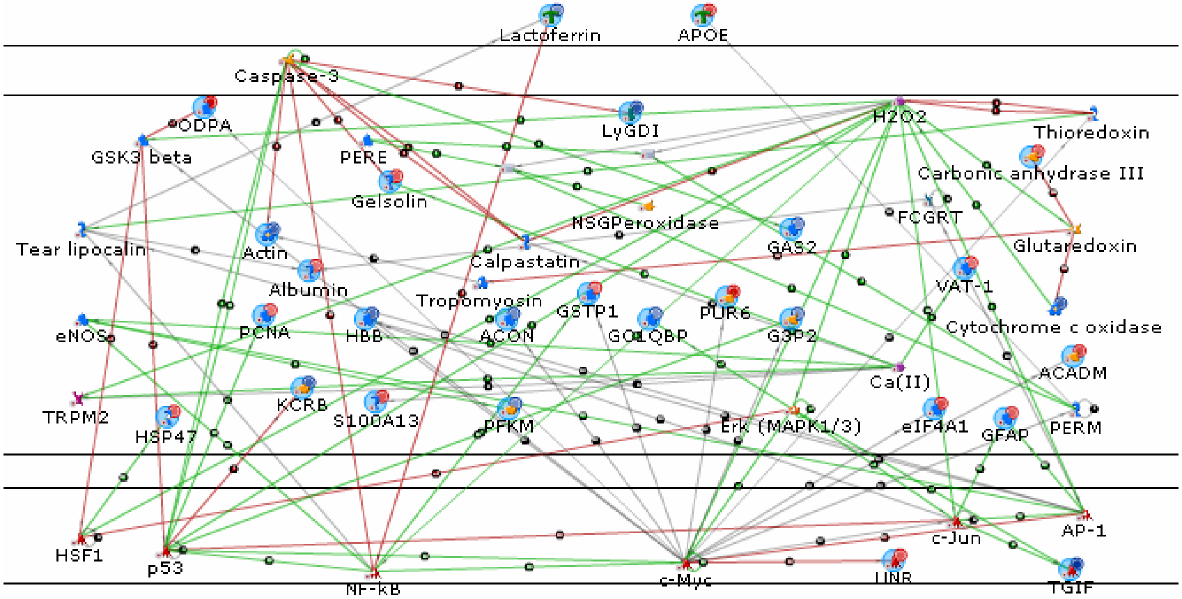
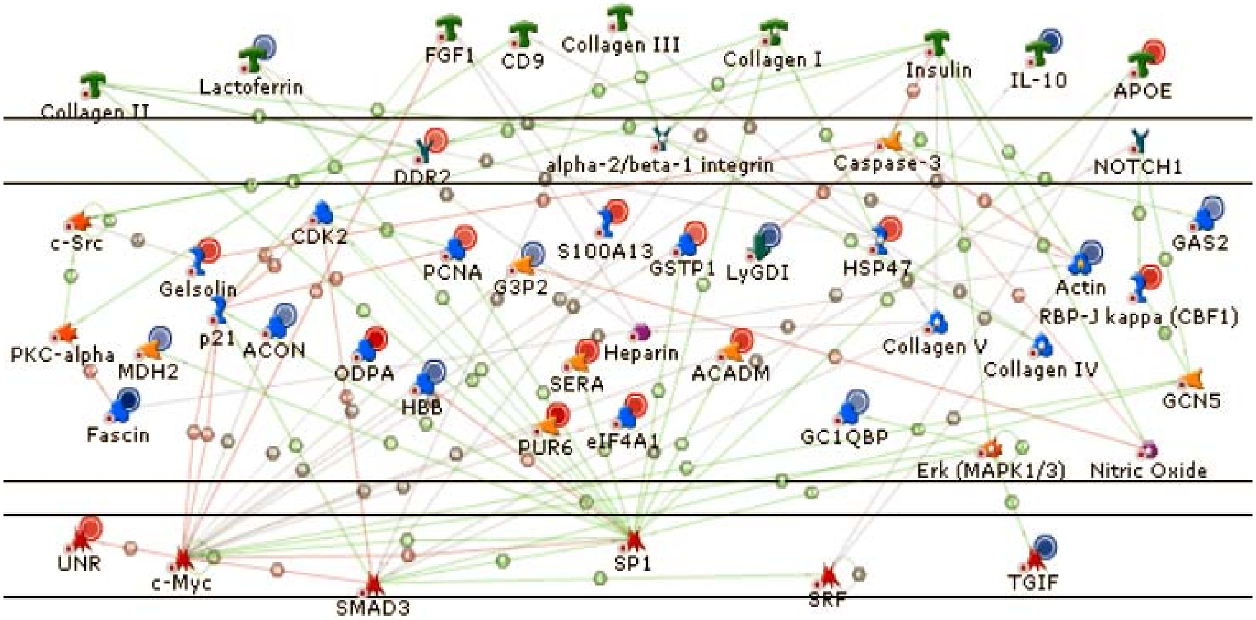
Supplemental Figure 1: Network 1 showing confident interactions



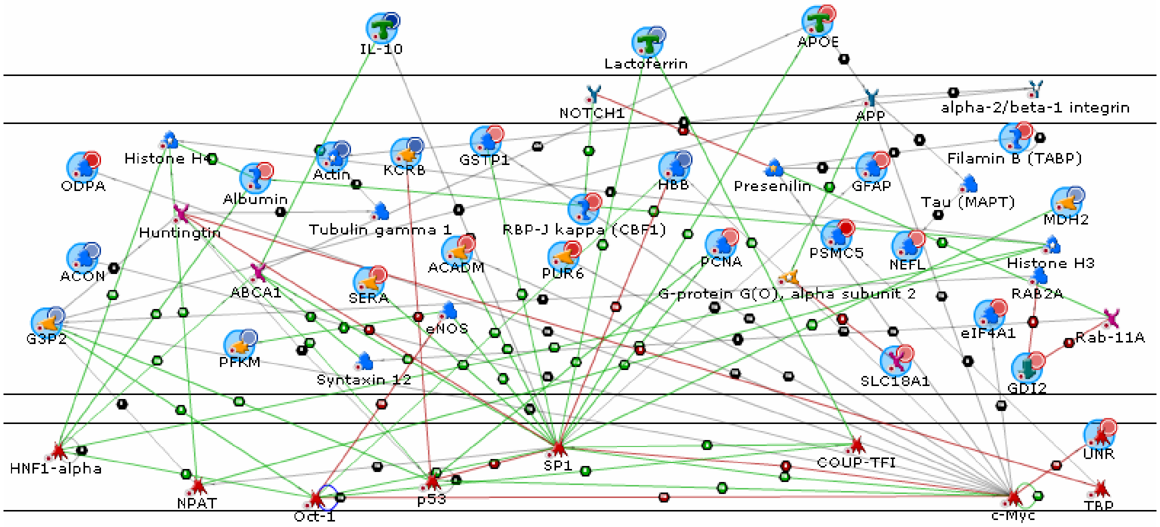
Supplemental Figure 2: Network 2 showing confident interactions



Supplemental Figure 3: Network 3 showing confident interactions



Supplemental Figure 4: Network 4 showing confident interactions



Supplemental Table 1: List of differentially expressed proteins

Spot No.	T-test	Av. Ratio MT/WT	GI #	Protein name	Protein Probability	Peptide (Coverage %)
173	0.0082	1.46	28916693	gelsolin	6.7E-13	10 (16)
			21450287	upstream of NRAS	3.4E-10	14 (20)
186	0.026	1.23	28916693	gelsolin	1.1E-15	17 (29)
			33859506	albumin 1	3.4E-11	33 (48)
187	0.037	1.31	28916693	gelsolin	5.2E-14	17 (31)
205	0.012	-1.16	18079339	aconitase 2, mitochondrial	1.6E-12	25 (36)
206	0.02	-1.15	31560677	lactotransferrin	5.7E-12	12 (19)
			31981185	phosphofructokinase, muscle	2.6E-11	11 (16)
			18079339	aconitase 2, mitochondrial	9.4E-11	37 (53)
436	0.016	1.12	6678359	transketolase	1.0E-30	20 (47)
			33667042	heterogeneous nuclear ribonucleoprot	5.2E-11	8 (17)
510	0.0072	1.27	7305565	t-complex protein 1	2.0E-12	7 (15)
			12963757	myo-inositol 1-phosphate synthase A1	3.00E-10	11 (21)
522	0.0047	1.52	12963757	myo-inositol 1-phosphate synthase A1	7.30E-10	11 (24)
599	0.0057	1.2	6679687	glucose regulated protein	4.00E-09	11 (25)
709	0.0052	1.17	31981273	CNDP dipeptidase 2 (metallopeptidase	1.50E-11	19 (50)
715	0.0017	-1.13	6679745	fascin homolog 1, actin bundling prot	6.40E-12	12 (32)
723	0.099	-1.7	6679745	fascin homolog 1, actin bundling prot	4.20E-10	6 (16)
			6677981	vacuolar protein sorting 4b	1.30E-08	6 (17)
			6671700	chaperonin subunit 2 (beta)	5.60E-08	4 (13)
743	0.0078	-1.21	31980648	ATP synthase, H+ transporting mitoch	5.10E-10	23 (44)
810	0.045	1.41	26080422	glial fibrillary acidic protein	3.60E-10	14 (35)
			19527048	heterogeneous nuclear ribonucleoprot	7.30E-08	4 (10)
			30794476	protein kinase, cAMP dependent regul	7.20E-07	5 (19)
861	0.014	1.23	56119103	guanosine diphosphate (GDP) dissocia	2.50E-13	22 (51)

			33859662	vesicle amine transport protein 1 ho	7.10E-11	7 (22)
894	0.008	1.62	21450625	eukaryotic translation initiation fa	1.00E-09	3 (10)
907	0.0094	1.28	8393866	ornithine aminotransferase	9.00E-11	7 (21)
912	0.0046	1.32	38198665	p47 protein	2.0E-06	1 (4)
917	0.0054	1.21	8393866	ornithine aminotransferase	9.6E-12	11 (22)
939	0.0097	1.61	63518159	PREDICTED: phosphogluconate dehydrog	1.0E-12	4 (11)
			6680956	coagulation factor C homolog (Limulus	1.1E-12	13 (28)
942	0.0027	1.51	63518159	PREDICTED: phosphogluconate dehydrog	5.6E-12	2 (5)
			6680956	coagulation factor C homolog (Limulus	1.6E-11	14 (24)
			7305363	platelet-activating factor acetylhydr	2.0E-10	12 (30)
945	0.00084	1.73	6680956	coagulation factor C homolog (Limulus	1.3E-11	16 (28)
			33859554	fumarate hydratase 1	1.1E-08	4 (12)
947	0.00018	1.44	6679261	pyruvate dehydrogenase E1 alpha 1	2.4E-14	22 (52)
			6680956	coagulation factor C homolog (Limulus	3.0E-13	26 (54)
962	0.0014	1.32	33859554	fumarate hydratase 1	8.9E-15	19 (37)
			6680956	coagulation factor C homolog (Limulus	1.8E-14	25 (51)
969	0.01	1.4	33859554	fumarate hydratase 1	1.0E-15	22 (40)
			6753304	serine (or cysteine) proteinase inhib	2.0E-15	9 (9)
985	0.0053	-1.31	10946574	creatine kinase, brain	6.3E-13	17 (46)
			6753416	chitinase 3-like 3	8.5E-11	19 (51)
			46593021	ubiquinol-cytochrome c reductase cor	6.8E-10	5 (11)
			6671509	actin, beta, cytoplasmic	2.6E-08	9 (24)
991	0.0008	2.55	6680956	coagulation factor C homolog (Limulus	1.1E-16	29 (56)
			7110703	protease (prosome, macropain) 26S sub	8.3E-12	12 (32)
992	0.00023	1.69	6680956	coagulation factor C homolog (Limulus	2.0E-15	23 (46)
995	3.10E-05	2.18	6680956	coagulation factor C homolog (Limulus	1.0E-30	23 (40)
			6679261	pyruvate dehydrogenase E1 alpha 1	1.0E-30	9 (23)
1002	0.013	1.91	6680956	coagulation factor C homolog (Limulus	2.0E-13	27 (59)

			21313144	GTP-binding protein PTD004	6.0E-11	12 (33)
			6753428	creatine kinase, mitochondrial 1, ubi	2.9E-10	13 (35)
1004	0.0012	2.22	7110703	protease (prosome, macropain) 26S sub	5.9E-14	24 (19)
			6753476	cyclic nucleotide phosphodiesterase 1	4.9E-13	6 (17)
			51766806	PREDICTED: similar to Pgk1 protein	1.9E-12	7 (11)
1005	0.019	1.72	6680956	coagulation factor C homolog (Limulus	9.0E-15	21 (43)
			51766806	PREDICTED: similar to Pgk1 protein	2.0E-10	15 (42)
1010	0.032	1.53	6680956	coagulation factor C homolog (Limulus	2.7E-14	18 (35)
1011	0.0031	1.68	6680956	coagulation factor C homolog (Limulus	4.2E-11	10 (26)
			13386272	citrate synthase-like protein	1.4E-10	2 (5)
1019	0.00093	2.12	7110703	protease (prosome, macropain) 26S sub	5.5E-13	24 (52)
			6680956	coagulation factor C homolog (Limulus	2.1E-12	15 (36)
			13385434	phosphoribosylaminoimidazole carboxy	4.0E-10	10 (26)
			6679261	pyruvate dehydrogenase E1 alpha 1	1.9E-09	12 (31)
1039	0.045	1.89	51766806	PREDICTED: similar to Pgk1 protein	3.3E-15	19 (58)
			6680956	coagulation factor C homolog (Limulus	1.1E-14	11 (28)
1042	0.013	1.47	6680956	coagulation factor C homolog (Limulus	4.4E-15	9 (22)
			51766806	PREDICTED: similar to Pgk1 protein	4.8E-11	14 (43)
1065	0.0027	-1.16	1338474	aminoacylase 1	5.8E-14	17 (48)
			6754816	septin 2	2.2E-12	7 (18)
1087	0.052	1.6	51766806	PREDICTED: similar to Pgk1 protein	1.1E-15	21 (62)
			6680618	acetyl-Coenzyme A dehydrogenase, medi	4.3E-14	4 (16)
			6680956	coagulation factor C homolog (Limulus	7.3E-14	21 (44)
1100	0.015	1.26	31543747	spermine synthase	1.8E-09	8 (28)
			26080422	glial fibrillary acidic protein	9.2E-09	10 (23)
			39204499	neurofilament, light polypeptide	1.1E-08	6 (10)
1106	0.048	-1.59	6680956	coagulation factor C homolog (Limulus	4.2E-11	17 (33)
1112	0.0068	-1.12	51890205	succinate-Coenzyme A ligase, GDP-for	6.3E-11	8 (27)

1113	0.0089	-1.54	6680956	coagulation factor C homolog (Limulus	3.3E-12	17 (33)
			9789985	isovaleryl coenzyme A dehydrogenase	1.8E-10	10 (28)
1114	0.015	-1.57	6680956	coagulation factor C homolog (Limulus	1.9E-13	19 (38)
1127	0.015	-1.58	6680956	coagulation factor C homolog (Limulus	1.3E-12	17 (31)
1138	0.021	-1.17	51766806	PREDICTED: similar to Pgk1 protein	1.00E-15	11 (32)
			22267442	ubiquinol cytochrome c reductase cor	3.00E-15	22 (49)
1166	0.0069	-1.29	6671507	actin, alpha 2, smooth muscle, aorta	6.40E-11	7 (22)
			6679022	neutrophil cytosolic factor 4	5.60E-10	9 (34)
1212	0.0024	-1.12	13195624	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex	4.00E-12	19(48)
1248	0.027	1.18	33859801	F-box only protein 2	1.20E-12	7 (37)
1329	0.032	-1.42	6678674	lactate dehydrogenase 2, B chain	1.60E-11	13 (48)
1356	0.0073	-1.17	18152793	pyruvate dehydrogenase (lipoamide) b	5.60E-15	20 (53)
			6680045	guanine nucleotide-binding protein, b	7.90E-11	6 (25)
1415	0.01	-1.13	31982186	malate dehydrogenase 2, NAD (mitocho	2.00E-15	20 (63)
			6679943	growth arrest specific 2	2.00E-12	12 (45)
			47607490	glyceraldehyde-3-phosphate dehydr	3.00E-11	4 (18)
1434	0.0027	1.22	6753060	annexin A5	3.20E-14	17 (59)
			19527388	OTU domain, ubiquitin aldehyde bindi	4.10E-12	4 (19)
			7242171	proliferating cell nuclear antigen	9.30E-12	21 (67)
1451	0.0011	1.48	6753060	annexin A5	4.8E-12	4 (16)
			54287684	eukaryotic translation elongation fa	2.0E-08	4 (19)
1454	0.0077	1.39	6753060	annexin A5	2.0E-10	18 (53)
1458	0.0024	1.59	6753102	apolipoprotein E	2.6E-07	3 (15)
1460	0.0055	1.33	6753060	annexin A5	1.4E-11	8 (18)
			1952738	OTU domain, ubiquitin aldehyde bindi	1.1E-09	6 (28)
1485	0.022	1.19	6753060	annexin A5	5.0E-11	15 (56)
1488	0.013	-1.48	31982825	TG-interacting factor	8.8E-04	1 (8)
1595	0.009	-1.12	6680816	complement component 1, q subcomponen	6.7E-15	6 (25)

1652	0.0053	-1.6	34098931	calbindin 2	1.8E-10	13 (49)
1654	0.025	-1.45	34098931	calbindin 2	6.10E-11	18(59)
			6756039	tyrosine 3-monooxygenase/tryptophan 5	1.00E-10	2(18)
			31543976	3-monooxgenase/tryptophan 5-monooxyg	5.54E-10	4(17)
1655	0.033	-1.37	33563236	Rho, GDP dissociation inhibitor (GDI	2.00E-13	12(58)
			31982030	Rho GDP dissociation inhibitor (GDI)	8.25E-11	2(12)
1698	0.017	1.31	31982861	carbonic anhydrase 3	1.5E-10	12 (67)
1869	0.0062	1.13	10092608	glutathione S-transferase, pi	2.9E-13	14(54)
			32401425	glutathione S-transferase, pi	2.9E-13	9(40)
2067	0.0038	-1.13	19482160	coactosin-like 1	1.3E-06	4(20)
2109	0.037	-1.31	6680986	cytochrome c oxidase, subunit Va	2.0E-09	4 (30)
2149	0.0065	-1.26	5176389	PREDICTED: similar to Hemoglobin bet	2.0E-12	8 (65)
			31982300	hemoglobin, beta adult major chain	2.0E-12	7 (56)
2175	0.0031	1.51	6677835	S100 calcium binding protein A13	2.0E-06	2 (20)

List of proteins differentially expressed in the cochlea of the *av* mouse compared to controls. The table includes spot number from the gel, significance (t-test), fold change expressed as mutant vs. wild-type, genome identifier (gi#), protein name, probability of SEQUEST identification and peptide coverage for the protein of interest.

Supplemental Table 2: Replicate Cts data for cochlin

COCH	**AV-3J #1**	**AV-3J #2**	**AV-3J #3**	**NC #1**	**NC #2**	**NC #3**
	20.2	20	19.3	20.4	19.8	19.1
	19.9	19.8	19.1	20.1	19.8	18.9
	19.8	19.6	18.9	20	19.6	18.7
Average	19.97	19.80	19.10	20.17	19.73	18.90
STDEV	0.21	0.20	0.20	0.21	0.12	0.20
%CV	0.01	0.01	0.01	0.01	0.01	0.01

GAPDH	**AV-3J #1**	**AV-3J #2**	**AV-3J #3**	**NC #1**	**NC #2**	**NC #3**
	24.2	21.9	22.7	21.3	22	21.2

	24.1	21.7	22.2	21.3	22.2	21.2
	24.1	21.8	22.4	21.7	22	20.9
Average	24.13	21.80	22.43	21.43	22.07	21.10
STDEV	0.06	0.10	0.25	0.23	0.12	0.17
%CV	0.00	0.00	0.01	0.01	0.01	0.01

Replicate Cts data from the qPCR assays involving *Coch.* The Cts (cross-over thresholds) data are shown in the table. A higher Ct value represents lower gene expression. The replicate data points are very tight (little variation), and are therefore very reliable and may be biologically significant. AV-3J represents the strand of *av* mice used in the assays. NC means normal control. STDEV is standard deviation. CV is coefficient of variation. %CV is calculated using the formula STDEV/average.

Supplemental Table 3: Replicate Cts data for p53, Nrf2, and Brn3a

TRP53	**AV-3J #1**	**AV-3J #2**	**AV-3J #3**	**NC #1**	**NC #2**	**NC #3**
	27	26.7	26.7	26.6	26.7	26
	26.9	26.7	26.7	26.6	26.5	25.7
	26.7	26.6	26.5	26.5	25.8	25.5
Average	26.87	26.67	26.63	26.57	26.33	25.73
STDEV	0.15	0.06	0.12	0.06	0.47	0.25
%CV	0.01	0.00	0.00	0.00	0.02	0.01

NFE2L2	**AV-3J #1**	**AV-3J #2**	**AV-3J #3**	**NC #1**	**NC #2**	**NC #3**
	28.5	26.9	27.2	27	26.9	26
	28.9	26.8	26.9	26.8	27	26.6
	28.8	27	27.1	27.2	26.8	26.3
Average	28.73	26.90	27.07	27.00	26.90	26.30
STDEV	0.21	0.10	0.15	0.20	0.10	0.30
%CV	0.01	0.00	0.01	0.01	0.00	0.01

POU4F1	**AV-3J #1**	**AV-3J #2**	**AV-3J #3**	**NC #1**	**NC #2**	**NC #3**
	34.5	32.9	32.7	33.8	32.4	31.9
	33.3	32.7	33.1	33.7	33.4	31.9
	33.7	33.1	32.9	34.1	33.7	32.2
Average	33.83	32.90	32.90	33.87	33.17	32.00
STDEV	0.61	0.20	0.20	0.21	0.68	0.17
%CV	0.02	0.01	0.01	0.01	0.02	0.01

GAPDH	**AV-3J #1**	**AV-3J #2**	**AV-3J #3**	**NC #1**	**NC #2**	**NC #3**

	25.7	23.5	24.1	23.7	24.1	22.9
	25.7	23.3	24.4	23.8	24.2	22.9
	26.7	23.8	24.7	24.1	24.3	23.1
Average	26.03	23.53	24.40	23.87	24.20	22.97
STDEV	0.58	0.25	0.30	0.21	0.10	0.12
%CV	0.02	0.01	0.01	0.01	0.00	0.01

Replicate Cts data from the qPCR assays involving *Trp53*, *Nfe2l2*, and *Pou4f1*. The Cts (cross-over thresholds) data are shown in the table. A higher Ct value represents lower gene expression. The replicate data points are very tight (little variation), and are therefore very reliable and may be biologically significant. AV-3J represents the strand of *av* mice used in the assays. NC means normal control. STDEV is standard deviation. CV is coefficient of variation. %CV is calculated using the formula STDEV/average.