

Signaling Effects of Demethylasterriquinone B1, a Selective Insulin Receptor Modulator (SIRM)

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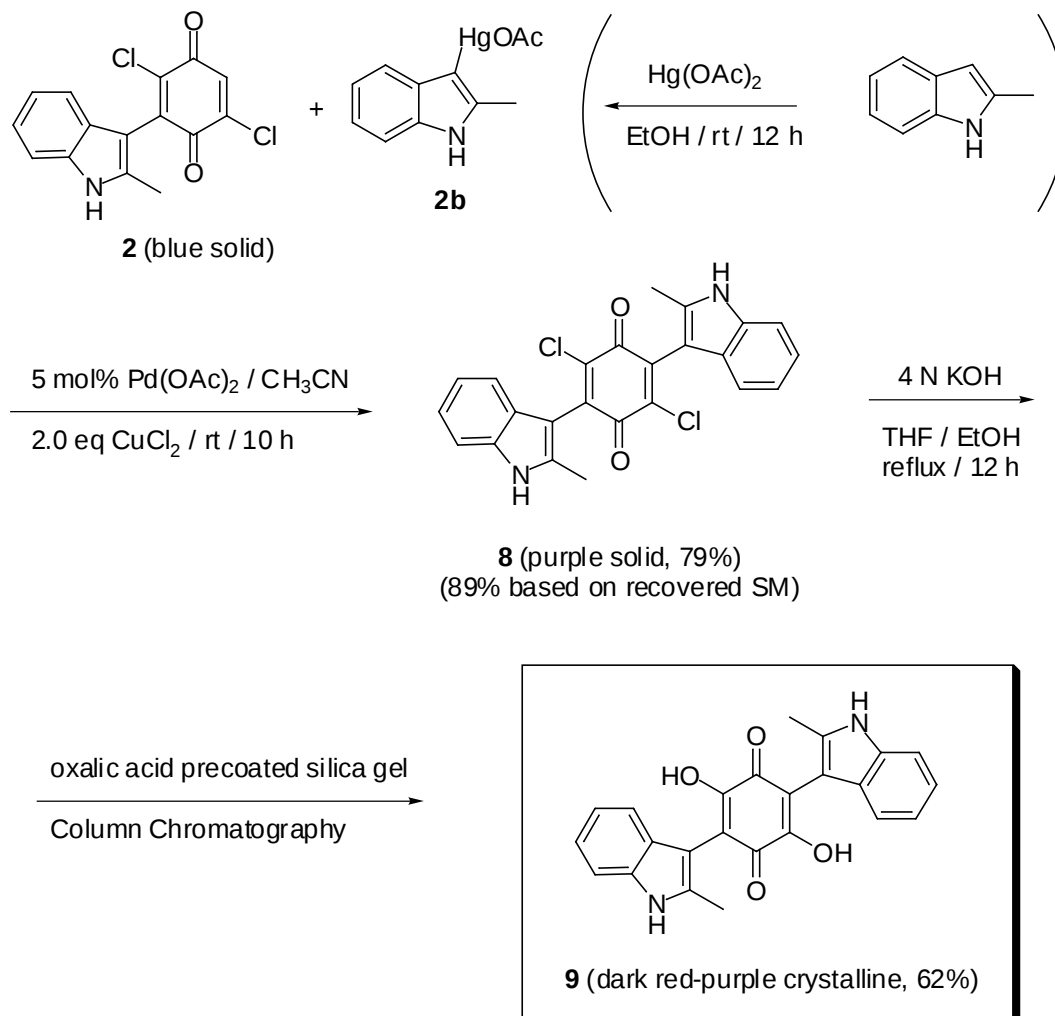
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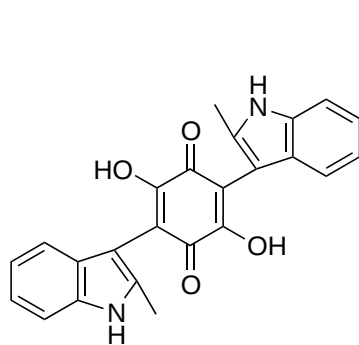
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2,5-Dichloro-3,6-bis-(2-methyl-1*H*-indol-3-yl)-[1,4]benzoquinone (8). To a solution of 2,5-dichloro-3-(2-methyl-1*H*-indol-3-yl)-[1,4]benzoquinone (**2**, 200 mg, 0.653 mmol) in CH₃CN (5 mL) were added 3-mercurial-2-methylindole **2a** (382 mg, 0.980 mmol), CuCl₂ (176 mg, 1.31 mmol) and Pd(OAc)₂ (7.3 mg, 0.0327 mmol) at room temperature. After stirred for 24 h at room temperature, the reaction mixture was filtered through Celite. The filtrate was concentrated and the residue was purified by flash column chromatography using 30% EtOAc in hexane as eluent to afford pure 2,5-dichloro-3,6-bis-(2-methyl-1*H*-indol-3-yl)-[1,4]benzoquinone (233 mg, 89% based on the recovered SM, **2** (7.5%)) as a blue solid. R_f = 0.29 (2:3, EtOAc/hexane); ¹H NMR (300 MHz, acetone-d₆) δ 10.6 (bs, 2NH), 7.40 - 7.31 (m, 4H), 7.14 - 7.02 (m, 4H), 2.42 (s, 3H), 2.40 (s, 3H); ¹³C NMR (75 MHz, acetone-d₆) δ 177.9, 140.7, 140.2, 137.8, 137.7, 136.5, 128.1, 121.8, 120.5, 120.4, 120.2, 111.5, 105.7, 13.6 (2C); LRMS (FAB) calcd for C₂₄H₁₇N₂O₂Cl₂ [M]⁺: 436.07. Found: 436.09.

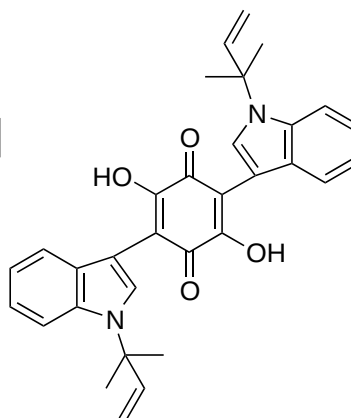
2,5-Dihydroxy-3,6-bis-(2-methyl-1*H*-indol-3-yl)-[1,4]benzoquinone (9). To a solution of 2,5-dichloro-3,6-bis-(2-methyl-1*H*-indol-3-yl)-[1,4]benzoquinone (**8**, 0.50 g, 1.15 mmol) in THF/EtOH (15/30 mL) were added aqueous 4 N KOH (15 mL, 60 mmol) at room temperature. The reaction mixture was refluxed for 10 h. The organic solvents, THF and EtOH, were removed *in vacuo* and the crude mixture was acidified with 1N HCl. The resulting solution was extracted with EtOAc (3 x 50 mL). The extracts were washed with brine and dried over Na₂SO₄. The residue was concentrated and purified by flash column chromatography using oxalic acid-precoated silicagel and 30% EtOAc in hexane as eluent to afford pure 2,5-dihydroxy-3,6-bis-(2-methyl-1*H*-indol-3-yl)-[1,4]benzoquinone (282 mg, 62%) as a dark red-purple solid. mp = 277 - 278 °C; IR (thin film) 3395, 2926, 1617, 1460 cm⁻¹; ¹H NMR (300 MHz, CD₃OD) δ 10.40 (bs, 2NH), 7.27 (d, J = 7.8 Hz, 4H), 7.06 - 6.94 (m, 4H), 2.32 (s, 6H); ¹³C NMR (75 MHz,

CD₃OD) d 137.0, 136.5, 129.3, 121.4, 120.3, 119.8, 112.6, 111.3, 102.7, 13.4; HRMS (FAB) calcd for C₂₄H₁₉N₂O₄ [M + H]⁺: 399.1345. Found: 399.1340.





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DAQ A1

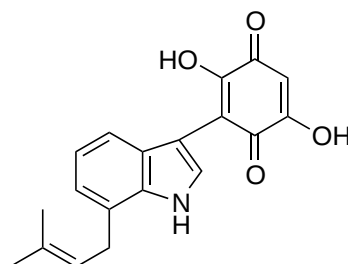
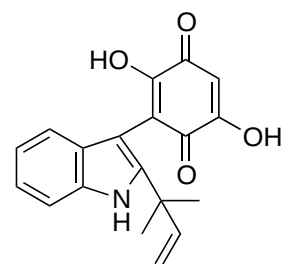
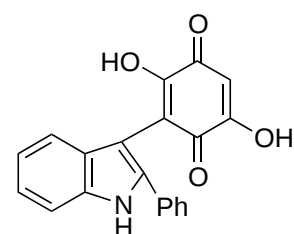
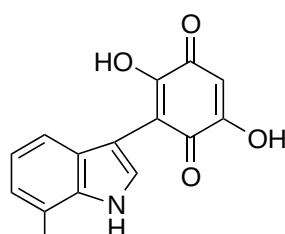
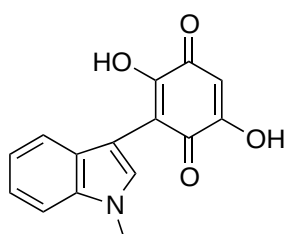
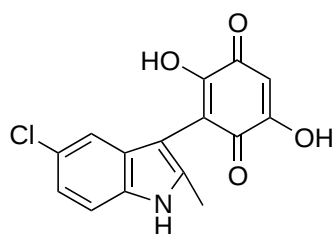
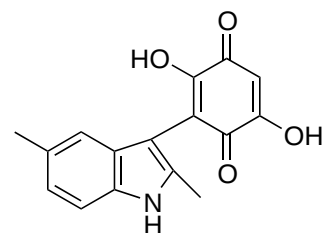
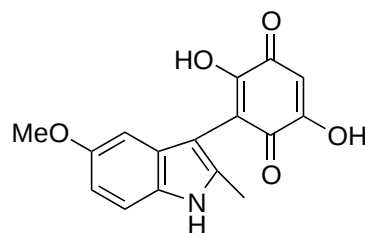
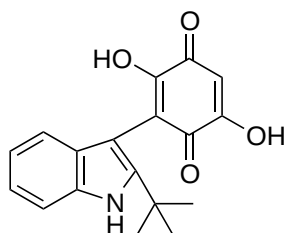
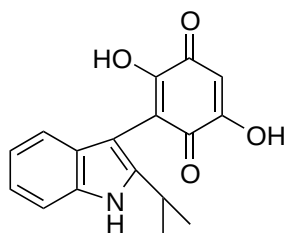
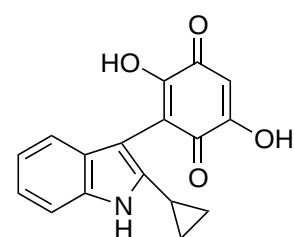
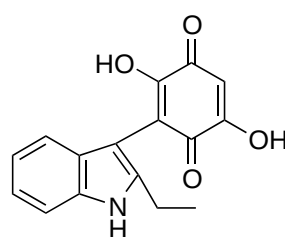
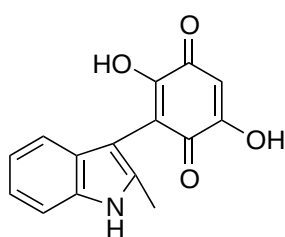
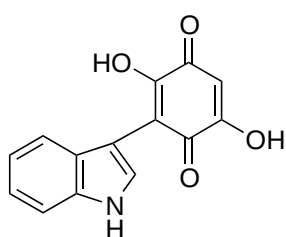


Table S1. RNAs Upregulated > 2× by DAQ Only

Genbank Accession #	Product	Fold
Z21966	mPOU homeobox protein	2
M11567	angiogenin	3
L27943	cytidine deaminase	2
D45248	proteasome activator hPA28 subunit beta	2
H12458	placenta Nb2HP cDNA IMAGE:148517 3' similar to SP:WNT6_MOUSE P22727 WNT-6	3
S81916	phosphoglycerate kinase	3
U93868	RNA polymerase III (DNA directed) (32kD)	3
X15183	90 kDa heat-shock protein (AA 1-732)	3
AC006271	BC319430_5	2
L05144	phosphoenolpyruvate carboxykinase 1 (soluble)	3
J03626	uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5'-decarboxylase)	3
U96915	sin3-associated polypeptide, 18kD	2
U39573	salivary peroxidase	4
D84454	solute carrier family 35 (UDP-galactose transporter), member 2	2
AF006087	actin related protein 2/3 complex, subunit 4 (20 kD)	2
AI819948	wj88e11.x1 NCI_CGAP_Lym12 cDNA clone IMAGE:2409932 3', mRNA	2
U89505	RNA binding motif protein 4	2
X12901	villin 1	2
AF044311	synuclein, gamma (breast cancer-specific protein 1)	*100
AF001461	transcription factor involved in hepatic wound healing, core promoter element binding protein	3
U93305	integral membrane protein; SP: O04901; may play role in cell differentiation in intestinal epithelium; LIM domain only 6	2
D61391	phosphoribosyl pyrophosphate synthetase-associated protein 1	2
AF061812	keratin 16	2
D42047	ha3662 gene product related to mouse glycerophosphate dehydrogenase.	2
AI961220	wt15b04.x1 NCI_CGAP_Ut1 cDNA IMAGE:2507503 3' similar to gb:M11949 pancreatic secretory trypsin inhibitor	3
AD001528	spermine synthase	2
AF042384	putative breast adenocarcinoma marker (32kD)	2
N95168	zb55f11.s1 fetal lung NbHL19W cDNA IMAGE:307533	2
X54942	CDC28 protein kinase 2	3
W28255	retina cDNA	2
AA978033	NCI_CGAP_Kid5 cDNA IMAGE:1590270 3' similar to gb:X15822 cytochrome c oxidase polypeptide VIIa precursor	2
D87673	heat shock transcription factor 4	2
U17969	eukaryotic translation initiation factor 5A	5
J04423	7,8-diamino-pelargonic acid aminotransferase	2

*basal level was 0

Table S2. RNAs Downregulated > 2× by DAQ Only

Genbank Accession #	Product	Fold
Y08200	rab geranylgeranyl transferase	2
M37238	phospholipase C, gamma 2 (phosphatidylinositol-specific)	100
L76191	interleukin-1 receptor-associated kinase	3
M22092	neural cell adhesion molecule	3
L07597	ribosomal protein S6 kinase, 90kD, polypeptide 1	100
U07695	tyrosine kinase	2
J03161	serum response factor (c-fos serum response element-binding transcription factor)	2
L38487	estrogen-related receptor alpha	2
U19796	melanoma-associated antigen recognised by T lymphocytes	3
U07563	v-abl Abelson murine leukemia viral oncogene homolog 1 isoform a	2
U09578	mitogen-activated protein kinase-activated protein kinase 3	2
U61836	putative cyclin G1 interacting protein	2
U51096	homeobox protein Cdx2	3
S75174	E2F transcription factor 4, p107/p130-binding	6
M62403	insulin-like growth factor-binding protein 4	3
U33053	protein kinase C-like 1	13
D50683	transforming growth factor, beta receptor II (70-80kD)	3
AF005775	CASP8 and FADD-like apoptosis regulator	2
AF024710	vascular endothelial growth factor	3
U29656	non-metastatic cells 3, protein expressed in	8
M73554	cyclin D1 (PRAD1: parathyroid adenomatosis 1)	13
M23410	junction plakoglobin	4
M64673	heat shock transcription factor 1	4
L29277	signal transducer and activator of transcription 3 (acute-phase response factor)	3
U78575	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha	2
U78110	neurturin precursor	3
X96744	paired box gene 7, isoform 1	2
L13385	platelet-activating factor acetylhydrolase, isoform Ib, alpha subunit (45kD)	9
U07802	butyrate response factor 2 (EGF-response factor 2)	3
X78992	butyrate response factor 2 (EGF-response factor 2)	7
U90552	butyrophilin, subfamily 3, member A1	2
D79992	KIAA0170 gene product, similar to Drosophila photoreceptor cell-specific protein, calphotin	8
AB018247	FE65-LIKE 2	3
M59287	protein kinase	8
AF104913	eukaryotic translation initiation factor 4 gamma, 1	5
AI052224	liver/spleen 1NFLS_S1 cDNA:1675946 similar to SW:PKBS_MOUSE P50637 peripheral benzodiazepine receptor	3

U37012	cleavage and polyadenylation specific factor 1, 160kD subunit	4
L25270	SMC (mouse) homolog, X chromosome, escapes X-chromosome inactivation	10
L41143	T-cell leukemia translocation altered gene	100
AF016903	agrin precursor	2
AF009225	conserved helix-loop-helix ubiquitous kinase	2
AL034374	dJ483K16.1.1 (novel protein (isoform 1))	2
AC002045	nuclear pore complex interacting protein	3
U76702	follistatin-like 3 glycoprotein	3
AI829701	NFL_T_GBC_S1 cDNA IMAGE:2350101 3' similar to gb:L23556 IG heavy chain V-II region	3
AB019529	8-oxoguanine DNA glycosylase, isoform 1a	2
W22541	retina cDNA Tsp509I-cleaved sublibrary	5
AL050141	clone DKFZp586O031	3
Y00486	adenine phosphoribosyltransferase	3
D31766	KIAA0060, similar to E.coli N-acetylglucosamine transport protein	3
AA173896	zp03b02.s1 Stratagene ovarian cancer (#937219) cDNA IMAGE:595275	3
X85237	splicing factor 3a, subunit 1, 120kD	2
U59151	dyskeratosis congenita 1, dyskerin	2
AB029012	KIAA1089 protein	8
U65090	carboxypeptidase D precursor	3
U43318	frizzled 5	3
U61232	beta-tubulin cofactor E	2
AL050280	DKFZP586B0519 protein	2
AF015553	TFII-I protein	2
U40571	syntrophin, alpha 1(dystrophin-associated protein A1, 59kD, acidic component)	3
AB014587	mitogen-activated protein kinase kinase kinase 4	2
AF006082	ARP2 (actin-related protein 2, yeast) homolog	3
H93123	fetal liver/spleen 1NFLS cDNA IMAGE:241884	2
W25936	retina cDNA randomly primed sublibrary	2
D00265	cytochrome c	3
AB020712	yeast Sec31p homolog	4
AL049654	protein kinase C, alpha binding protein	2
AI417075	NhHMPu_S1 cDNA IMAGE:2114920 3' similar to SW:MOF_DROME O02193 males-absent on the first protein	2
X98261	M-phase phosphoprotein 5	2
L13848	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 9 (RNA helicase A, nuclear DNA helicase II)	3
L37368	RNA-binding protein S1, serine-rich domain	2
M63959	low density lipoprotein-related protein-associated protein 1 (alpha-2-macroglobulin receptor-associated protein 1)	2
D42040	RING3	3
AB018314	KIAA0771 protein	2
Z24725	mitogen inducible gene mig-2	2

X51405	carboxypeptidase E precursor	2
U09585	interferon-related developmental regulator 2	3
D21261	transgelin 2	3
M64936	retinoic acid-inducible endogenous retroviral DNA.	3
X90908	gastrotropin	3
Z24727	tropomyosin isoform	3
X80692	mitogen-activated protein kinase 6	9
U70063	N-acylsphingosine amidohydrolase (acid ceramidase)	2
Y08262	ataxin 2	2
U83981	growth arrest and DNA-damage-inducible 34	2
AF040628	ectodermal dysplasia 1, anhidrotic	6
AF020044	stem cell growth factor; lymphocyte secreted C-type lectin	3
Z29481	3-hydroxyanthranilate 3,4-dioxygenase	2
X81625	eukaryotic translation termination factor 1	2
U79716	reelin	2
AF007150	clone 23767 and 23782	5
M55268	casein kinase 2, alpha prime polypeptide	2
D31764	KIAA0064 gene product	3
U16799	ATPase, Na ⁺ /K ⁺ transporting, beta 1 polypeptide	2
AB020687	solute carrier family 21 (organic anion transporter), member 9	10
U26266	deoxyhypusine synthase isoform a	4
X74008	protein phosphatase 1, catalytic subunit, gamma isoform	2
X80200	TNF receptor-associated factor 4	5
U70370	paired-like homeodomain transcription factor 1	2
U94905	diacylglycerol kinase, zeta (104kD)	3
D84110	RNA-binding protein gene with multiple splicing	3
M65028	heterogeneous nuclear ribonucleoprotein A/B	2
AB011151	KIAA0579 protein	3
X70218	protein phosphatase 4 (formerly X), catalytic subunit	2
U90916	clone 23815	2
M91029	adenosine monophosphate deaminase 2 (isoform L)	3
M95627	angio-associated, migratory cell protein	3
U50733	dynamitin (dynactin complex 50 kD subunit)	2
AJ012008	dimethylarginine dimethylaminohydrolase 2	21
AF047863	microtubule-associated protein tau, isoform 2	6
AB011087	KIAA0515 protein	3
Y08685	serine palmitoyltransferase, long chain base subunit 1	2
U94831	transmembrane 9 superfamily member 1	3
AB021663	activating transcription factor 5	3

AI074025	NCI_CGAP_CLL1 cDNA IMAGE:1670854 similar to gb:M23419 initiation factor 5A	2
N98667	multiple_sclerosis_2NbHMSP cDNA IMAGE:278505	3
AL008583	chromobox homolog 6	7
X16416	v-abl Abelson murine leukemia viral oncogene homolog 1 isoform a	2
D87437	KIAA0250 gene product	8
U20982	insulin-like growth factor-binding protein 4	2
L77567	mitochondrial citrate transport protein (CTP)	4
AI526089	DU3.2-7.H07.r DU-145 cDNA	2
D43951	KIAA0099 protein	2
AB002312	bromodomain adjacent to zinc finger domain, 2A	3
J03161	serum response factor (c-fos serum response element-binding transcription factor)	2
D89937	folistatin-like 1	3
X96484	DiGeorge syndrome critical region gene 6	100
AC005053	six transmembrane epithelial antigen of the prostate	8
AB015718	serine/threonine kinase 10	9
S69189	peroxisomal acyl-coenzyme A oxidase	4
AB011144	minichromosome maintenance deficient (S. cerevisiae) 3-associated protein	2
AJ010059	SHP2 interacting transmembrane adaptor	2
X64228	nucleoporin 214kD (CAIN)	100
AJ005259	endothelial differentiation-related factor 1	3
AI660963	Dieckgraefe_colon_NHUC cDNA IMAGE:2351166 similar to gb:U07358 mixed lineage kinase 2	3
U68723	checkpoint suppressor 1	2
X52221	ercc2 gene product	3
AC005943	methyl-CpG binding domain protein 3	5
AB014888	MRJ gene for a member of the DNAJ protein family	2
AA194159	NhHMPu_S1 cDNA IMAGE:665617	2
AF037339	cleft lip and palate associated transmembrane protein 1	2
X56681	jun D proto-oncogene	3
AW044624	NSF_F8_9W_OT_PA_P_S1 cDNA IMAGE:2554662 3' similar to TR:O15258 O15258 rer1 protein	2
AF034373	ataxin 2 related protein, isoform 1	9
U43572	N-acetylglucosaminidase, alpha- (Sanfilippo disease IIIB)	5
U79297	clone 23589	2
U89896	casein kinase 1, gamma 2	3
AL040137	DKFZp434D1813_s1 434 (synonym: htes3)	2
AB018274	KIAA0731 protein	3
U77948	general transcription factor II, i	3
U70987	docking protein 1	3
S62539	insulin receptor substrate 1	3
M74524	ubiquitin-conjugating enzyme E2A (RAD6 homolog)	6

M91670	ubiquitin carrier protein	2
L33243	polycystic kidney disease 1 (autosomal dominant)	100
X59812	cytochrome P450, subfamily XXVIIA (steroid 27-hydroxylase, cerebrotendinous xanthomatosis), polypeptide 1	2

Table S3. RNAs Upregulated > 2× by Insulin Only

Genbank Accession #	Product	Fold
L07597	ribosomal protein S6 kinase, 90kD, polypeptide 1	2
L27080	melanocortin 5 receptor	3
D00591	chromosome condensation 1	4
S81914	immediate early response 3	5
U15655	ERF	2
L22005	ubiquitin conjugating enzyme	3
D12686	eIF-4 gamma	3
L04270	lymphotoxin B receptor	2
J04102	v-ets avian erythroblastosis virus E26 oncogene homolog 2	2
L13720	growth arrest-specific 6	3
Z23115	BCL2-like 1	*100
U61836	putative cyclin G1 interacting protein	3
M14764	nerve growth factor receptor precursor	2
U08023	c-mer proto-oncogene tyrosine kinase	3
U67092	ATM protein	2
AB000584	prostate differentiation factor	2
Z36714	cyclin F	3
AF024710	vascular endothelial growth factor	2
V00568	c-myc oncogene	3
X55504	nucleolar protein 1 (120kD)	3
M73554	cyclin D1 (PRAD1: parathyroid adenomatosis 1)	5
M80261	apurinic endonuclease	2
M31328	guanine nucleotide binding protein (G protein), beta polypeptide 3	3
AL031737	dJ8B22.1 (similar to cytoplasmic dynein light chain 1)	2
M55630	topoisomerase I pseudogene 2.	2
AL050136	DKFZp586L141	2
D86967	KIAA0212 gene product	3
AF017995	3-phosphoinositide dependent protein kinase-1	2
AF098462	stanniocalcin 2	4
AF057164	solute carrier family 22 (organic cation transporter), member 5	5
AB007915	KIAA0446 protein	2
S46950	adenosine A2a receptor	2
U00968	sterol regulatory element binding transcription factor 1	3
AB000461	gene with multiple splice variants near HD locus on 4p16.3	3
AB002386	enhancer of zeste (Drosophila) homolog 1	4
M20470	clathrin, light polypeptide B (Lcb) isoform a	3

Y11525	CCAAT/enhancer binding protein (C/EBP), alpha	2
L13385	platelet-activating factor acetylhydrolase, isoform Ib, alpha subunit (45kD)	3
AF000560	TTF-I interacting peptide 20	2
U84720	RAE1 (RNA export 1, S.pombe) homolog	2
U84720	RAE1 (RNA export 1, S.pombe) homolog	2
L08246	myeloid cell leukemia sequence 1 (BCL2-related)	2
C18655	placenta cDNA GEN-565G08	2
AB011133	KIAA0561 protein	3
M16941	DR7 beta-chain glycoprotein	2
D88827	zinc finger protein 263	3
X57348	stratifin	2
X76040	protease, serine, 15	8
AI535653	P9-C4.T3.P9.D4 conorm cDNA	2
AB005754	topoisomerase-related function protein 4	3
L41143	T-cell leukemia translocation altered gene	5
AF067420	SNC73 protein	2
U87459	cancer/testis antigen	2
X02344	tubulin, beta, 2	2
X98494	M phase phosphoprotein 10	2
AC002045	nuclear pore complex interacting protein	4
W28892	randomly primed retina cDNA sublibrary	3
U76702	folliculin-like 3 glycoprotein	3
U81375	solute carrier family 29 (nucleoside transporters), member 1	3
AB007144	death-associated protein kinase 3	2
W28869	53h2 randomly primed retina cDNA sublibrary	2
AB018325	KIAA0782 protein	2
L03426	DNA segment on chromosome X and Y (unique) 155 expressed sequence	2
D83778	KIAA0194 protein	2
AB018338	KIAA0795 protein	2
AI352450	NCI_CGAP_GC4 cDNA IMAGE:1947812 similar to SW:MAZ_HUMAN P56270 myc-associated zinc finger protein	2
AJ005893	polyglutamine binding protein 1	2
X97324	adipose differentiation-related protein	2
AB002352	KIAA0354 gene product	2
M25753	cyclin B	2
AF047473	BUB3 (budding uninhibited by benzimidazoles 3, yeast) homolog	2
Y12065	nucleolar protein (KKE/D repeat)	2
X79536	heterogeneous nuclear ribonucleoprotein A1	2
D28423	pre-mRNA splicing factor SRp20	3
AF084481	Wolfram syndrome	2

AB007929	KIAA0460 protein	2
U31501	fragile X mental retardation, autosomal homolog 2	3
AJ132712	nuclear RNA export factor 1	2
U78525	eukaryotic translation initiation factor	2
U38276	Semaphorin IV	3
AF035287	similar to synaptic membrane glycoprotein	3
AI986201	NCI_CGAP_Ut1 cDNA IMAGE:2494056 3' similar to SW:DYI2_RAT Q62871 cytosolic dynein intermed. chain 2,	2
AF026816	putative oncogene protein	4
D78130	squalene monooxygenase	3
M62831	immediate early protein	3
AF022375	vascular endothelial growth factor	3
X75755	splicing factor, arginine/serine-rich 2	2
L40397	putative	3
U29185	prion protein (p27-30) (Creutzfeld-Jakob disease)	2
U61234	beta-tubulin cofactor C	2
Z15108	protein kinase C, zeta	2
D42040	RING3	3
S78771	RING3	3
AI827895	NFL_T_GBC_S1 cDNA IMAGE:2350347	6
AB011093	KIAA0521 protein	2
M33308	vinculin isoform VCL	2
X87949	BiP protein	3
X77956	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	10
X77956	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	4
X06272	signal recognition particle receptor ('docking protein')	3
AB002324	KIAA0326 protein	11
AF022991	circadian period protein, period 1	*100
X70394	zinc finger protein 146	5
U39400	chromosome 11 open reading frame 4	2
U89278	early development regulator 2	3
X17025	isopentenyl-diphosphate delta isomerase	2
Z56281	interferon regulatory factor 3	3
AF040628	ectodermal dysplasia 1, anhidrotic	3
U44755	small nuclear RNA activating complex, polypeptide 2, 45kD	3
Z50115	thimet oligopeptidase 1	2
AI140857	fetal_heart_NbHH19W cDNA IMAGE:1693364	3
AB030506	B9 protein	3
X64318	nuclear factor, interleukin 3 regulated	3
AF007150	clone 23767 and 23782	4

X78678	ketoheokinase, isoform a	2
U28811	Golgi apparatus protein 1	2
V00568	c-myc oncogene	4
AB015019	BAI1-associated protein 2, isoform 1	2
AF112972	TJ6 protein	4
J02943	corticosteroid binding globulin precursor	2
AL049942	hypothetical protein	2
AL050269	DKFZP564C103 protein	2
L25665	guanine nucleotide binding protein-like 1	4
X66436	hsr1 g protein	4
X63422	ATP synthase, H ⁺ transporting, mitochondrial F1 complex, delta subunit	2
J02939	antigen identified by monoclonal antibodies 4F2, TRA1.10, TROP4, and T43	3
U90909	clone 23722	3
D38555	SEC24 (S. cerevisiae) related gene family, member C	2
M14083	serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	3
AF050110	TGFB inducible early growth response	3
U34683	glutathione synthetase	3
S81752	diphtheria toxin resistance protein required for diphthamide biosynthesis (Saccharomyces)-like 1	2
U08377	splicing factor, arginine/serine-rich 8 (suppressor-of-white-apricot, Drosophila homolog)	3
D88667	galactosylceramide sulfotransferase	3
M14630	prothymosin, alpha (gene sequence 28)	2
U80760	trinucleotide repeat containing 1	3
X80230	cyclin-dependent kinase 9 (CDC2-related kinase)	2
X79067	butyrate response factor 1 (EGF-response factor 1)	3
M81945	CD34 antigen	2
W26655	34c9 randomly primed retina cDNA sublibrary	3
H98552	melanocyte 2NbHM cDNA IMAGE:250709	3
AI262789	NCI_CGAP_Co8 cDNA IMAGE:1870970 similar to gb:J05016 protein disulfide isomerase-related protein precursor	2
AJ006973	target of myb1 (chicken) homolog	2
X99720	papillary renal cell carcinoma (translocation-associated)	3
X58521	nucleoporin 62kD	2
U72514	C2f	3
W28264	44c9 randomly primed retina cDNA sublibrary	2
S62138	TLS-CHOP	3
X97671	erythropoietin receptor precursor	2
AL080209	DKFZp586F2423	2
J03075	protein kinase C substrate 80K-H	2
AA522530	NCI_CGAP_Lu1 cDNA IMAGE:979127	7
M24069	cold shock domain protein A	2

AI246730	NCI_CGAP_Co8 cDNA IMAGE:1871401	3
AI935420	NCI_CGAP_Kid11 cDNA IMAGE:2462030	3
U63090	sialyltransferase 4B (beta-galactosidase alpha-2,3-sialyltransferase)	3
D10040	fatty-acid-Coenzyme A ligase, long-chain 2	2
AF035444	tumor suppressing subtransferable candidate 3	4
AC005053	six transmembrane epithelial antigen of the prostate	3
AF091890	G-protein coupled receptor	2
X52425	interleukin 4 receptor precursor	3
AB020710	KIAA0903 protein	2
AF047469	arsenite translocating ATPase	3
X64228	nucleoporin 214kD (CAIN)	4
AB004066	differentiated embryo chondrocyte expressed gene 1	2
X63564	polymerase (RNA) II (DNA directed) polypeptide A (220kD)	2
M34715	pregnancy specific beta-1-glycoprotein 1	2
U63541	hemochromatosis protein	2
L49380	zinc finger protein 162	2
D84273	asparaginyl-tRNA synthetase	2
W27997	43e3 randomly primed retina cDNA sublibrary	5
AB002344	KIAA0346	2
M64174	janus kinase 1	3
AF047442	SEC22, vesicle trafficking protein (S. cerevisiae)-like 1	2
AI688299	NCI_CGAP_Co3 cDNA IMAGE:2325667	2
AB018337	KIAA0794 protein	4
AC004770	BC269730_1	2
AF048977	Ser/Arg-related nuclear matrix protein (plenty of prolines 101-like)	2
Z83840	non-histone chromosome protein 2 (S. cerevisiae)-like 1	2
AL049851	dJ889J22B.1 (novel protein (isoform 2))	3
X00734	tubulin, beta, 5	2
U89896	casein kinase 1, gamma 2	4
M59465	tumor necrosis factor, alpha-induced protein 3	6
L41351	protease, serine, 8 (prostasin)	2
U84487	small inducible cytokine subfamily D (Cys-X3-Cys), member 1 (fractalkine, neurotactin)	3
J04423	7,8-diamino-pelargonic acid aminotransferase	2
X00351	beta actin	3
M33197	glyceraldehyde-3-phosphate dehydrogenase	2

*basal level was 0

Table S4. RNAs Downregulated > 2× by Insulin Only

Genbank Accession #	Product	Fold
M11717	70 kDa heat shock protein	4
M74587	insulin-like growth factor binding protein 1	5
X04297	ATPase alpha subunit (aa 1-1023)	3
AI885852	NCI_CGAP_Brn25 cDNA IMAGE:2429487 similar to gb:L19779 histone H2A.1	2
AI541050	pec1.2-1.E08.recnorm	2
M34309	v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 3	2
L10379	CTG-B45d	2
W29087	ex. randomly primed retina cDNA sublibrary	3
Y09445	T-box 5	3
L38941	ribosomal protein L34	2
M94314	ribosomal protein L24	2
AC004770	BC269730_1	3
W52024	ribosomal protein S15a	3
X02596	breakpoint cluster region, isoform 1	2
W27541	ex. randomly primed retina cDNA sublibrary	100
Y17169	protein tyrosine kinase 9-like (A6-related protein)	2
Y00815	protein tyrosine phosphatase, receptor type, f polypeptide	3
U01120	glucose-6-phosphatase, catalytic	9
M81141	lymphocyte antigen	2
AI246726	NCI_CGAP_Co8 cDNA IMAGE:1871416 similar to gb:X61970 proteasome zeta chain	2
X79389	glutathione S-transferase theta 1	2
D88308	fatty-acid-Coenzyme A ligase, very long-chain 1	2
D86961	KIAA0206	2
L40802	hydroxysteroid (17-beta) dehydrogenase 2	2
D50402	solute carrier family 11 (sodium/phosphate symporters), member 1	3
AB014520	KIAA0620 protein	100
AL050159	hypothetical protein	2
X13916	low density lipoprotein-related protein 1 (alpha-2-macroglobulin receptor)	3
AB022718	decidual protein induced by progesterone	37
S73885	transcription factor AP-4 (activating enhancer-binding protein 4)	2
AI708983	Barstead aorta HPLRB6 cDNA IMAGE:2353949 similar to gb:M15661 60S ribosomal protein L44	9
J02984	ribosomal protein S15	3
M57730	ephrin A1 precursor	2
U57721	kynureninase (L-kynurenine hydrolase)	3
X95808	zinc finger protein 261	2
U49785	D-dopachrome tautomerase	2

D26068	eukaryotic translation initiation factor 4H	2
AJ007583	acetylglucosaminyltransferase-like protein	142
M99435	transducin-like enhancer of split 1, homolog of Drosophila E (sp1)	2
AF062346	zinc finger protein 216	3
L13698	growth arrest-specific 1 (gas1)	5

Table S5. RNAs Upregulated > 2× by DAQ and Insulin

Genbank Accession #	Product	Fold by Ins	Fold by DAQ
AF008442	RNA polymerase I subunit	100	100
L78207	ATP-binding cassette, sub-family C, member 8	100	100
AI521453	cDNA similar to SW:P15_HUMAN P53999 RNA polymerase II transcriptional coactivator P15	83	127
L40402	Zap2	*100	*100
W28931	ex. randomly primed retina cDNA sublibrary	100	100
D84239	Fc fragment of IgG binding protein	100	100
J03764	plasminogen activator-1	100	100
S78187	Cdc25B	100	100
D00408	cytochrome P450, subfamily IIIA, polypeptide 7	100	100
M60974	growth arrest and DNA-damage-inducible, alpha	100	100
U88629	ELL-related RNA polymerase II, elongation factor	*100	*100
D79985	DiGeorge syndrome critical region gene 2	*100	*100
X51804	putative receptor protein	63	57
U08998	TAR (HIV) RNA-binding protein 2	52	40
L29217	CDC-like kinase 3 isoform hclK3/152	34	32
AB018316	KIAA0773 gene product	43	21
AB020626	KIAA0819 protein	35	9
V01512	v-fos FBJ murine osteosarcoma viral oncogene homolog	6	9
L17075	activin A receptor type II-like 1	7	8
AF052151	clone 24574	16	8
M62324	modulator recognition factor I	9	7
AB023192	imidazoline receptor candidate	12	6
AI347155	cDNA IMAGE:2062868 3' similar to TR:O00233 O00233 proteasome subunit P27.	9	6
D83542	cadherin-15	3	5
U52522	partner of RAC1 (arfaptin 2)	9	5
AF035313	clone 23851	44	5
M12174	ras homolog gene family, member B	20	5
D14874	adrenomedullin	2	4
AJ224335	similar to yeast BET3 (S. cerevisiae)	7	4
AB014547	myotubularin related protein 4	5	4
U41804	putative T1/ST2 receptor binding protein	5	4
S81439	TGFB inducible early growth response	12	4
AB029016	KIAA1093 protein	5	4
M12792	cytochrome P450, subfamily XXIA (steroid 21-hydroxylase,), polypeptide 2	3	4
AB023167	lifeguard	7	4
N36638	melanocyte 2NbHM cDNA IMAGE:268833	8	4

U47927	Ubiquitin isopeptidase T	3	3
AI254524	NCI_CGAP_Ov32 cDNA IMAGE:1984837 3' similar to contains element L1 repetitive element	10	3
X74795	minichromosome maintenance deficient (S. cerevisiae) 5 (cell division cycle 46)	3	3
U48705	tyrosine kinase DDR	3	3
X68277	protein-tyrosine phosphatase	3	3
D14811	gene predicted from cDNA with a complete coding sequence	4	3
L13434	chromosome 3p21.1 gene sequence	4	3
AF046001	zinc finger protein 207	2	3
D38535	inter-alpha (globulin) inhibitor H4 (plasma Kallikrein-sensitive glycoprotein)	3	3
U91543	chromodomain helicase DNA binding protein 3	3	3
L13738	activated p21cdc42Hs kinase	4	3
AJ005866	Sqv-7-like protein	5	3
D76444	zinc finger protein homologous to Zfp103 in mouse	3	3
J04423	7,8-diamino-pelargonic acid aminotransferase	2	3
U46691	suppressor of Ty (S.cerevisiae) 6 homolog	14	3
D88208	suppressor of S. cerevisiae gcr2	3	2
AF039945	synaptojanin 2B	2	2
U01147	active breakpoint cluster region-related protein	3	2
X63753	SON DNA binding protein	3	2
AF010315	p53-induced protein	3	2
W28356	ex. 48e3 randomly primed retina cDNA sublibrary	5	2
AL096857	hypothetical protein	4	2
AB011174	KIAA0602 protein	4	2
U94362	glycogenin 2	3	2
M28170	CD19 antigen	2	2
U41668	deoxyguanosine kinase	2	2
AI553745	NCI_CGAP_Brn25 cDNA IMAGE:2168948 3' similar to WP:ZK265.6 CE15299	8	2
D89618	karyopherin alpha 3	2	2
AF052155	clone 24761	3	2
U14391	myosin IC	3	2
M64929	protein phosphatase-2A subunit-alpha	3	2
U31556	E2F-5	4	2
AA160724	zo72h04.r1 Stratagene pancreas (#937208) cDNA IMAGE:592471	3	2
AI127424	cDNA IMAGE:1705899 similar to gb:M31211 myosin light chain 1, slow-twitch muscle A isoform	2	2
D63876	KIAA0154 gene product related to mouse gamma adaptin.	3	2
D63861	peptidylprolyl isomerase D (cyclophilin D)	3	2
Y09723	zinc finger protein 151 (pHZ-67)	3	2
AC004382	CC chemokine STCP-1	3	2

*basal level was 0

Table S6. RNAs Downregulated > 2× by DAQ and Insulin

Genbank Accession #	Product	Fold by Ins	Fold by DAQ
AB002356	MAP-kinase activating death domain	100	4
AF070598	ABC transporter, ATP-binding cassette, sub-family B, member 6	5	3
L05624	mitogen-activated protein kinase kinase 1	3	2
AL080061	DKFZp564H182 (CLIC4)	3	3
M63167	rac protein kinase alpha	3	3
AB002310	upstream regulatory element binding protein 1 (KIAA0312)	3	100
Z35093	surfeit 1 (SURF-1)	3	3
U03105	proline-rich protein with nuclear targeting signal	3	2
S75174	E2F transcription factor 4, p107/p130-binding	3	3
Y07661	upstream transcription factor 2, c-fos interacting	3	3
AI004207	fetus_Nb2HF8_9w cDNA IMAGE:1624472 like WP:F57C12.4 CE04674 ATP-binding transport	2	4
R54564	infant brain 1NIB cDNA IMAGE:39876	2	3
X75252	prostatic phosphatidylethanolamine binding protein	2	3
D50863	testis-specific kinase 1 (TESK1)	2	7
M64673	heat shock transcription factor 1 (TCF5)	2	4
AL050395	DKFZp586D1020	2	2
Z30093	general transcription factor IIH, polypeptide 3 (34kD subunit)	2	2