

Supplementary Material:

Table S1: List of the most significant deregulated transcripts regarding *CDKN2A* status (p.G101W vs wild-type), adjusted P-value < 0.0001. Only genes identified in both *MC1R* wild-type and *MC1R* RHC variant carriers are included (N=108)

Abbreviations: FC: Fold Change; P-value: adjusted P-Value of such comparison; wt: wild-type.

*Statistical values of mutant *CDKN2A* vs wild-type in *MC1R* RHC skin cells (individual A1 vs individual A2).

**Statistical values of mutant *CDKN2A* vs wild-type in wild-type *MC1R* skin cells (individual B1 vs individual B2)

Gene ID	Gene Name	FC in <i>MC1R</i> RHC *	P-value in <i>MC1R</i> RHC *	FC in wt <i>MC1R</i> **	P-value in wt <i>MC1R</i> **
NM_002121	<i>HLA-DPB1</i>	-4.83	4.05E-13	-2.60	5.79E-10
NM_005766	<i>FARP1</i>	-3.6	1.32E-11	-1.53	5.80E-07
NM_152270	<i>SLFN11</i>	-3.4	1.87E-06	-2.08	7.47E-07
NM_005110	<i>GFPT2</i>	-3.2	5.49E-06	-2.50	5.64E-05
NM_015719	<i>COL5A3</i>	-3.1	1.87E-06	-2.28	3.91E-05
NM_000550	<i>TYRP1</i>	-2.76	1.43E-06	-2.34	6.40E-06
NM_016269	<i>LEF1</i>	-2.69	1.73E-09	-1.64	6.46E-07
NM_000423	<i>KRT2</i>	-2.45	7.93E-05	-2.70	1.58E-05
NM_000304	<i>PMP22</i>	-2.41	9.22E-10	-1.80	3.50E-08
NM_152996	<i>ST6GALNAC3</i>	-2.38	1.38E-08	-1.44	4.65E-06
NM_138284	<i>IL17D</i>	-2.31	7.53E-06	-2.02	2.08E-05
AF086044	<i>unknown</i>	-2.23	1.74E-10	-3.42	5.23E-13
NM_198951	<i>TGM2</i>	-2.08	4.10E-06	-2.42	4.33E-07
NM_138375	<i>CABLES1</i>	-2.08	5.78E-09	-3.31	8.92E-12
NM_006426	<i>DPYSL4</i>	-2.03	3.01E-05	-3.92	6.81E-09
NM_032048	<i>EMILIN2</i>	-1.83	5.82E-06	-2.04	1.00E-06
AK074473	<i>unknown</i>	-1.83	6.09E-06	-2.43	1.29E-07
NM_001129	<i>AEBP1</i>	-1.81	2.43E-07	-1.40	3.91E-06
NM_014070	<i>unknown</i>	-1.78	2.71E-07	-1.31	8.02E-06
BC004343	<i>C21orf122</i>	-1.66	5.99E-06	-1.47	1.48E-05
NM_148897	<i>SDR9C7</i>	-1.63	3.91E-05	-1.83	6.51E-06
AF131834	<i>unknown</i>	-1.53	2.07E-06	-2.60	1.81E-09
NM_080647	<i>TBX1</i>	-1.53	4.46E-06	-1.21	3.80E-05
NM_012131	<i>CLDN17</i>	-1.47	4.17E-05	-1.79	2.57E-06
NM_000635	<i>RFX2</i>	-1.38	2.98E-06	-1.08	2.98E-05
ENST00000224809	<i>unknown</i>	-1.28	6.59E-06	-1.81	6.37E-08
NM_032534	<i>KRBA1</i>	-1.21	2.92E-06	-0.97	2.25E-05
NM_152359	<i>CPT1C</i>	-1.08	1.08E-05	-1.48	1.50E-07
NM_001077263	<i>TMPRSS13</i>	-0.87	4.43E-05	-2.81	9.51E-12
NM_000396	<i>CTSK</i>	-0.74	7.83E-05	-1.81	1.05E-09
NM_003798	<i>CTNNA1</i>	0.71	6.15E-05	0.81	9.91E-06
NM_015920	<i>RPS27L</i>	0.77	4.43E-05	0.86	8.34E-06
NM_001015509	<i>unknown</i>	0.79	1.13E-05	0.68	3.46E-05
THC2657938	<i>unknown</i>	0.81	4.28E-05	2.08	2.37E-10
NM_000022	<i>ADA</i>	0.87	8.65E-06	1.08	3.92E-07
THC2698177	<i>unknown</i>	0.89	6.21E-05	1.75	1.38E-08
NM_005760	<i>CEBPZ</i>	0.90	3.14E-05	2.20	3.14E-10
NM_004346	<i>CASP3</i>	0.91	1.50E-05	1.31	1.23E-07
NM_004487	<i>GOLGB1</i>	0.95	5.49E-06	1.17	2.84E-07
BC027178	<i>PRPF40A</i>	0.99	8.74E-05	2.62	3.74E-10
NM_004280	<i>EEF1E1</i>	1.00	7.97E-05	1.06	2.48E-05
NM_004986	<i>KTN1</i>	1.04	2.90E-06	2.53	1.59E-11
ENST00000377156	<i>unknown</i>	1.07	1.97E-05	1.09	9.97E-06
NM_007047	<i>BTN3A2</i>	1.09	1.77E-05	1.11	9.31E-06

NM_020169	LXN	1.11	3.10E-05	1.97	1.97E-08
ENST00000306024	LSM3	1.12	2.45E-05	0.99	5.33E-05
NM_001033719	ZNF404	1.13	4.49E-05	2.13	1.58E-08
NM_016010	FAM164A	1.13	1.23E-05	0.99	3.29E-05
NM_001007234	unknown	1.15	1.63E-06	1.42	7.87E-08
NM_001012334	MDK	1.16	6.19E-05	1.20	2.48E-05
NM_181453	GCC2	1.19	6.48E-05	1.56	1.83E-06
NM_033514	LIMS3	1.20	8.85E-07	1.16	8.49E-07
NM_033316	MF12	1.20	9.60E-05	1.87	3.91E-07
NM_002890	RASA1	1.22	1.18E-06	0.86	3.86E-05
NM_018300	ZNF83	1.23	5.73E-05	1.70	8.63E-07
NM_201612	unknown	1.23	1.19E-05	2.28	4.38E-09
NM_207014	WDR78	1.30	6.81E-05	1.50	8.56E-06
NM_002078	GOLGA4	1.31	4.03E-05	1.21	5.59E-05
AK075484	SAMD4B	1.31	1.52E-05	3.52	3.01E-11
NM_003566	EEA1	1.33	9.48E-05	2.36	7.47E-08
NM_144777	SCEL	1.33	5.55E-07	1.01	9.54E-06
CB050071	unknown	1.41	5.52E-05	1.53	1.31E-05
NM_022154	SLC39A8	1.43	8.09E-05	1.54	2.19E-05
CR603437	unknown	1.44	1.33E-06	1.35	1.75E-06
NM_018169	C12orf35	1.48	2.17E-05	2.02	3.71E-07
NM_207331	unknown	1.49	9.36E-06	1.28	3.07E-05
AB075826	FAM171B	1.49	5.31E-05	1.47	3.83E-05
NM_004510	SP110	1.53	1.66E-07	0.94	3.63E-05
NM_172174	IL15	1.55	5.30E-08	1.29	4.08E-07
NM_000888	ITGB6	1.55	3.99E-05	2.52	8.05E-08
NM_005059	RLN2	1.58	1.97E-05	1.38	5.37E-05
NM_025114	CEP290	1.67	1.90E-05	2.70	3.88E-08
AK096536	unknown	1.70	3.16E-06	1.36	2.52E-05
THC2683448	unknown	1.72	2.01E-06	1.91	3.87E-07
NM_001013728	unknown	1.74	1.34E-05	2.23	4.47E-07
BC029919	unknown	1.78	4.62E-06	1.40	4.30E-05
NM_001712	CEACAM1	1.80	1.35E-06	1.56	4.49E-06
NM_003020	SCG5	1.83	2.10E-08	2.37	5.14E-10
NM_004921	unknown	1.86	8.41E-05	1.74	9.87E-05
NM_018429	BDP1	1.90	1.48E-05	2.05	3.60E-06
THC2676635	unknown	1.93	2.93E-08	1.27	3.49E-06
NM_178445	CCRL1	1.99	1.68E-05	1.98	1.08E-05
THC2740317	unknown	2.04	7.85E-06	1.75	2.63E-05
NM_182762	MACC1	2.05	5.66E-09	0.89	8.55E-05
XR_015158	unknown	2.15	6.40E-10	1.91	2.32E-09
NM_001547	IFIT2	2.16	4.68E-08	2.17	3.56E-08
NM_152737	RNF182	2.19	1.05E-05	1.78	5.97E-05
NM_014314	DDX58	2.22	3.99E-08	1.53	2.66E-06
AK022351	unknown	2.26	4.01E-05	2.74	2.66E-06
THC2526509	unknown	2.26	6.31E-08	1.19	7.99E-05
NM_181501	ITGA1	2.38	1.07E-08	1.09	8.38E-05
NM_018284	GBP3	2.40	1.80E-07	2.10	6.58E-07
AI078143	unknown	2.60	2.11E-07	1.52	7.46E-05
THC2510656	unknown	2.62	8.54E-06	2.91	1.51E-06
THC2549494	unknown	2.72	4.74E-06	2.48	8.65E-06
NM_020124	IFNK	2.74	7.98E-07	2.36	3.02E-06
NM_152703	SAMD9L	2.98	8.72E-06	2.94	6.15E-06
NM_005532	IFI27	3.03	3.42E-11	0.92	5.22E-05
NM_017654	SAMD9	3.04	1.08E-07	1.98	1.26E-05
NM_006417	IFI44	3.07	3.28E-12	2.71	7.74E-12
THC2679528	unknown	3.18	4.40E-07	2.89	9.26E-07
AK023743	unknown	3.18	1.52E-10	1.95	7.56E-08
NM_001548	IFIT1	3.28	6.99E-11	1.59	5.54E-07
BF213738	unknown	3.46	3.06E-11	1.34	2.66E-06
NM_006820	IFI44L	3.49	6.99E-11	2.28	1.49E-08
D89479	SULT1B1	3.56	1.70E-08	3.24	4.36E-08

NM_005127	<i>CLEC2B</i>	3.66	1.61E-13	1.20	1.33E-07
NM_017523	<i>XAF1</i>	5.11	1.98E-08	3.00	9.40E-06

Table S2: List of the most significant deregulated transcripts regarding *MC1R* status (p.R106W and p.R151C vs wild-type) identified in both comparisons. Adjusted P-value < 0.0000001. Only genes identified in both analyses are included (N=159). Abbreviations: FC: Fold Change; P-value: adjusted P-Value of such comparison; wt: wild-type. *Statistical values of *MC1R* RHC vs wild-type in mutant *CDKN2A* skin cell (individual A1 vs individual B1). **Statistical values of *MC1R* RHC vs wild-type in wild-type *CDKN2A* skin cell (individual A2 vs individual B2).

Gene ID	Gene Name	FC in mutant <i>CDKN2A</i> *	P-value in mutant <i>CDKN2A</i> *	FC in wt <i>CDKN2A</i> **	P-value in wt <i>CDKN2A</i> **
NM_005672	<i>PSCA</i>	-7.30	2.39E-12	-7.02	1.20E-12
NM_000550	<i>TYRP1</i>	-7.24	2.85E-12	-6.82	2.14E-12
NM_000095	<i>COMP</i>	-6.79	3.34E-13	-5.08	2.95E-12
NM_005511	<i>MLANA</i>	-5.74	2.51E-09	-6.96	7.05E-11
NM_000372	<i>TYR.TYRL</i>	-5.59	1.29E-12	-7.19	1.62E-14
NM_002443	<i>MSMB</i>	-5.30	1.03E-14	-4.05	1.47E-13
NM_006928	<i>SILV</i>	-4.79	1.66E-08	-6.05	3.02E-10
NM_000166	<i>GJB1</i>	-4.72	2.43E-10	-2.76	9.95E-08
NM_000014	<i>A2M</i>	-4.52	3.06E-08	-7.21	2.40E-11
NM_000698	<i>ALOX5</i>	-4.17	3.63E-11	-2.19	6.05E-08
NM_016190	<i>CRNN</i>	-4.14	8.50E-10	-4.68	5.89E-11
THC2711870	<i>unknown</i>	-3.98	8.16E-09	-6.00	1.27E-11
THC2675163	<i>unknown</i>	-3.73	6.81E-12	-6.37	5.96E-15
NM_032588	<i>TRIM63</i>	-3.70	6.23E-10	-5.36	1.70E-12
NM_004750	<i>CRLF1</i>	-3.70	1.31E-10	-2.14	6.30E-08
NM_013358	<i>PADI1</i>	-3.61	1.08E-08	-4.16	6.97E-10
ENST00000366930	<i>TGFB2</i>	-3.56	3.31E-10	-2.27	4.78E-08
NM_004864	<i>GDF15</i>	-3.31	8.19E-11	-4.23	1.09E-12
NM_020182	<i>PMEPA1</i>	-3.18	2.39E-12	-1.98	4.44E-10
NM_001712	<i>CEACAM1</i>	-3.12	6.03E-10	-3.36	7.97E-11
NM_005512	<i>LRRC32</i>	-3.11	8.78E-08	-3.21	2.37E-08
NM_144497	<i>AKAP12</i>	-3.10	8.04E-08	-2.91	7.23E-08
NM_130808	<i>CPNE4</i>	-2.97	4.58E-09	-2.69	6.33E-09
NM_001901	<i>CTGF</i>	-2.94	9.98E-10	-4.13	4.12E-12
NM_001039212	<i>unknown</i>	-2.87	9.12E-11	-3.14	9.05E-12
NM_024101	<i>MLPH</i>	-2.86	1.13E-08	-4.17	3.06E-11
ENST00000264554	<i>SHC2</i>	-2.80	1.77E-08	-2.97	3.32E-09
NM_000201	<i>ICAM1</i>	-2.75	2.83E-09	-2.45	4.99E-09
NM_000222	<i>KIT</i>	-2.75	6.97E-09	-5.47	3.15E-13
NM_201631	<i>TGM5</i>	-2.69	6.67E-09	-2.57	4.59E-09
NM_002193	<i>INHBB</i>	-2.61	3.47E-10	-2.46	2.87E-10
NM_001001547	<i>CD36</i>	-2.60	1.37E-08	-2.58	6.28E-09
NM_001945	<i>HBEGF</i>	-2.59	4.84E-08	-2.56	2.20E-08
NM_002463	<i>MX2</i>	-2.59	2.72E-09	-5.66	4.69E-14
NM_173198	<i>NR4A3</i>	-2.45	2.44E-10	-4.42	5.15E-14
NM_001343	<i>DAB2</i>	-2.42	2.64E-08	-3.27	1.92E-10
NM_138375	<i>CABLES1</i>	-2.23	1.35E-09	-3.46	1.49E-12
NM_001012964	<i>KLK6</i>	-2.19	2.71E-09	-4.55	8.27E-14
NM_016463	<i>CXXC5</i>	-2.10	3.00E-08	-2.26	4.70E-09
NM_001453	<i>FOXC1</i>	-1.94	1.02E-09	-1.72	2.04E-09
NM_003793	<i>CTSF</i>	-1.92	4.54E-08	-3.15	2.38E-11
NM_022910	<i>NDRG4</i>	-1.84	9.53E-09	-1.55	3.44E-08
NM_006989	<i>RASA4</i>	-1.67	7.49E-08	-2.15	1.08E-09
NM_145804	<i>ABTB2</i>	-1.45	7.91E-08	-2.40	3.58E-11

NM_003565	<i>ULK1</i>	-1.39	7.35E-08	-1.75	1.36E-09
NM_030912	<i>TRIM8</i>	-1.25	5.80E-08	-1.13	8.84E-08
NM_206836	<i>PECI</i>	1.33	6.12E-08	1.23	6.13E-08
NM_005915	<i>MCM6</i>	1.33	9.39E-08	1.69	1.62E-09
AY163812	<i>C17orf80</i>	1.34	6.62E-08	1.47	7.72E-09
CR600585	<i>unknown</i>	1.45	8.28E-09	1.35	7.88E-09
NM_033514	<i>LIMS3</i>	1.46	3.69E-08	1.42	2.13E-08
NM_016126	<i>HSPB11</i>	1.47	6.42E-08	1.48	2.29E-08
NM_001079525	<i>PAICS</i>	1.50	1.12E-08	2.03	7.45E-11
NM_016448	<i>DTL</i>	1.53	5.00E-09	1.85	1.41E-10
NM_003579	<i>RAD54L</i>	1.54	6.67E-09	1.87	1.86E-10
NM_032636	<i>PSRC1</i>	1.59	5.94E-08	1.67	1.21E-08
NM_033417	<i>HAUS8</i>	1.59	6.77E-08	1.71	1.05E-08
NM_018455	<i>CENPN</i>	1.61	2.25E-08	2.40	4.13E-11
NM_030771	<i>CCDC34</i>	1.64	3.02E-09	3.26	1.47E-13
NM_017868	<i>TTC12</i>	1.67	7.74E-10	2.18	7.74E-12
NM_003258	<i>TK1</i>	1.72	8.63E-08	1.83	1.53E-08
NM_003504	<i>CDC45L</i>	1.75	6.55E-09	1.99	4.57E-10
NM_002916	<i>RFC4</i>	1.76	1.32E-09	2.19	2.50E-11
ENST00000367003	<i>C1orf97</i>	1.77	2.25E-08	2.65	4.11E-11
NM_145231	<i>C14orf143</i>	1.84	1.04E-08	1.86	3.46E-09
NM_003798	<i>CTNNAL1</i>	1.85	2.44E-10	1.94	4.44E-11
NM_014317	<i>PDSS1</i>	1.86	3.58E-08	2.19	1.71E-09
NM_004219	<i>PTTG1</i>	1.87	9.03E-09	1.92	2.48E-09
NM_001159	<i>AOX1</i>	1.87	8.16E-09	2.23	3.05E-10
NM_018186	<i>C1orf112</i>	1.94	5.99E-09	1.94	2.12E-09
NM_001826	<i>CKS1B</i>	1.96	5.59E-09	2.00	1.55E-09
BX640843	<i>unknown</i>	1.99	5.94E-09	2.51	9.73E-11
NM_182620	<i>FAM33A</i>	2.01	1.76E-09	1.72	5.18E-09
NM_003686	<i>EXO1</i>	2.01	2.93E-10	2.19	3.22E-11
NM_004282	<i>BAG2</i>	2.02	9.45E-10	2.61	1.14E-11
NM_014051	<i>TMEM14A</i>	2.09	1.45E-08	2.14	4.46E-09
NM_016095	<i>GINS2</i>	2.12	7.82E-10	2.14	2.35E-10
NM_145014	<i>HYLS1</i>	2.13	5.04E-08	2.66	1.08E-09
NM_024037	<i>C1orf135</i>	2.13	8.41E-10	2.22	1.78E-10
NM_003384	<i>VRK1</i>	2.15	6.03E-10	2.37	5.77E-11
BC040051	<i>unknown</i>	2.15	5.79E-08	2.00	5.83E-08
NM_001254	<i>CDC6</i>	2.20	8.16E-08	2.57	4.42E-09
NM_014176	<i>UBE2T</i>	2.23	1.12E-11	2.18	5.39E-12
NM_203467	<i>PPIL5</i>	2.23	9.58E-10	1.82	5.22E-09
NM_000057	<i>BLM</i>	2.26	7.59E-08	2.85	1.45E-09
NM_024808	<i>C13orf34</i>	2.27	8.38E-08	2.54	7.74E-09
NM_006607	<i>PTTG2</i>	2.27	2.24E-10	1.92	7.20E-10
NM_001928	<i>CFD</i>	2.30	3.69E-08	2.45	6.65E-09
NM_015895	<i>GMNN</i>	2.31	1.29E-10	1.77	1.51E-09
NM_018101	<i>CDCA8</i>	2.34	7.82E-10	2.36	2.52E-10
AK027541	<i>unknown</i>	2.35	2.05E-08	2.34	8.84E-09
NM_001766	<i>CD1D</i>	2.36	6.03E-09	2.53	9.33E-10
NM_002876	<i>RAD51C</i>	2.37	4.47E-10	2.20	4.50E-10
NM_000946	<i>PRIM1</i>	2.38	2.14E-09	2.22	1.94E-09
NM_005030	<i>PLK1</i>	2.40	8.38E-08	2.41	3.33E-08
NM_031299	<i>CDCA3</i>	2.41	2.46E-09	2.09	6.11E-09
NM_012415	<i>RAD54B</i>	2.43	6.39E-08	2.34	4.24E-08
NM_006479	<i>RAD51AP1</i>	2.46	3.02E-08	3.80	3.48E-11
NM_138555	<i>KIF23</i>	2.48	8.16E-09	2.87	4.69E-10
NM_018193	<i>FANCI</i>	2.50	4.23E-11	2.38	2.70E-11
NM_014791	<i>MELK</i>	2.50	1.91E-09	2.50	7.39E-10
NM_175617	<i>MT1E</i>	2.52	6.20E-10	2.12	2.36E-09
NM_012177	<i>FBXO5</i>	2.54	1.32E-09	2.45	8.26E-10
NM_001012271	<i>BIRC5</i>	2.55	9.58E-10	2.63	2.35E-10
NM_001012267	<i>CENPP</i>	2.56	2.85E-12	1.76	1.78E-10
NM_001827	<i>CKS2</i>	2.57	1.36E-10	2.22	3.37E-10

BC044246	<i>TMEM200A</i>	2.57	7.02E-09	2.04	5.61E-08
NM_012310	<i>KIF4A</i>	2.57	3.81E-09	2.48	2.30E-09
NM_199420	<i>POLQ</i>	2.58	6.02E-08	3.45	5.20E-10
NM_001274	<i>CHEK1</i>	2.58	1.29E-10	3.00	5.77E-12
NM_001005414	<i>unknown</i>	2.62	6.03E-10	1.95	1.10E-08
NM_182751	<i>MCM10</i>	2.62	2.54E-08	3.10	1.09E-09
NM_001010897	<i>SERP2</i>	2.65	3.23E-09	2.27	9.59E-09
NM_001034	<i>RRM2</i>	2.67	1.05E-08	2.47	1.16E-08
NM_145018	<i>C11orf82</i>	2.71	1.68E-10	2.95	1.85E-11
NM_031966	<i>CCNB1</i>	2.74	2.63E-11	2.84	5.39E-12
NM_005059	<i>RLN2</i>	2.78	9.81E-09	2.58	1.05E-08
NM_006845	<i>KIF2C</i>	2.80	1.74E-09	2.78	7.12E-10
NM_001211	<i>BUB1B</i>	2.81	4.88E-08	3.45	1.32E-09
NM_198433	<i>AURKA</i>	2.85	1.71E-08	2.81	8.31E-09
NM_004701	<i>CCNB2</i>	2.92	2.85E-12	3.11	5.71E-13
NM_020242	<i>KIF15</i>	2.93	5.10E-09	4.62	4.38E-12
NM_004523	<i>KIF11</i>	2.96	1.80E-08	3.18	2.81E-09
NM_001255	<i>CDC20</i>	3.05	4.70E-09	2.92	3.13E-09
BC013418	<i>C13orf3</i>	3.10	3.10E-09	3.42	3.24E-10
AL834537	<i>CCDC150</i>	3.11	3.65E-08	4.61	7.45E-11
NM_004336	<i>BUB1</i>	3.13	2.15E-10	3.42	2.35E-11
NM_004117	<i>FKBP5</i>	3.14	4.53E-08	3.43	5.67E-09
NM_052913	<i>TMEM200A</i>	3.14	8.40E-08	2.96	7.23E-08
NM_001067	<i>TOP2A</i>	3.14	9.65E-11	3.93	1.70E-12
NM_005733	<i>KIF20A</i>	3.15	1.78E-11	2.96	1.38E-11
NM_001813	<i>CENPE</i>	3.18	6.03E-10	4.69	1.24E-12
NM_152515	<i>CKAP2L</i>	3.18	8.97E-08	3.74	4.49E-09
NM_001237	<i>CCNA2</i>	3.19	2.93E-10	3.25	8.24E-11
NM_018136	<i>ASPM</i>	3.20	1.92E-09	3.55	1.78E-10
NM_007280	<i>OIP5</i>	3.21	1.51E-11	2.87	2.37E-11
NM_138419	<i>FAM54A</i>	3.23	3.04E-11	3.07	2.01E-11
NM_020675	<i>SPC25</i>	3.26	1.59E-12	3.45	1.87E-13
NM_018492	<i>PBK</i>	3.28	3.26E-09	3.95	9.92E-11
NM_022346	<i>NCAPG</i>	3.29	5.95E-13	3.50	7.81E-14
NM_024094	<i>DSCC1</i>	3.31	3.47E-10	3.99	1.02E-11
NM_032117	<i>MND1</i>	3.35	6.71E-12	3.77	5.71E-13
NM_001809	<i>CENPA</i>	3.38	7.61E-11	3.90	3.72E-12
NM_001786	<i>CDC2</i>	3.38	2.39E-12	3.27	1.24E-12
NM_145697	<i>NUF2</i>	3.40	8.28E-09	4.81	3.22E-11
NM_021186	<i>ZP4</i>	3.49	1.03E-14	4.91	3.21E-17
NM_016343	<i>CENPF</i>	3.52	1.25E-09	2.85	7.88E-09
NM_001790	<i>CDC25C</i>	3.60	3.47E-08	3.67	1.06E-08
NM_018131	<i>CEP55</i>	3.63	4.13E-10	3.89	5.89E-11
NM_016195	<i>KIF20B</i>	3.68	4.08E-10	2.62	1.36E-08
NM_014750	<i>DLGAP5</i>	3.71	2.39E-12	4.17	1.87E-13
NM_005192	<i>CDKN3</i>	4.04	7.94E-08	4.03	3.28E-08
NM_018365	<i>MNS1</i>	4.09	5.55E-10	3.31	3.38E-09
NM_012484	<i>HMMR</i>	4.51	2.85E-12	5.25	1.87E-13
NM_080672	<i>PHACTR3</i>	4.53	8.83E-10	3.81	3.34E-09
NM_001956	<i>EDN2</i>	4.78	2.38E-09	4.67	1.19E-09
NM_153046	<i>TDRD9</i>	4.83	1.87E-12	4.59	1.08E-12
NM_032935	<i>MT4</i>	5.04	2.85E-12	5.54	4.26E-13
BC004565	<i>unknown</i>	5.05	1.16E-11	2.65	2.23E-08

Table S3: List of genes inversely deregulated between *CDKN2A* and *MC1R* analyses. Abbreviations: F.C: Fold Change; P-value: adjusted P-Value of such comparison; wt: wild-type.

HGNC_symbol	Ensembl_link	mutant <i>CDKN2A</i> vs wt <i>CDKN2A</i> (both RHC <i>MC1R</i>)		mutant <i>CDKN2A</i> vs wt <i>CDKN2A</i> (both wt <i>MC1R</i>)		RHC <i>MC1R</i> vs wt <i>MC1R</i> (both mutant <i>CDKN2A</i>)		RHC <i>MC1R</i> vs wt <i>MC1R</i> (both wt <i>CDKN2A</i>)	
		log F.C	adj.p.value	log F.C	adj.p.value	log F.C	adj.p.value	log F.C	adj.p.value
<i>XAF1</i>	NM_017523	5.11	1.98E-08	3.00	9.40E-06	-1.11	0.041921124	-3.22	1.59E-06
<i>MX2</i>	NM_002463	4.14	1.32E-11	1.06	0.000133758	-2.59	2.72E-09	-5.66	4.69E-14
<i>IFI44L</i>	NM_006820	3.49	6.99E-11	2.28	1.49E-08	-0.93	0.000400236	-2.14	9.59E-09
<i>IFIT3</i>	NM_001549	3.26	8.18E-09	1.26	0.00036059	-1.57	3.37E-05	-3.57	5.21E-10
<i>CAPN14</i>	AK092257	3.25	3.91E-05	2.20	0.00113099	-1.37	0.032844763	-2.42	0.0002558
	AK023743	3.18	1.52E-10	1.95	7.56E-08	-0.49	0.039372674	-1.71	1.27E-07
<i>IFI44</i>	NM_006417	3.07	3.28E-12	2.71	7.74E-12	-0.76	5.31E-05	-1.12	2.60E-07
<i>KRT19</i>	NM_002276	2.86	3.59E-10	0.81	0.000744197	-1.31	4.49E-06	-3.36	8.78E-12
<i>IFNK</i>	NM_020124	2.74	7.98E-07	2.36	3.02E-06	-1.04	0.007725554	-1.43	0.000326988
<i>IFI6</i>	NM_022873	2.56	3.45E-08	1.05	0.000601236	-0.79	0.00606156	-2.30	2.96E-08
<i>BTN3A3</i>	NM_006994	2.42	1.07E-05	1.55	0.000669858	-1.08	0.011856791	-1.95	3.31E-05
<i>LMO2</i>	NM_005574	2.41	1.43E-10	0.79	1.00E-04	-1.12	1.67E-06	-2.75	5.51E-12
<i>GBP3</i>	NM_018284	2.40	1.80E-07	2.10	6.58E-07	-0.70	0.020231435	-1.00	0.000961856
<i>RNF182</i>	NM_152737	2.19	1.05E-05	1.78	5.97E-05	-0.93	0.015597153	-1.33	0.000585284
<i>RHOBTB3</i>	NM_014899	2.17	1.04E-05	1.01	0.008209935	-1.98	1.59E-05	-3.14	2.33E-08
<i>IFIT2</i>	NM_001547	2.16	4.68E-08	2.17	3.56E-08	-1.48	3.08E-06	-1.47	1.46E-06
<i>USP18</i>	NM_017414	2.14	1.55E-08	0.52	0.018990885	-0.69	0.002714314	-2.31	1.21E-09
<i>EPST11</i>	NM_033255	2.12	3.99E-05	1.77	0.000160602	-1.70	0.0002321	-2.05	1.60E-05
	A_32_P53976	2.01	3.17E-05	1.10	0.005270514	-0.86	0.026819981	-1.77	3.55E-05
<i>RSAD2</i>	NM_080657	1.96	0.001691807	1.44	0.012103521	-2.71	4.60E-05	-3.23	2.96E-06
	AK023660	1.96	4.65E-08	0.92	0.000195518	-0.81	0.000669435	-1.85	2.23E-08
	THC2676635	1.93	2.93E-08	1.27	3.49E-06	-0.86	0.000221405	-1.52	1.43E-07
<i>CLCA3</i>	NM_004921	1.86	8.41E-05	1.74	9.87E-05	-1.54	0.000333218	-1.65	8.58E-05
<i>PARP9</i>	NM_031458	1.83	2.21E-06	1.21	0.000138412	-0.63	0.024137843	-1.26	4.46E-05
<i>SCG5</i>	NM_003020	1.83	2.10E-08	2.37	5.14E-10	-1.87	8.28E-09	-1.32	2.93E-07
<i>HS3ST1</i>	NM_005114	1.80	2.00E-05	1.12	0.001411596	-1.00	0.003458263	-1.69	1.14E-05
<i>CEACAM1</i>	NM_001712	1.80	1.35E-06	1.56	4.49E-06	-3.12	6.03E-10	-3.36	7.97E-11
	NM_002534	1.76	0.000121473	0.79	0.039773363	-1.04	0.007622258	-2.01	7.90E-06
	L06175	1.75	0.000889078	1.36	0.004950943	-1.82	0.000403092	-2.22	2.73E-05
	AK124281	1.75	5.68E-05	1.40	0.00033138	-0.90	0.011971445	-1.25	0.000538014
<i>C5orf56</i>	ENST00000378953	1.73	0.000157045	0.84	0.030463445	-1.03	0.008749111	-1.93	1.47E-05
<i>CRNN</i>	NM_016190	1.67	0.000105303	1.13	0.002501087	-4.14	8.50E-10	-4.68	5.89E-11

	AK025669	1.67	0.000315954	1.77	0.000112469	-1.00	0.013197622	-0.90	0.017900911
<i>PADI1</i>	NM_013358	1.66	0.000201315	1.12	0.004289502	-3.61	1.08E-08	-4.16	6.97E-10
	THC2640099	1.63	0.003962305	1.41	0.008167973	-1.45	0.006843443	-1.67	0.001407815
<i>TNFSF10</i>	NM_003810	1.61	3.76E-05	1.04	0.001525958	-1.37	0.000112711	-1.93	1.06E-06
<i>F3</i>	NM_001993	1.56	0.007308907	1.28	0.019400875	-1.14	0.039539591	-1.42	0.007227404
<i>IL15</i>	NM_172174	1.55	5.30E-08	1.29	4.08E-07	-0.82	5.92E-05	-1.09	1.10E-06
<i>SP110</i>	NM_004510	1.53	1.66E-07	0.94	3.63E-05	-0.67	0.000916414	-1.26	4.53E-07
<i>BST2</i>	NM_004335	1.49	0.00349873	1.52	0.00211498	-3.36	4.60E-07	-3.33	2.09E-07
<i>CLCA4</i>	NM_012128	1.49	0.001612926	1.67	0.000362464	-1.67	0.000354497	-1.48	0.000637245
	BX090412	1.48	0.001281109	1.47	0.000930605	-0.87	0.037340541	-0.88	0.025448576
	BC045163	1.45	3.62E-05	0.58	0.040103551	-1.39	3.12E-05	-2.25	3.73E-08
<i>HOXA10</i>	NM_018951	1.43	4.44E-06	0.86	0.000579266	-0.53	0.022134445	-1.10	2.33E-05
<i>TLR2</i>	NM_003264	1.42	0.000310032	1.80	1.61E-05	-2.33	7.17E-07	-1.95	2.78E-06
	THC2657493	1.38	0.000134482	1.47	4.25E-05	-2.16	4.46E-07	-2.07	3.14E-07
<i>OASL</i>	NM_003733	1.34	1.66E-05	0.58	0.01676382	-0.78	0.001967307	-1.54	7.42E-07
	CR625594	1.34	0.000464881	1.05	0.002484941	-0.70	0.03890031	-0.98	0.002738176
<i>PSCA</i>	NM_005672	1.32	0.002415497	1.59	0.000301512	-7.30	2.39E-12	-7.02	1.20E-12
	A_24_P476718	1.31	0.000870782	2.24	1.89E-06	-1.93	9.86E-06	-1.00	0.00360047
<i>SPINK1</i>	NM_003122	1.29	0.005034924	0.96	0.024954425	-3.40	1.10E-07	-3.73	1.34E-08
	CR612518	1.28	0.006785661	1.14	0.011308172	-0.96	0.032090928	-1.11	0.009489293
	A_32_P169353	1.20	0.045002273	1.48	0.010727271	-2.84	2.98E-05	-2.56	4.67E-05
	BC062324	1.19	0.01579769	1.22	0.010153956	-1.67	0.00082046	-1.64	0.000563989
<i>DHX58</i>	NM_024119	1.18	5.99E-06	0.71	0.000741093	-0.68	0.001151375	-1.15	2.09E-06
	BM989848	1.16	0.011329228	0.98	0.023865075	-0.89	0.042562201	-1.07	0.010191815
<i>MDK</i>	NM_001012334	1.16	6.19E-05	1.20	2.48E-05	-1.55	1.14E-06	-1.51	7.03E-07
<i>S100A4</i>	NM_002961	1.12	0.000446466	0.72	0.010561535	-0.77	0.007225432	-1.17	0.000100805
<i>BTN3A2</i>	NM_007047	1.09	1.77E-05	1.11	9.31E-06	-0.57	0.00559599	-0.55	0.004476681
<i>ALDH1L1</i>	NM_012190	1.09	0.006504537	1.35	0.000801896	-1.46	0.000386161	-1.20	0.001386589
<i>SEPP1</i>	NM_005410	1.08	0.017795719	2.85	1.26E-06	-2.78	1.49E-06	-1.00	0.01532286
	THC2671679	1.07	3.76E-05	0.73	0.001017835	-1.24	3.55E-06	-1.58	7.50E-08
<i>HCP5</i>	NM_006674	1.06	0.007759651	1.33	0.000898615	-1.84	3.33E-05	-1.57	9.87E-05
	AK026517	1.05	0.002902491	1.06	0.001900336	-0.80	0.015527585	-0.79	0.011579443
	THC2754005	1.02	0.000456872	1.29	2.63E-05	-1.03	0.000244525	-0.77	0.002241279
<i>ITGA2</i>	NM_002203	1.01	0.022552265	0.94	0.026376749	-1.06	0.012631859	-1.13	0.005479826
<i>WNT7A</i>	NM_004625	0.99	0.000464881	0.53	0.033957447	-1.77	4.27E-07	-2.24	8.20E-09

<i>NEBL</i>	NM_006393	0.99	3.91E-05	0.73	0.000558386	-0.52	0.008729268	-0.78	0.000141682
<i>PLAT</i>	NM_000930	0.98	0.000875467	1.35	2.25E-05	-2.14	8.14E-08	-1.77	3.78E-07
<i>EIF2AK2</i>	NM_002759	0.98	0.020075442	1.52	0.000512242	-1.38	0.001188256	-0.84	0.027870165
	AF086052	0.98	0.009230344	1.53	0.000138634	-1.38	0.000353702	-0.83	0.013843783
<i>ALDH1A3</i>	NM_000693	0.96	0.000531565	0.60	0.014677759	-1.10	8.25E-05	-1.46	1.54E-06
	BC056662	0.96	0.014386956	1.04	0.006439966	-1.04	0.006569774	-0.96	0.007518063
<i>FMO2</i>	NM_001460	0.96	0.037434212	2.94	1.09E-06	-3.92	2.36E-08	-1.94	5.37E-05
	A_32_P35031	0.95	0.000214111	0.62	0.005152449	-0.59	0.00820823	-0.91	0.000104052
	K03200	0.93	0.005429992	0.89	0.005220606	-1.51	3.96E-05	-1.55	1.55E-05
	AK130514	0.91	0.017250913	0.93	0.011913737	-1.39	0.000462002	-1.38	0.00028677
<i>ZSCAN4</i>	NM_152677	0.90	0.014937773	1.41	0.000279708	-1.54	0.000105108	-1.03	0.002697114
<i>APOL6</i>	NM_030641	0.89	0.018487069	1.35	0.000505697	-1.98	8.89E-06	-1.51	9.06E-05
<i>STS</i>	NM_000351	0.87	0.014650689	1.50	0.000108672	-2.58	1.92E-07	-1.95	2.61E-06
	THC2543120	0.86	0.009788415	1.06	0.001361535	-0.83	0.009051891	-0.63	0.035366686
<i>PPARG</i>	NM_138711	0.86	0.001039611	1.19	2.54E-05	-0.84	0.000819453	-0.50	0.023893587
<i>IFITM1</i>	NM_003641	0.85	0.002663548	0.62	0.018223872	-0.67	0.012012196	-0.90	0.000693909
	CA314451	0.84	0.016043784	0.89	0.00853883	-1.83	9.45E-06	-1.79	6.00E-06
	THC2551769	0.84	0.004358863	0.73	0.008331505	-0.69	0.012821531	-0.79	0.003004577
<i>ENC1</i>	NM_003633	0.83	0.002044084	1.05	0.000153929	-1.96	1.05E-07	-1.74	2.01E-07
<i>KCNN4</i>	NM_002250	0.82	0.006830609	1.03	0.000785576	-1.34	5.13E-05	-1.14	0.000158723
<i>SPINK5</i>	NM_006846	0.76	0.001825778	0.47	0.033705902	-0.70	0.002501485	-0.99	5.08E-05
<i>MSMB</i>	NM_002443	0.73	0.000832073	1.96	6.81E-09	-5.28	1.03E-14	-4.05	1.47E-13
<i>PARP12</i>	NM_022750	0.73	0.001230432	0.63	0.002667999	-1.18	4.95E-06	-1.27	8.66E-07
	THC2545454	0.71	0.02260588	0.95	0.002276893	-0.95	0.002311169	-0.71	0.012721232
<i>LYN</i>	NM_002350	0.71	0.003114957	1.27	7.07E-06	-1.32	3.92E-06	-0.76	0.000708175
	AK022020	0.71	0.004745127	0.59	0.012998879	-1.12	4.23E-05	-1.25	6.53E-06
<i>LAYN</i>	NM_178834	0.71	0.01514181	1.04	0.000500006	-1.28	5.82E-05	-0.95	0.000706483
<i>PPP1R12B</i>	NM_032105	0.68	0.009014906	0.68	0.00660204	-0.86	0.00096841	-0.86	0.000563989
<i>ATP1B1</i>	NM_001677	0.67	0.040190654	0.78	0.013887884	-0.84	0.008541899	-0.73	0.014330567
<i>CAMK2G</i>	NM_172171	0.66	0.009630083	0.77	0.001946373	-0.83	0.001095948	-0.71	0.002542575
	AK023696	0.64	0.030845413	0.63	0.025358095	-0.64	0.025179173	-0.64	0.017239992
<i>TMEM132A</i>	NM_017870	0.60	0.015740285	0.64	0.007383258	-1.72	3.16E-07	-1.68	1.76E-07
<i>TRIM2</i>	NM_015271	0.59	0.004377494	0.42	0.029710532	-0.50	0.009901857	-0.67	0.000579911
<i>LRAT</i>	NM_004744	0.51	0.043998571	0.78	0.00198053	-1.46	2.88E-06	-1.19	1.50E-05
<i>CCNDBP1</i>	NM_037370	0.48	0.009949949	0.67	0.00049834	-0.61	0.001068743	-0.43	0.01171219

<i>SMAD3</i>	U68019	0.45	0.047091148	0.52	0.017762701	-0.74	0.001205253	-0.68	0.001635126
<i>TMEM51</i>	NM_018022	0.45	0.028015892	0.43	0.029372403	-0.56	0.005094908	-0.58	0.002388652
	AK025166	0.39	0.028250766	0.37	0.030166685	-0.45	0.008515843	-0.47	0.004029612
<i>NPEPPS</i>	NM_006310	0.38	0.044356931	0.45	0.014074734	-0.79	0.000114668	-0.72	0.000155666
<i>ALG9</i>	NM_001077691	-0.31	0.031798838	-0.29	0.034627663	0.28	0.044702714	0.30	0.023463075
	BC002724	-0.42	0.014772148	-0.81	3.29E-05	0.93	6.18E-06	0.54	0.000991685
<i>MPP1</i>	NM_002436	-0.42	0.047666353	-0.78	0.000483518	1.51	2.71E-07	1.16	3.00E-06
<i>MYO19</i>	NM_001033580	-0.43	0.026532957	-1.00	1.21E-05	0.98	1.38E-05	0.41	0.02114696
<i>FANCC</i>	NM_000136	-0.51	0.011609739	-0.47	0.014584719	0.48	0.012959276	0.52	0.004986322
<i>OVOL2</i>	NM_021220	-0.52	0.001084197	-0.39	0.007292061	0.47	0.001844654	0.60	0.000100716
<i>SIN3B</i>	BC025026	-0.57	0.011569948	-0.75	0.00103124	1.01	5.47E-05	0.83	0.000227367
<i>CDT1</i>	NM_030928	-0.58	0.019198248	-0.90	0.000479465	1.44	2.66E-06	1.13	2.30E-05
<i>PON3</i>	NM_000940	-0.62	0.005105333	-0.84	0.000276722	0.93	8.48E-05	0.72	0.000647845
<i>ADRB2</i>	NM_000024	-0.63	0.001524882	-0.73	0.000236914	0.59	0.001792781	0.48	0.005629305
<i>PLK1</i>	NM_005030	-0.63	0.042808398	-0.63	0.034901844	2.40	8.38E-08	2.41	3.33E-08
	CR611847	-0.66	0.000634076	-0.51	0.003687258	0.35	0.044627807	0.50	0.002990718
	A_23_P216071	-0.70	0.00958912	-0.58	0.022202131	0.54	0.033583338	0.66	0.00706467
<i>CTSK</i>	NM_000396	-0.74	7.83E-05	-1.81	1.05E-09	1.64	2.75E-09	0.58	0.000331696
<i>ASF1B</i>	NM_018154	-0.76	0.048590758	-0.83	0.022912812	1.00	0.007299284	0.92	0.008832468
<i>NMNAT3</i>	NM_178177	-0.76	0.000552736	-0.87	9.23E-05	0.76	0.000345671	0.65	0.000881113
<i>REEP2</i>	NM_016606	-0.78	0.005759911	-0.93	0.001039901	1.69	1.66E-06	1.54	2.21E-06
<i>ABCF2</i>	NM_007189	-0.80	0.000944624	-0.74	0.001305162	0.60	0.00667932	0.66	0.001912744
<i>LMCD1</i>	NM_014583	-0.95	0.002645754	-0.76	0.010312363	0.74	0.012418953	0.93	0.001307708
<i>NRP2</i>	NM_201264	-0.97	0.002390052	-0.63	0.031835409	1.17	0.000297324	1.51	9.74E-06
<i>ST7OT1</i>	NR_002330	-0.99	0.000144723	-0.44	0.048099669	0.80	0.00068922	1.36	1.07E-06
<i>PKMYT1</i>	NM_182687	-0.99	0.001983455	-0.74	0.012491031	1.23	0.000180492	1.48	1.20E-05
<i>CPT1C</i>	NM_152359	-1.08	1.08E-05	-1.48	1.50E-07	0.94	2.56E-05	0.54	0.003391166
<i>BEX5</i>	NM_001012978	-1.26	0.001348714	-0.76	0.032521061	2.00	7.09E-06	2.50	2.08E-07
<i>DHRS13</i>	NM_144683	-1.45	0.00088615	-1.72	0.000114616	1.32	0.001366222	1.05	0.005333513
<i>CLDN17</i>	NM_012131	-1.47	4.17E-05	-1.79	2.57E-06	1.34	6.23E-05	1.01	0.000593411
<i>STAC</i>	NM_003149	-1.57	0.001093743	-1.23	0.005257075	0.88	0.043609023	1.22	0.003788264
	AK074473	-1.83	6.09E-06	-2.43	1.29E-07	1.71	7.39E-06	1.11	0.000405428
	CR602075	-2.00	0.007381353	-1.87	0.008773947	1.59	0.024722861	1.73	0.010382231
<i>CD248</i>	NM_020404	-2.04	2.85E-05	-1.14	0.004130168	0.77	0.049370648	1.67	7.16E-05