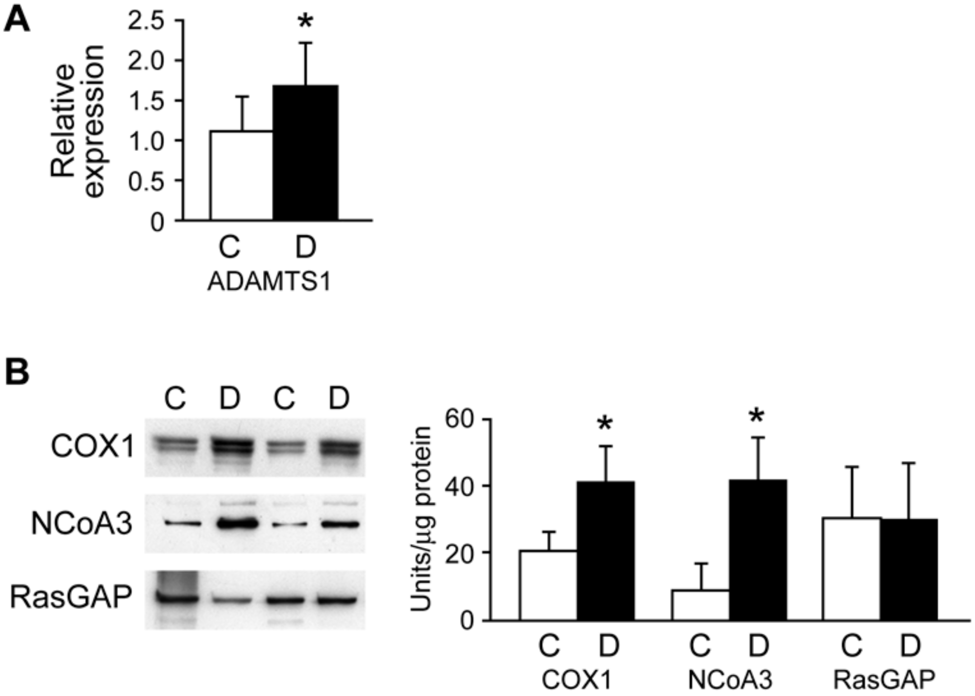
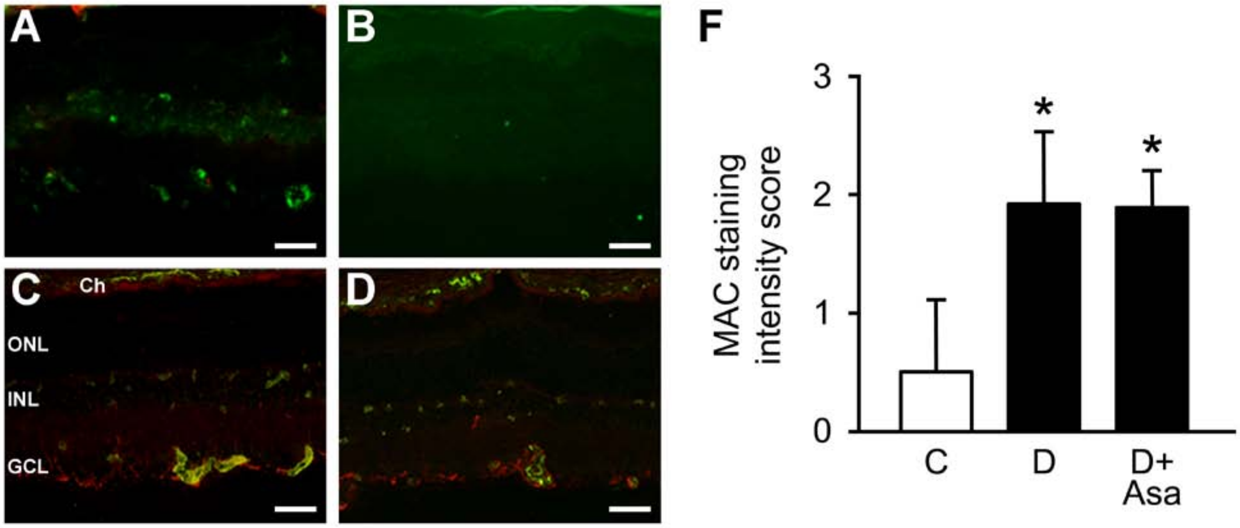
Supplemental Table 1: Primary antibodies used in immunoblotting

Antigen	Antibody	Source (catalog #)	Dilution
TGFβR1	rabbit polyclonal V-22	Santa Cruz Biotechnology (sc-398)	1:500
COX-1	rabbit polyclonal	Cayman Chemical (160109)	1:500
NCoA3	goat polyclonal R-19	Santa Cruz Biotechnology (sc-32348)	1:200
RasGAP	rabbit antiserum	gift of Dr. A. Kazlauskas	1:10,000
β-actin	mouse monoclonal AC-15	Sigma-Aldrich (A 5441)	1:10,000
phosphorylated Smad2 (ser465/467)	rabbit polyclonal	Cell Signaling Technology (3101)	1:1000
Smad2/3	rabbit polyclonal	Millipore (07-408)	1:1000



Supplemental Figure 1. Confirmation of microarray results for selected genes. Total RNA and protein lysates were prepared from retinal vessels isolated by hypotonic lysis from the retina of diabetic (D) and age-matched control (C) rats. **(A)** ADAMTS-1 mRNA levels assayed by quantitative real-time PCR. Relative expression was calculated by the comparative C_T method using β-actin as endogenous control. Values are mean ± SD. n = 7 rats per group. * $P = 0.05$. **(B)** Representative Western blots of COX1 and NCoA3, and bar plot of the quantitative analysis. Immunoblotting for RasGAP served as control for loading. Values are mean ± SD. n = 3-5 rats per group. * $P < 0.02$.



Supplemental Figure 2. Aspirin treatment does not prevent complement activation in the retinal vessels of diabetic rats (3 months diabetes duration). Complement activation was detected by immunostaining retinal sections for the membrane attack complex (MAC, C5b-9) of complement. The secondary antibody was Cy3-conjugated, yielding red fluorescence. Double-staining for vWf (FITC, green fluorescence) was used to identify the vessels. The intensity and frequency of MAC staining were scored by masked observers on a scale from 0 (no staining) to 4 (maximal staining) as previously described (10). **(A-C)** Representative photographs of retinal sections immunostained for MAC and vWf. **(A)** The retina of a control rat shows only vWf staining, MAC is not detected. **(B)** Negative control. (**C)** The retina of a diabetic rat shows colocalization of MAC and vWf, indicating deposition of MAC in the retinal vessels. **(D)** The retina of an aspirin-treated diabetic rat shows colocalization of MAC and vWf, as in untreated diabetes. ONL, outer nuclear layer; INL, inner nuclear layer; GCL, ganglion cell layer; Ch, choroid. Scale bar = 50 micron. **(F)** Bar plot of the quantitative analysis of MAC staining intensity; values are mean ± SD. C, control rats, n=5; D, diabetic rats, n=7; D+ASA, diabetic rats treated with aspirin, n=4. * *P*< 0.003 vs C.

Supplemental Table 2: Gene expression profile of retinal vessels in diabetes. Differentially expressed genes related to **TGF-β/BM Ps pathway**.

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
TGF-β PATHWAY ACTIVATION									
1376636_at	BE111972	29591	transforming growth factor, beta receptor 1	Tgfbr1	2.06	0.99700	YES	YES	**ALK-5.** Receptor serine/threonine kinase. TGF-β receptor complex. Both TGFBRI and TGFBRII are required for TGF-β signaling. Upregulated in ischemia-reperfusion injury and atherosclerotic lesions. **Upregulated by glucose (mesangial cells, MDCK cells, VSMC) and in diabetes (kidney).**
1368921_a_at	NM_012924	25406	CD44 antigen	Cd44	2.05	0.99900	NO	NO	Cell-surface glycoprotein. Receptor for hyaluronic acid (HA) and other ligands (osteopontin, collagens, MMPs). Multiple isoforms (alternative splicing). Cell-cell and cell-matrix interactions, cell adhesion and migration. Cytokines/growth factors presentation. Binding of HA to CD44 leads to NF-κB activation. Induced in inflammation by cytokines and growth factors (TNFα, IL-1β, TGF-β, IFN, HGF, VEGF, and FGF). Upregulated in vascular injury. Pro-angiogenic. Interacts with TGFβR1 = enhances TGF-β signaling. Interacts with CD74.
1382189_at	AI574779	25615	syndecan 2	Sdc2	2.09	0.99900	NO	YES	**Heparan sulfate proteoglycan 1.** Proteoglycan receptor of the ECM. Connection between ECM and actin cytoskeleton. Binds laminin, FN, growth factors, and a variety of other molecules. Highly expressed in brain vessels. Cell proliferation and migration. Interacts with FGF2, VEGF, and TGF-β superfamily = growth factor presentation to the specific receptor and co-receptor. Upregulated by TNF-α (HUVEC), TGF-β1, and BMP-2. Syndecan-2 overexpression leads to upregulation of TGF-β RI and RII. **Increased in diabetes (kidney) = regulates TGF-β activity.**
1396074_at	BF525157	25573	ubiquitin-conjugating enzyme E2I	Ube2i	1.92	0.99302	YES	YES	**Ubc9.** Member of the E2 ubiquitin-conjugating enzyme family. Ube2i is the key enzyme of the sumoylation reaction. The Sumo pathway is a key regulator of numerous processes: transcriptional regulation, nuclear transport, maintenance of genome integrity, signal transduction. Sumoylation occurs in proteins involved in: cell-cycle regulation, proliferation, apoptosis and DNA repair. Regulation of cell growth (mitotic progression chromosome segregation, sister-chromatid regulation). Ubc9 and, by implication, the SUMO pathway, is critical for early embryonic development. Overexpressed in tumors. Interacts with FAS (also UP) and modulates FAS activity. Interacts with p53-p63 (also UP). Regulates Smad4 stability and transcriptional activity.
1367631_at	NM_022266	64032	connective tissue growth factor	Ctgf	2.11	0.99200	YES	YES	Member of the CNN family of matricellular proteins initially discovered as a protein secreted by EC. Induced by TGF-β is a downstream mediator of TGF-β = fibrosis. Promotes EC proliferation, migration, adhesion, survival = pro-angiogenic. Binds BMPs (inhibition of BMP signaling) and TGF-β1 (activation of TGF-β signaling). Upregulated in wound healing and fibrotic diseases. **Upregulated in diabetes (retina and kidney glomeruli) and by high glucose (mesangial cells) via TGF-β.**
1367712_at	NM_053819	116510	tissue inhibitor of metallopeptidase 1	Timp1	4.01	1.00000	NO	NO	Inhibitor of MMPs. Promotes cell proliferation and may have an anti-apoptotic function. Upregulated by cytokines (IL-1β, TNF-α, IFNγ, IL-6, TGF-β) and hormones. Induced by TGF-β via CTGF. Inflammatory response. Anti-angiogenic. Upregulated in vascular injury = prevents neointima formation. **Upregulated in diabetes (glomeruli, retinal Müller cells) and by high glucose (via CTGF).**
1371310_s_at	BI285495	29345	serine (or cysteine) proteinase inhibitor, clade H, member 1	Serpinh1	2.49	1.00000	NO	NO	**HSP47, colligin.** Member of the serpin superfamily of serine proteinase inhibitors. Molecular chaperone involved in the maturation of collagen molecules. Upregulated by TGF-β in rat skeletal myoblasts, mouse osteoblasts, and human embryonic lung fibroblast =fibrosis. Upregulated in atherosclerotic lesions (SMC) and in lesions of fibrotic diseases. Interacts with Cd9.
1368259_at	NM_017043	24693	prostaglandin-endoperoxide synthase 1	Ptgs1	2.04	0.99900	NO	YES	**Cyclooxygenase 1, COX-1.** Prostaglandin synthesis. Constitutive isoform. Inhibited by aspirin. Upregulated in EC in tissue injury (cirrhotic liver, traumatic brain injury) and by estrogen/progesterone. Upregulated by TGF-β. **In diabetes: upregulated in kidney medulla, downregulated in aorta and sciatic nerve.**

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1380638_at	BI294907	84584	nuclear receptor coactivator 3	Ncoa3	2.12	0.99232	YES	NO	**Steroid receptor coactivator 3 (SRC3), thyroid hormone receptor activator molecule 1 (TRAM-1), CBP-interacting protein.** Nuclear receptor coactivator. Interacts with nuclear-hormone receptors. Enhances NF-κB activity (interaction with IKK). Highly expressed in VSMC and EC. Induced by TGF-β.
1371131_a_at	U30789	117514	Thioredoxin interacting protein	Txnip	2.66	0.99899	YES	NO	**VDUP1.** Negative regulator of thioredoxin. Upregulation promotes oxidative stress. Pro-apoptotic. Upregulated by vitamin D3 and TGF-β. **Upregulated by high glucose (glucose responsive elements in the promoter). Induced in diabetes (aorta, kidney, islets).**
1386913_at	NM_019358	54320	podoplanin	Pdpn	2.02	0.99600	YES	NO	Mucin-type small membrane glycoprotein. Expressed in lymphatic EC, podocytes, alveolar type I cells, and epithelial cells. Induced in HUVEC and microvascular EC by IFNγ, IL-3, TNF-α. Induced by TGF-β (tumor cells). Lymphatic development. Promotes cell adhesion, migration, and tube formation. Ectopic expression = actin reorganization and cell motility.
1389617_at	BM392135	362871	ELK3, member of ETS oncogene family (predicted)	Elk3_predicted	2.00	0.99027	NO	NO	Transcription factor member of the ETS-domain transcription factor family and the ternary complex factor (TCF) subfamily. Proteins in this subfamily regulate transcription when recruited by serum response factor to bind to serum response elements. Activated by signal-induced phosphorylation; transcriptional inhibitor in the absence of Ras, but activates transcription when Ras is present. Repressor of NOS2 and HO1; upregulated by TGF-β1; downregulated by LPS
1374976_a_at	AI548897	81782	Sterol O-acyltransferase 1	Soat1	2.01	0.99137	NO	YES	**Acat-1.** Endoplasmic reticulum. Catalyzes the formation of cholesterol esters from cholesterol. Upregulated by TGF-β. Upregulated in atheroma. **Activity increased in diabetic rats.**
1368963_at	NM_013160	25701	Max interacting protein 1	Mxi1	2.20	0.98943	YES	NO	Member of the Myc/Max/Mad protein family. Transcriptional repressor. Negative regulator of Myc oncoprotein activity. Induced by hypoxia. Induced by TGF-β.
1390426_at	BF389398	25496	Notch gene homolog 1 (Drosophila)	Notch1	3.01	0.99998	NO	YES	Notch signaling pathway. Receptor for membrane bound ligands. Development/vascular development. Required in part for the TGF-β cytostatic response. Expressed in EC and upregulated in vascular injury (EC and SMC). Both anti-apoptotic and pro-apoptotic. Activation of NF-κB.
1374601_at	BI274482	360697	interferon gamma receptor 2 (predicted)	Ifngr2_predicted	1.96	0.99485	YES	NO	IFNγ receptor β chain. Signaling chain of the IFNγ receptor. IFN-γ signaling is activated in neointimal SMC. Upregulated in vascular injury and atherosclerosis. Potentiates the proliferative effect of PDGF on VSMC. IFN γ is antifibrotic = inhibits the activity of p300--Smad coactivator/TGF-β pathway.
BMPs PATHWAY ACTIVATION									
1390398_at	AI179372	81507	Bone morphogenetic protein receptor, type 1A	Bmpr1a	2.46	0.99803	NO	NO	**ALK-3.** Serine/threonine kinase closely related to the TGF-β receptor I. Receptors for BMPs
1380442_at	AI235507	368178	homeo box C8	Hoxc8	0.33	0.99325	YES	YES	Transcription factor. Spatial patterning during embryogenesis. Interacts with Smad1 and smad6. Overexpression inhibits Smad1-dependent transcription of bone related genes
1370256_at	AA944349	58868	frizzled homolog 1 (Drosophila)	Fzd1	2.05	0.99272	YES	NO	Wnt receptor. G protein-coupled receptor. Wnt signaling pathways. Development, vascular development. Upregulated by BMP2.
1373911_at	BM389026	361945	periostin, osteoblast specific factor (predicted)	Postn_predicted	2.41	0.99700	YES	NO	**Osteoblast specific factor 2.** Secreted adhesion molecule. Binds to integrins and promotes integrin-dependent cell adhesion and motility. Promotes SMC migration and proliferation, tumor survival, and angiogenesis. Upregulated by hypoxia, BMP2, TGF-β, and growth factors. Upregulated in vascular injury (SMC).

Supplemental Table 3: Gene expression profile of retinal vessels in diabetes. Differentially expressed genes related to **oxidative stress**

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
PRO-OXIDANT									
1387328_at	NM_019184	29277	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	Cyp2c	2.20	0.99950	YES	NO	Most abundant member of the p450 xenobiotic-inducible superfamily. ROS production. Metabolizes arachidonic acid to epoxyeicosatrienoic acids (EETs). EETs are vasodilator, inhibit platelet adhesion, and elicit endothelial cell proliferation and angiogenesis.
1371774_at	AA893220	302642	spermidine/spermine N1-acetyl transferase (mapped)	Sat	2.09	0.99800	YES	NO	Rate-limiting enzyme of polyamine catabolism. Overexpression leads to generation of H2O2 and oxidative stress, inhibition of cell growth and apoptosis, and increased integrin-mediated cell migration. Upregulated in ischemia-reperfusion and by H2O2 (kidney, liver)
1371131_a_at	U30789	117514	Thioredoxin interacting protein	Txnip	2.66	0.99899	YES	NO	**VDUP1.** Negative regulator of thioredoxin. Upregulation promotes oxidative stress. Pro-apoptotic. Upregulated by vitamin D3 and TGF-β. **Upregulated by high glucose (glucose responsive elements in the promoter). Induced in diabetes (aorta, kidney, islets).**
ANTI-OXIDANT									
1369321_s_at	NM_012840	25310	cytochrome c, testis	Cyct	0.30	0.99459	NO	YES	Testis specific cytochrome c; expressed during spermatogenesis. Involved in H2O2 detoxification: antioxidant.
1381650_at	BM389433	291314	selenophosphate synthetase 1	Sephs1	1.99	0.99092	YES	YES	Synthesis of selenophosphate from selenide and ATP. Selenophosphate is used to synthesize selenocysteine, which is co-translationally incorporated into selenoproteins at in-frame UGA codons. Most selenoproteins are involved in redox balance (glutathione peroxidase, thioredoxin reductase) Overexpression leads to increasead cell death in response to genotoxic conditions in a p53-dependent mechanism.
1390416_at	H35736	361074	solute carrier family 25, member 30	Slc25a30	2.16	0.99600	YES	NO	**Kidney mitochondrial carrier protein-1.** Mitochondrial carrier. Upregulated by fasting and during the regenerative phase of glycerol-induced renal failure in association with upregulation of superoxide-generating enzymes. Proposed function: shift from carbohydrate to lipid metabolism and protection from oxidative damage.
PRO-/ANTI-OXIDANT									
1368418_a_at	AF202115	24268	ceruloplasmin	Cp	3.68	1.00000	NO	NO	Copper-containing ferroxidase. Copper and iron metabolism and homeostasis. Inflammatory response, acute-phase response protein. Exerts both anti-oxidant and pro-oxidant (on lipoproteins) effects. **Upregulated in retinal Müller cells in diabetes.**
1368419_at	AF202115	24268	ceruloplasmin	Cp	2.65	1.00000	NO	NO	Copper-containing ferroxidase. Copper and iron metabolism and homeostasis. Inflammatory response, acute-phase response protein. Exerts both anti-oxidant and pro-oxidant (on lipoproteins) effects. **Upregulated in retinal Müller cells in diabetes.**
1368420_at	NM_012532	24268	ceruloplasmin	Cp	4.80	1.00000	NO	NO	Copper-containing ferroxidase. Copper and iron metabolism and homeostasis. Inflammatory response, acute-phase response protein. Exerts both anti-oxidant and pro-oxidant (on lipoproteins) effects. **Upregulated in retinal Müller cells in diabetes.**

Supplemental Table 4: Gene expression profile of retinal vessels in diabetes. Differentially expressed genes related to **inflammation/response to injury.**

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
INFLAMMATORY MEDIATORS									
1386987_at	NM_017020	24499	interleukin 6 receptor, alpha	Il6ra	2.02	0.99925	YES	NO	**IL-6Rα, CD126.** Subunit α of the IL-6 receptor complex. Binds IL-6 and recruits gp130. IL-6 signals by phosphorylating STAT3 and it is pro-angiogenic.
1370224_at	BE113920	25125	signal transducer and activator of transcription 3	Stat3	2.38	0.99769	YES	NO	Transcription factor downstream of IL-6 and other IL-6 family members that use the gp130 receptor. Pro-angiogenic. Upregulated in retina neovessels (hyperoxia model of ROP).
1371781_at	BI285863	25125	signal transducer and activator of transcription 3	Stat3	2.20	0.99719	YES	NO	Transcription factor downstream of IL-6 and other IL-6 family members that use the gp130 receptor. Pro-angiogenic. Upregulated in retina neovessels (hyperoxia model of ROP).
1372064_at	BI296385	497942	similar to chemokine (C-X-C motif) ligand 16	Cxcl16	2.04	0.99174	YES	NO	Chemokine family similar to fractalkine. Transmemrane form is an adhesion molecule, the cleaved soluble form is a chemokine = recruitment of CXCR6 expressing T, NK, NKT cells to site of inflammation/injury. CXCL16 also functions as a scavenger receptor for phosphatidylserine and oxidized LDL = promotes foam cell formation. Induces SMC proliferation.
1368259_at	NM_017043	24693	prostaglandin-endoperoxide synthase 1	Ptgs1	2.04	0.99900	NO	YES	**Cyclooxygenase 1, COX-1.** Prostaglandin synthesis. Constitutive isoform. Inhibited by aspirin. Upregulated in EC in tissue injury (cirrhotic liver, traumatic brain injury) and by estrogen/progesterone. Upregulated by TGF-β. **In diabetes: upregulated in kidney medulla, downregulated in aorta and sciatic nerve.**
1386879_at	NM_031832	83781	lectin, galactose binding, soluble 3	Lgals3	5.10	0.99931	YES	NO	**Galectin 3.** IgE-binding lectin. Multiple extracellular and intracellular functions. Immediate early gene. Cell-cell and cell-matrix interaction. Laminin-binding. RAGE ligand. Amplifier of inflammation. Anti-apoptotic. Pro-angiogenic. Upregulated in vascular injury. **Upregulated in diabetes (kidney, retinal Müller cells, hippocampus) and by glucose (mesangial cell).**
ACUTE-PHASE RESPONSE PROTEINS									
1367794_at	NM_012488	24153	alpha-2-macroglobulin	A2m	2.90	1.00000	YES	NO	Broad spectrum protease inhibitor. Inflammatory response, acute-phase response protein. Antiangiogenic. Binds cytokines and growth factors and regulates their biological activity. **Upregulated in retinal Müller cells in diabetes.**
1370907_at	M83143	25197	Beta galactoside alpha 2,6 sialyltransferase 1	St6gal1	2.19	0.99629	YES	NO	Sialylation of N-linked oligosaccharide of glycoproteins/ glycolipids. Ubiquitously expressed with tissue-specific isoforms/regulation. The hepatic form is an Acute-Phase Protein (induced by IL-6). Membrane protein (golgi) and secreted (cleavage by cathepsin-S-like). Upregulated in HUVEC by LPS, and cytokines. Upregulated by Ras oncogene leads to changes in integrin sialylation.
1368418_a_at	AF202115	24268	ceruloplasmin	Cp	3.68	1.00000	NO	NO	Copper-containing ferroxidase. Copper and iron metabolism and homeostasis. Inflammatory response, acute-phase response protein. Exerts both anti-oxidant and pro-oxidant (on lipoproteins) effects. **Upregulated in retinal Müller cells in diabetes.**
1368419_at	AF202115	24268	ceruloplasmin	Cp	2.65	1.00000	NO	NO	Copper-containing ferroxidase. Copper and iron metabolism and homeostasis. Inflammatory response, acute-phase response protein. Exerts both anti-oxidant and pro-oxidant (on lipoproteins) effects. **Upregulated in retinal Müller cells in diabetes.**
1368420_at	NM_012532	24268	ceruloplasmin	Cp	4.80	1.00000	NO	NO	Copper-containing ferroxidase. Copper and iron metabolism and homeostasis. Inflammatory response, acute-phase response protein. Exerts both anti-oxidant and pro-oxidant (on lipoproteins) effects. **Upregulated in retinal Müller cells in diabetes.**
1387893_at	D88250	192262	complement component 1, s subcomponent	C1s	2.91	0.99916	YES	NO	Classical complement pathway. Acute-phase response protein. Inhibited by SERPING1 (UP). Increased in aortic tissue of hypercholesterolemic mice. Increased in serum in familiar hypercholesterolemia. **Upregulated in retinal Müller cells in diabetes.**
1383391_a_at	AI716125	24231	complement component 2	C2	2.42	0.99837	YES	NO	Classical complement pathway. Acute-phase response protein. Induced by IFNγ, and other cytokines.

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1368000_at	NM_016994	24232	complement component 3	C3	3.50	0.99990	NO	NO	Complement pathway. Acute-phase response protein. Induced by IFNg, and other cytokines. Increased in aortic tissue of hypercholesterolemic mice. Increased in serum in familiar hypercholesterolemia. **Upregulated in retinal Müller cells in diabetes.**
1389470_at	AI639117	294257	Complement factor B	Cfb	2.27	0.99545	YES	NO	Complement alternative pathway. Acute-phase response protein. Induced by IFNg, and other cytokines. **Upregulated in retinal Müller cells in diabetes.**
1387011_at	NM_130741	170496	lipocalin 2	Lcn2	4.21	0.99947	NO	NO	**Neutrophil gelatinase-associated lipocalin (NGAL), oncogene24p3.** Member of the lipocalin family. Iron delivery pathway. Acute-phase response protein upregulated in inflammation. Modulates the activity of matrix MMPs (by preventing inactivation by TIMP1). Upregulated in atheroma and MI (vascular inflammation, plaque instability). **Upregulated in retinal Müller cells in diabetes.**
1368224_at	NM_031531	24795	Serine (or cysteine) peptidase inhibitor, clade A, member 3N	Serpina3n	5.46	0.99158	YES	NO	Homolog of human and mouse antichimotrypsin. Acute-phase response protein. Induced by IL-6 via STAT3 (liver). **Upregulated in retinal Müller cells in diabetes.**
IFNγ PATHWAY									
1374601_at	BI274482	360697	interferon gamma receptor 2 (predicted)	Ifngr2_predicted	1.96	0.99485	YES	NO	IFNγ receptor β chain. Signaling chain of the IFNγ receptor. IFN-γ signaling is activated in neointimal SMC. Upregulated in vascular injury and atherosclerosis. Potentiates the proliferative effect of PDGF on VSMC. IFN γ is antifibrotic = inhibits the activity of p300--Smad coactivator/TGF-β pathway.
1370913_at	AI409634	65190	Best5 protein	Best5	2.10	0.99432	NO	NO	Induced by IFNγ. Ossification. **Upregulated in retinal Müller cells in diabetes.**
1367595_s_at	NM_012512	24223	beta-2 microglobulin	B2m	2.03	0.99700	YES	NO	Induced by IFNγ in HUVEC. Induced in inflammation and injury. Pro- apoptotic. Inhibits NF-kB and activates STAT3. Chaperone of MHC class I molecules. Antigen presentation. Interacts with CD1d1 antigen. Iron metabolism.
1387005_at	NM_017320	50654	cathepsin S	Ctss	2.10	0.99900	YES	NO	Lysosomal cysteine protease. Elastolytic and collagenolytic activity. Degradation of proteoglycans. Upregulated by IFNγ. Mediates interferon-induced apoptosis. MHCII antigen presentation (degradation of the MHC invariant chain CD74). Upregulated in EC by cytokine/growth factors. Pro-angiogenic. Upregulated in atheroma and vascular injury. **Serum levels increased in DM with atherosclerosis and obesity.**
1386913_at	NM_019358	54320	podoplanin	Pdpn	2.02	0.99600	YES	NO	Mucin-type small membrane glycoprotein. Expressed in lymphatic EC, podocytes, alveolar type I cells, and epithelial cells. Induced in HUVEC and microvascular EC by IFNγ, IL-3, TNF-α. Induced by TGF-β (tumor cells). Lymphatic development. Promotes cell adhesion, migration, and tube formation. Ectopic expression = actin reorganization and cell motility.
1367786_at	NM_080767	24968	proteosome (prosome, macropain) subunit, beta type 8	Psmb8	2.73	0.99846	YES	NO	Member of the proteasome B-type family. Induced by IFN-γ. Antigen presentation.
1396268_at	BF523991	301570	SP110 nuclear body protein	Sp110	2.38	0.99606	NO	NO	**IF-induced P 41 30kD; IF-induced P 75 52kD.** Induced by IFNγ. Negative regulation of RARα-mediated transcription.
1397221_s_at	BE108106	246097	Tumor necrosis factor receptor superfamily, member 6	Tnfrsf6	2.60	1.00000	NO	NO	**FAS, CD95 antigen.** Member of the TNF-receptor superfamily. Induces apoptosis. EC are usually resistant, while VSMC are susceptible to FAS-induced apoptosis. Induced by cytokines (IFNγ, TNF-α, IL-1β in EC and VSMC; TGFβ in gastric carcinoma cells). Upregulated in vascular injury. FAS/FASL deficiency increases neovascularization. **Upregulated in retinal vessels in diabetes.**
ANTIGEN PRESENTATION									
1368593_at	NM_017079	25109	CD1d1 antigen	Cd1d1	2.09	0.99943	YES	NO	Antigen presentation (lipid antigen). MHC class 1b. Expressed in T cells, NKT cells, and VSMC. Interacts with β-2 microglobulin and CD74.

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1367679_at	NM_013069	25599	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)	Cd74	4.47	1.00000	NO	NO	**Ii, Ia-associated invariant chain.** Antigen presentation. Accessory signaling molecule. The cleaved cytosolic fragment of CD74 translocates to the nucleus and activates transcription mediated by NF-kB. Interacts with CD1d1 and CD44. Induced by IFN. **Upregulated in retinal Müller cells in diabetes.**
1387568_at	NM_031713	65146	paired-Ig-like receptor B	Pirb	0.31	0.99827	YES	NO	Immunoglobulin-like receptor. MHC class I recognition system. Inhibits chemokine and integrin signaling.
1388071_x_at	M24024	24737	RT1 class Ib, locus Aw2	RT1-Aw2	2.08	0.99462	YES	NO	Class Ib gene of the rat major histocompatibility complex. Antigen presentation and processing. **Upregulated in retinal Müller cells in diabetes.**
ANTI-INFLAMMATORY									
1392171_at	AA945643	89824	chitinase 3-like 1	Chi3l1	2.19	0.98982	YES	NO	**Cartilage glycoprotein-39.** Member of chi-lectin family. Induced in inflammation, tissue remodeling (connective tissue turnover), atheroma, and tumors. Promotes migration and adhesion of VSMC and EC. Induces HUVEC tubulogenesis. Mitogenic (via AKT). Inhibits cytokines signaling = anti-inflammatory.
1372254_at	AW915763	295703	serine (or cysteine) peptidase inhibitor, clade G, member 1	Serping1	4.10	0.99896	YES	NO	**C1 inhibitor.** Inhibitor of complement activation (C1s and C1r, classical pathway) and other proteases (kallicrein, plasmin and coagulation factors). Inhibits leukocytes adhesion (anti-inflammatory). Inhibits vascular leakage (deficiency = angioedema hereditary, knockout=increased vascular permeability). Prevents ischemia/reperfusion injury. **Upregulated in retinal Müller cells in diabetes.**
1385397_at	AA859085	499991	Ab1-219	LOC499991	2.00	0.99261	NO	NO	Rat homolog of mouse and human STEAP4/STAMP2 (Tiarp, Tnfa-induced adipose-related protein) expressed during adipocyte differentiation. Induced by TNFa, IL6, GH, and FA in adipocytes. Regulated by androgen. Metalloreductase involved in iron and copper uptake. Suppressor of inflammation under nutrient-rich condition.

Supplemental Table 5: Gene expression profile of retinal vessels in diabetes. Differentially expressed genes related to **matrix and vascular remodeling.**

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
MATRIX									
1382189_at	AI574779	25615	syndecan 2	Sdc2	2.09	0.99900	NO	YES	**Heparan sulfate proteoglycan 1.** Proteoglycan receptor of the ECM. Connection between ECM and actin cytoskeleton. Binds laminin, FN, growth factors, and a variety of other molecules. Highly expressed in brain vessels. Cell proliferation and migration. Interacts with FGF2, VEGF, and TGF-β superfamily = growth factor presentation to the specific receptor and co-receptor. Upregulated by TNF-α (HUVEC), TGF-β1, and BMP-2. Syndecan-2 overexpression leads to upregulation of TGF-β RI and RII. **Increased in diabetes (kidney) = regulates TGF-β activity.**
1379300_at	AW520944	367145	carbohydrate sulfotransferase 2 (predicted)	Chst2_predicted	1.98	0.99600	YES	NO	Sulfation of chondroitin at position 6-O. Keratan sulfate biosynthesis. Lymphocyte homing.
1391022_at	BE101834	305078	laminin, beta 3	Lamb3	0.38	0.99247	NO	NO	Components of laminin-5. Binds dystroglycan, syndecan, and integrins.
1371310_s_at	BI285495	29345	serine (or cysteine) proteinase inhibitor, clade H, member 1	Serpinh1	2.49	1.00000	NO	NO	**HSP47, colligin.** Member of the serpin superfamily of serine proteinase inhibitors. Molecular chaperone involved in the maturation of collagen molecules. Upregulated by TGF-β in rat skeletal myoblasts, mouse osteoblasts, and human embryonic lung fibroblast =fibrosis. Upregulated in atherosclerotic lesions (SMC) and in lesions of fibrotic diseases. Interacts with Cd9.
1392990_at	AI031004	312936	SRY-box containing gene 17 (predicted)	Sox17_predicted	2.58	0.99873	NO	NO	Transcriptional regulator. Enhances fibronectin and laminin transcription. Inhibits Wnt signaling by binding to β-catenin.
CELL ADHESION									
1370907_at	M83143	25197	Beta galactoside alpha 2,6 sialyltransferase 1	St6gal1	2.19	0.99629	YES	NO	Sialylation of N-linked oligosaccharide of glycoproteins/ glycolipids. Ubiquitously expressed with tissue-specific isoforms/regulation. The hepatic form is an Acute-Phase Protein (induced by IL-6). Membrane protein (golgi) and secreted (cleavage by cathepsin-S-like). Upregulated in HUVEC by LPS, and cytokines. Upregulated by Ras oncogene leads to changes in integrin sialylation.
1389095_at	BE110539	360715	biregional cell adhesion molecule-related/down-regulated by oncogenes (Cdon) binding protein (predicted)	Boc_predicted	2.11	0.99528	NO	YES	Receptor of the Ig/fibronectin type III repeat family. Involved in myogenic differentiation. Cell-cell contact. Interacts with cadherin.
1371499_at	AI227627	24936	CD9 antigen	Cd9	2.00	0.99184	YES	NO	**Tetraspanin 29.** Cell surface glycoprotein member of the tetraspanin family (tetraspanins forms membrane microdomains involved in integrin-dependent adhesion strengthening, migration, and signaling). Highly abundant on EC surface. Involved in cell adhesion and migration (via integrin). Inhibits SMC migration (by inhibiting integrin clustering). Leukocyte adhesion and transmigration. Triggers platelet activation. Interacts with tetraspanin 8, Serpinh1, and Ifitm3/fragilis.
1375936_at	BI279663	291760	desmocollin 2	Dsc2	3.13	0.99961	NO	NO	Desmosomal cadherin. Expressed primarily in epithelial cells. Desmocollin (and desmogleins) are the adhesive proteins of the desmosome cell-cell junction and are required for cell adhesion and desmosome formation.
1371430_at	AW251326	114489	dystroglycan 1	Dag1	2.06	0.99600	YES	NO	Non-integrin adhesion molecule. Laminin-binding component of the dystrophin-glycoprotein complex (linkage between the cytoskeleton and the extracellular matrix). Required for basement membrane organization. Expressed in EC at the blood-brain barrier. Upregulated in tumor EC.

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1392888_at	AI071251	317322	glypican 4	Gpc4	1.97	0.98575	NO	NO	**k-glypican.** GPI-anchored heparan sulphate proteoglycans that modulate signaling by growth factors: HSPGs are low-affinity accessory binding sites that facilitate or stabilize binding of the ligand to its high-affinity receptor. Control of cell division and growth regulation. Glypican-4 is expressed in synovial vessels (EC, pericytes and SMC), HUVEC, renal tubular cells. Glypican-4 binds: endostatin and mediates endostatin anti-angiogenic function, FGF2: regulation of FGF2 action during cortical neurogenesis, and HGF.
1373911_at	BM389026	361945	periostin, osteoblast specific factor (predicted)	Postn_predicted	2.41	0.99700	YES	NO	**Osteoblast specific factor 2.** Secreted adhesion molecule. Binds to integrins and promotes integrin-dependent cell adhesion and motility. Promotes SMC migration and proliferation, tumor survival, and angiogenesis. Upregulated by hypoxia, BMP2, TGF-β, and growth factors. Upregulated in vascular injury (SMC).
1387568_at	NM_031713	65146	paired-Ig-like receptor B	Pirb	0.31	0.99827	YES	NO	Immunoglobulin-like receptor. MHC class I recognition system. Inhibits chemokine and integrin signaling.
ACTIN ORGANIZATION									
1392250_at	AI145827	56611	Annexin A2	Anxa2	0.37	0.99127	NO	YES	**Lipocortin2, calpactin 1 heavy chain. M**ember of the annexin family. Annexins (in combination with members of the S100A family) bind charged phospholipids in a Ca2+ dependent manner, a property required for membrane fusion=vesicles trafficking (endocytosis/exocytosis), and tight junction assembly (annexinA2/S100A10 heterotetramer). AnnexinA2 is also involved in the organization of membrane-associated actin at sites of cholesterol enriched membrane rafts. AnnnexinA2 on EC luminal surface binds PA and tPA = antithrombogenic; plasminogen receptor; interacts with CD44 (up).
1383546_at	BE097393	302421	glycerophosphodiester phosphodiesterase domain containing 2 (predicted)	Gdpd2_predicted	2.73	0.98718	YES	NO	Osteoblast differentiation: expressed at the stage of matrix maturation in association with actin filament disappearance. Actin cytoskeleton organization
1385433_at	AI576354	362918	metastasis suppressor 1 (predicted)	Mtss1_predicted	0.47	0.99210	NO	YES	Scaffold protein that interacts with Rac, actin, and actin-associated proteins to modulate lamellipodia formation. promotes actin organization. Mtss1 inhibits WASP-mediated actin polymerization. Overexpression inhibits cell motility.
1370339_at	L24775	117557	Tropomyosin 3, gamma	Tpm3	2.20	0.99800	YES	NO	**Tropomyosin γ, Tpm5.** Nonmuscle low-molecular weight tropomyosin (many isoforms). Promotes actin filament stability, vesicle trafficking, and cell motility. Overexpression = increased stress fiber.
1376124_at	BG375480	296936	Wiskott-Aldrich syndrome-like (human)	Wasl	1.97	0.99290	YES	YES	**N-WASP.** Regulation of the cortical actin cytoskeleton. Activator of the Arp2/3 complex = branching of actin filaments. Ubiquitously expressed.
VASCULAR REMODELING									
1379586_at	BF564116	361332	A disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 19 (predicted)	Adamts19_predicted	1.83	0.98966	YES	NO	member of the ADAMTS family (subgroup f).

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1368223_at	NM_024400	79252	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 1	Adamts1	2.72	1.00000	NO	NO	Member of the ADAMTS family of metalloprotease. Degradation of proteoglycans. Upregulated in inflammation, MI (early ischemic response gene), wound healing, atheroma. Antiangiogenic.
1374778_at	AI409046	25423	cathepsin C	Ctsc	2.19	0.99497	YES	NO	Cysteine dipeptidyl aminopeptidase. Activator of serine proteases involved in immune and inflammatory responses. Deficiency protects against acute arthritis. Proteoglycan degradation.
1387005_at	NM_017320	50654	cathepsin S	Ctss	2.10	0.99900	YES	NO	Lysosomal cysteine protease. Elastolytic and collagenolytic activity. Degradation of proteoglycans. Upregulated by IFNγ. Mediates interferon-induced apoptosis. MHCII antigen presentation (degradation of the MHC invariant chain CD74). Upregulated in EC by cytokine/growth factors. Pro-angiogenic. Upregulated in atheroma and vascular injury. **Serum levels increased in DM with atherosclerosis and obesity.**
1368921_a_at	NM_012924	25406	CD44 antigen	Cd44	2.05	0.99900	NO	NO	Cell-surface glycoprotein. Receptor for hyaluronic acid (HA) and other ligands (osteopontin, collagens, MMPs). Multiple isoforms (alternative splicing). Cell-cell and cell-matrix interactions, cell adhesion and migration. Cytokines/growth factors presentation. Binding of HA to CD44 leads to NF-κB activation. Induced in inflammation by cytokines and growth factors (TNFα, IL-1β, TGF-β, IFN, HGF, VEGF, and FGF). Upregulated in vascular injury. Pro-angiogenic. Interacts with TGFβR1 = enhances TGF-β signaling. Interacts with CD74.
1392171_at	AA945643	89824	chitinase 3-like 1	Chi3l1	2.19	0.98982	YES	NO	**Cartilage glycoprotein-39.** Member of chi-lectin family. Induced in inflammation, tissue remodeling (connective tissue turnover), atheroma, and tumors. Promotes migration and adhesion of VSMC and EC. Induces HUVEC tubulogenesis. Mitogenic (via AKT). Inhibits cytokines signaling = anti-inflammatory.
1367631_at	NM_022266	64032	connective tissue growth factor	Ctgf	2.11	0.99200	YES	YES	Member of the CNN family of matricellular proteins initially discovered as a protein secreted by EC. Induced by TGF-β is a downstream mediator of TGF-β = fibrosis. Promotes EC proliferation, migration, adhesion, survival = pro-angiogenic. Binds BMPs (inhibition of BMP signaling) and TGF-β1 (activation of TGF-β signaling). Upregulated in wound healing and fibrotic diseases. **Upregulated in diabetes (retina and kidney glomeruli) and by high glucose (mesangial cells) via TGF-β.**
1393067_at	AI710931	89804	endothelial-specific receptor tyrosine kinase	Tek	2.07	0.99197	NO	NO	Angiopoietins receptor. Expressed almost exclusively in EC both in quiescent vessels and angiogenesis. Defects in TEK are associated with inherited venous malformations: TEK signaling pathway is critical for endothelial cell-smooth muscle cell communication in venous morphogenesis. Required for physiological (development) and pathological angiogenesis. Tek/Tie2 signaling depends on the ligand: Ang1 leads to activation of an EC survival pathway and angiogenesis; Ang2 is a contest-dependent agonist/antagonist of Tie 2 signaling and can leads either to vascular regression or survival. Upregulated by IL-1β and TNF-α in EC in vitro. Upregulated by hypoxia in BRP in vitro. Upregulated in ROP. **In vivo upregulated in diabetic kidney (STZ rats)** and MI (rats), epiretinal membranes (retinal ischemic diseases), synovial tissue in RA and OA, hemangioma and psoriasis.
1383641_at	BF414702	24326	endothelin receptor type A	Ednra	2.57	1.00000	NO	YES	Endothelin receptor (ETA). Regulation of vascular resistance. Expressed in VSMC, pericytes, cardiomyocytes, mesangial cells, fibroblast. Activation of ETA induces CTGF (UP) in VSMC. ETA mediates the profibrotic effect of ET1 on vasculature (convergence of ET1 and TGF-β on a common signaling pathway for collagen 1 upregulation). ETA mediates the co-mitogenic effect of ET1 (ET1 potentiates the mitogenic effect of other GFs). ETA activation mediates renal inflammation and TGF-β production in diabetes. **Increased in the diabetic retina (STZ and BB rats).**

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1373093_at	AI169756	313729	ERBB receptor feedback inhibitor 1	Errfi1	2.14	0.99395	YES	NO	**Ralt, gene 33, Mig6.** Immediate early response gene encoding a non-kinase scaffolding adaptor protein. Physiological feedback inhibitor of EGFR and HGF/Met signaling. Induced by mitogens, stressors, hypoxia. Tumor suppressor. Activates NF-κB and SAPK/JNK (Mapk8/SAPK1/JNK1 is UP). Pro-apoptotic.
1386879_at	NM_031832	83781	lectin, galactose binding, soluble 3	Lgals3	5.10	0.99931	YES	NO	**Galectin 3**. IgE-binding lectin. Multiple extracellular and intracellular functions. Immediate early gene. Cell-cell and cell-matrix interaction. Laminin-binding. RAGE ligand. Amplifier of inflammation. Anti-apoptotic. Pro-angiogenic. Upregulated in vascular injury. **Upregulated in diabetes (kidney, retinal Müller cells, hippocampus) and by glucose (mesangial cell).**
1387011_at	NM_130741	170496	lipocalin 2	Lcn2	4.21	0.99947	NO	NO	**Neutrophil gelatinase-associated lipocalin (NGAL), oncogene24p3**. Member of the lipocalin family. Iron delivery pathway. Acute-phase response protein upregulated in inflammation. Modulates the activity of matrix MMPs (by preventing inactivation by TIMP1). Upregulated in atheroma and MI (vascular inflammation, plaque instability). **Upregulated in retinal Müller cells in diabetes.**
1390426_at	BF389398	25496	Notch gene homolog 1 (Drosophila)	Notch1	3.01	0.99998	NO	YES	Notch signaling pathway. Receptor for membrane bound ligands. Development/vascular development. Required in part for the TGF-β cytostatic response. Expressed in EC and upregulated in vascular injury (EC and SMC). Both anti-apoptotic and pro-apoptotic. Activation of NF-κB.
1386913_at	NM_019358	54320	podoplanin	Pdpn	2.02	0.99600	YES	NO	Mucin-type small membrane glycoprotein. Expressed in lymphatic EC, podocytes, alveolar type I cells, and epithelial cells. Induced in HUVEC and microvascular EC by IFNγ, IL-3, TNF-α. Induced by TGF-β (tumor cells). Lymphatic development. Promotes cell adhesion, migration, and tube formation. Ectopic expression = actin reorganization and cell motility.
1383290_at	BI280343	311331	serine peptidase inhibitor, Kunitz type 1	Spint1	2.00	0.99173	NO	YES	Regulator of HGF activity. Inhibits HGFA (HGF activator) = prevents HGF activation. The membrane form functions as a reservoir of HGFA at site of tissue injury = promotes local activation of HGF.
1367712_at	NM_053819	116510	tissue inhibitor of metallopeptidase 1	Timp1	4.01	1.00000	NO	NO	Inhibitor of MMPs. Promotes cell proliferation and may have an anti-apoptotic function. Upregulated by cytokines (IL-1β, TNF-α, IFNγ, IL-6, TGF-β) and hormones. Induced by TGF-β via CTGF. Inflammatory response. Anti-angiogenic. Upregulated in vascular injury = prevents neointima formation. **Upregulated in diabetes (glomeruli, retinal Müller cells) and by high glucose (via CTGF).**
1376102_at	BI292351	316516	transmembrane BAX inhibitor motif containing 1	Tmbim1	2.04	0.99135	YES	NO	**RECS1, responsive to centrifugal force and shear stress 1.** Identified as a shear stress responsive gene in EC. Expressed in EC and VSMC. Expressed in most tissues. Endosomal/ lysosomal protein. Negative regulator of aortic MMP9 production: vascular remodeling.

Supplemental Table 6: Gene expression profile of retinal vessels in diabetes. Differentially expressed genes related to **cell cycle**.

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
CELL CYCLE PROGRESSION									
1391374_at	BE106930	360962	transforming, acidic coiled-coil containing protein 3	Tacc3	0.29	0.99880	NO	YES	Member of the acidic coiled-coil (TACC) family = centrosomal proteins that interact with microtubules and tubulin. Involved in centrosome/mitotic spindle dynamics. TACC3 deficiency triggers p53-mediated apoptosis. May be involved in cell growth and differentiation.
1391063_at	BE113443	315740	kinesin family member 23 (predicted)	Kif23_predicted	0.29	0.99068	NO	YES	**Mitotic kinesin-like protein 1.** Member of the kinesin-like protein family (microtubule-dependent molecular motors that transport organelles within cells and move chromosomes during cell division). Drives microtubule movement in vitro. Cytokinesis.
1374565_at	BF282365	360161	NIMA (never in mitosis gene a)-related expressed kinase 6	Nek6	2.08	0.99235	YES	NO	Serine/threonine kinase. Cell-cycle progression. Histone kinase = regulates chromatin condensation. Positive regulator of NF-κB.
CELL CYCLE ARREST									
1369108_at	NM_019221	246334	transformation related protein 63	Trp63	0.39	0.98642	YES	YES	Member of the p53 gene family. TA isoforms = similar to p53, induce growth arrest and apoptosis. deltaN isoforms (prevalent isoforms) = dominant negative inhibitors of p53 and TA-p63.
1377659_at	BI302005	310483	myeloid leukemia factor 1 (predicted)	Mlf1_predicted	3.17	0.99988	YES	NO	Negative regulator of cell cycle progression. Expressed in many tissues. Overexpression associated with malignant transformation. Inhibits cell-cycle progression by activating p53.
PROLIFERATION INHIBITION									
1377100_at	AI172172	304218 493912	androgen-induced proliferation inhibitor (predicted)	Aprin_predicted	2.43	0.99778	NO	NO	Inhibitor of proliferation. Induced by androgen and vitamin D.
1390426_at	BF389398	25496	Notch gene homolog 1 (Drosophila)	Notch1	3.01	0.99998	NO	YES	Notch signaling pathway. Receptor for membrane bound ligands. Development/vascular development. Required in part for the TGF-β cytostatic response. Expressed in EC and upregulated in vascular injury (EC and SMC). Both anti-apoptotic and pro-apoptotic. Activation of NF-κB.

Supplemental Table 7: Gene expression profile of retinal vessels in diabetes. Differentially expressed genes related to **apoptosis.**

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
PRO-APOPTOTIC p53 PATHWAY									
1369108_at	NM_019221	246334	transformation related protein 63	Trp63	0.39	0.98642	YES	YES	Member of the p53 gene family. TA isoforms = similar to p53, induce growth arrest and apoptosis. deltaN isoforms (prevalent isoforms) = dominant negative inhibitors of p53 and TA-p63.
1377659_at	BI302005	310483	myeloid leukemia factor 1 (predicted)	Mlf1_predicted	3.17	0.99988	YES	NO	Negative regulator of cell cycle progression. Expressed in many tissues. Overexpression associated with malignant transformation. Inhibits cell-cycle progression by activating p53.
1370928_at	BI284739	65161	LPS-induced TN factor	Litaf	3.84	0.99886	NO	NO	Transcription factor. Mediates the LPS-dependent induction of TNF-α and other cytokines. Induced by LPS and p53. Activates NF-κB. Inhibited by salicylates.
1388776_at	AI169176	301013	scotin	MGC94600	1.98	0.99200	YES	NO	p53- and p73-dependent apoptosis. Endoplasmic reticulum. Induced and transactivated by p53 and p73. Activates NF-κB.
1381650_at	BM389433	291314	selenophosphate synthetase 1	Sephs1	1.99	0.99092	YES	YES	Synthesis of selenophosphate from selenide and ATP. Selenophosphate is used to synthesize selenocysteine, which is co-translationally incorporated into selenoproteins at in-frame UGA codons. Most selenoproteins are involved in redox balance (glutathione peroxidase, thioredoxin reductase) Overexpression leads to increasead cell death in response to genotoxic conditions in a p53-dependent mechanism.
1391374_at	BE106930	360962	transforming, acidic coiled-coil containing protein 3	Tacc3	0.29	0.99880	NO	YES	Member of the acidic coiled-coil (TACC) family = centrosomal proteins that interact with microtubules and tubulin. Involved in centrosome/mitotic spindle dynamics. TACC3 deficiency triggers p53-mediated apoptosis. May be involved in cell growth and differentiation.
1372564_at	AI411375	304063	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian) (mapped)	Ets2	2.37	0.99800	YES	NO	Transcription factor member of the ETS-domain transcription factor family. induced by oxidative stress; endothelial morphogenesis. Pro-apoptotic via activation of p53 pathway.
PRO-APOPTOTIC									
1397221_s_at	BE108106	246097	Tumor necrosis factor receptor superfamily, member 6	Tnfrsf6	2.60	1.00000	NO	NO	**FAS, CD95 antigen.** Member of the TNF-receptor superfamily. Induces apoptosis. EC are usually resistant, while VSMC are susceptible to FAS-induced apoptosis. Induced by cytokines (IFNγ, TNF-α, IL-1β in EC and VSMC; TGFβ in gastric carcinoma cells). Upregulated in vascular injury. FAS/FASL deficiency increases neovascularization. **Upregulated in retinal vessels in diabetes.**
1371131_a_at	U30789	117514	Thioredoxin interacting protein	Txnip	2.66	0.99899	YES	NO	**VDUP1.** Negative regulator of thioredoxin. Upregulation promotes oxidative stress. Pro-apoptotic. Upregulated by vitamin D3 and TGF-β. **Upregulated by high glucose (glucose responsive elements in the promoter). Induced in diabetes (aorta, kidney, islets).**
1371774_at	AA893220	302642	spermidine/spermine N1-acetyl transferase (mapped)	Sat	2.09	0.99800	YES	NO	Rate-limiting enzyme of polyamine catabolism. Overexpression leads to generation of H2O2 and oxidative stress, inhibition of cell growth and apoptosis, and increased integrin-mediated cell migration. Upregulated in ischemia-reperfusion and by H2O2 (kidney, liver)
1373093_at	AI169756	313729	ERBB receptor feedback inhibitor 1	Errfi1	2.14	0.99395	YES	NO	**Ralt, gene 33, Mig6.** Immediate early response gene encoding a non-kinase scaffolding adaptor protein. Physiological feedback inhibitor of EGFR and HGF/Met signaling. Induced by mitogens, stressors, hypoxia. Tumor suppressor. Activates NF-κB and SAPK/JNK (Mapk8/SAPK1/JNK1 is UP). Pro-apoptotic.
1392418_at	BE105603	116554	Mitogen-activated protein kinase 8	Mapk8	2.02	0.99125	YES	NO	**c-jun N-terminal kinase 1, JNK1, SAPK1.** Member of the MAP kinase family. Activated by various cell stimuli (cytokines, stressors) mediates immediate-early gene expression. Stress-induced apoptosis. Required for TNF-α induced apoptosis. Survival signaling in some cases. **Activated by high glucose** and hyperosmolarity in VSMC and EC.

REA 230 20 Index	Representative Public ID	Entrez Gene ID	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1387005_at	NM_017320	50654	cathepsin S	Ctss	2.10	0.99900	YES	NO	Lysosomal cysteine protease. Elastolytic and collagenolytic activity. Degradation of proteoglycans. Upregulated by IFNγ. Mediates interferon-induced apoptosis. MHCII antigen presentation (degradation of the MHC invariant chain CD74). Upregulated in EC by cytokine/growth factors. Pro-angiogenic. Upregulated in atheroma and vascular injury. **Serum levels increased in DM with atherosclerosis and obesity.**
1370694_at	AB020967	246273	tribbles homolog 3	Trib3	0.49	0.99200	NO	YES	Negative regulator of NF-κB and Akt1. Induced by NF-κB, hypoxia, and ER-stress. ER-stress-induced apoptosis. Sensitizes cells to TNF-induced apoptosis. **Upregulated in diabetes (liver db/db mice).**
1369959_at	NM_017172	29344	zinc finger protein 36, C3H type-like 1	Zfp36l1	2.03	0.99700	YES	YES	Member of the TIS11 family of early response genes. Regulates the response to growth factors. Control of both basal and ACTH-induced VEGF mRNA expression by decreasing VEGF mRNA stability. Pro-apoptotic.
ANTI-APOPTOTIC									
1370048_at	NM_053936	116744	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2	Edg2	0.26	0.98670	YES	YES	G-protein coupled receptor for lysophosphatidic acid (LPA). LPA is a growth factor that regulates EC and VSMC functions (promotes survival, proliferation, migration, and increases permeability). Anti-apoptotic.
1374904_at	AI175048	114634	sine oculis homeobox homolog 1 (Drosophila)	Six1	0.26	0.99300	YES	YES	Transcription factor. Cell survival and proliferation. Required for Pax3 expression in myogenesis (and vice versa).
1397478_at	AI030187	114766	Prohibitin 2	Phb2	2.94	0.99725	YES	NO	Anti-apoptotic (via interaction and regulation of Hax1 in mitochondria). Maintenance of mitochondrial morphology. Translocates to the nucleus: transcriptional repressor (Repressor of estrogen receptor activity). Inhibits myogenic differentiation (via interaction with Akt2).
1367725_at	NM_022602	64534	serine/threonine-protein kinase pim-3	Pim3	2.49	0.99685	NO	YES	Member of the proto-oncogene Pim family = downstream effectors of cytokines/growth factors signaling pathways. Aberrant expression promotes cell proliferation and prevents apoptosis. Two other members of this family --Pim1 and Pim2-- are induced by cytokines/growth factors via STAT3 and prevent cytokine-induced apoptosis.

Supplemental Table 8: Gene expression profile of retinal vessels in diabetes. Differentially expressed genes related to **other functions and of unknown function.**

REA 230 20 Index	Representative Public ID	Entrez Gene	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
METABOLISM									
1375944_at	AA849497	311569	acyl-CoA synthetase short-chain family member 2 (predicted)	Acss2_predicted	2.14	0.99200	NO	YES	Cytosolic enzyme that catalyzes the activation of acetate for use in lipid synthesis and energy generation. Expression regulated by sterol regulatory element-binding proteins, transcription factors that activate genes required for the synthesis of cholesterol and unsaturated fatty acids. Activity regulated by SIRT (deacetylation)
1390383_at	BI285616	298199	Adipose differentiation related protein	Adfp	2.10	0.99262	YES	NO	Adipophilin. Biogenesis of lipid droplets. Adipocytes differentiation. Ubiquitously expressed. Upregulated in atheroma (intima). **Upregulated in diabetes (kidney).**
1390850_at	AA874941	298199	Adipose differentiation related protein	Adfp	1.98	0.99800	YES	NO	Adipophilin. Biogenesis of lipid droplets. Adipocytes differentiation. Ubiquitously expressed. Upregulated in atheroma (intima). **Upregulated in diabetes (kidney).**
1388480_at	AI412863	288707	glycolipid transfer protein (predicted)	Gltp_predicted	3.01	0.99900	NO	NO	Glycosphingolipids and glyceroglycolipids transport across membranes. It is thought to be a cytoplasmic protein.
1383413_at	AW531481	301073	Gup1, glycerol uptake/transporter homolog (yeast) (predicted)	Gup1_predicted	0.48	0.98641	NO	NO	In yeasts involved in remodeling of the GPI-anchor lipids. No data on mammalians homologs. The human and mouse gene name is: HHATL, hedgehog acyltransferase-like [HHATL, C3orf3, MBOAT3, OACT3]
1386979_at	NM_133395	170907	developmentally regulated protein TPO1	Tpo1	2.50	0.99700	NO	NO	Serine incorporator 5. Serine and sphyngolipid synthesis. Human homolog (C5orf12) expressed in many tissues. Endoplasmic reticulum.
1389791_at	AI179775	306619	ceroid-lipofuscinosis, neuronal 8	Cln8	1.99	0.99700	NO	YES	Motor neuron degeneration. Mutation leads to neuronal ceroid-lipofuscinosis. Endoplasmic reticulum.
1379334_at	BF547086	309312	Glycine decarboxylase (predicted)	Gldc_predicted	2.04	0.99540	YES	NO	Component of the glycine decarboxilase system (mitochondrial).
1375426_a_at	BI295086	171137	KH-type splicing regulatory protein	Khsrp	2.01	0.98700	YES	NO	MAP2 RNA trans-acting protein MARTA1. mRNA destabilization factor. Nuclear-cytoplasmic mRNA targeting. Interacts with TNF.
1374621_at	AA892987	361420	TATA box binding protein (Tbp)-associated factor, RNA polymerase I, C	Taf1c	2.28	0.98969	NO	YES	This gene encodes the largest SL1-specific TAF (TBP-associated factors required for initiation of transcription by RNA polymerase I). P53 binds to SL1 and inhibits its function. [SL1, 110kD subunit; TBP-associated factor 1C; transcription factor SL1, transcription factor TAFI95]
OTHER FUNCTION									
1371245_a_at	BI287300	689064	beta-globin	LOC689064	2.16	0.98627	NO	YES	Homolog of human hemoglobin delta and mouse hemoglobin β adult major chain.
1368353_at	NM_017009	24387	glial fibrillary acidic protein	Gfap	5.84	0.99700	YES	NO	Intermediate filament protein. Upregulated in glial reactivity. **Upregulated in retinal Müller cells in diabetes.**
1368951_at	NM_022797	24412	glutamate receptor, ionotropic, N-methyl D-aspartate 2D	Grin2d	2.10	0.99700	YES	YES	N-methyl-D-aspartate receptor subunit. Myogenic differentiation; bind to microtubule MAP2. NMDA receptors are expressed also in EC. [NMDAR2D, NR2D].
1380048_at	BF401725	171297	Neuroligin 3	Nlgn3	1.95	0.98724	YES	NO	Neuronal cell surface protein that binds neurexins. Required for proper synapse maturation.

REA 230 20 Index	Representative Public ID	Entrez Gene	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1385752_at	BF394136	299016	neuronal PAS domain protein 3 (predicted)	Npas3_predicted	2.40	1.00000	NO	NO	Brain-enriched basic helix-loop-helix (bHLH) PAS domain transcription factor. Regulates FGF signaling in the dentate gyrus of mammalian brain by controlling expression of the FGFR1, and in turn also controls neurogenesis emanating from this region.
1392449_at	BI282152	362412	RAD18 homolog (S. cerevisiae) (predicted)	Rad18_predicted	0.39	0.99893	NO	YES	Postreplication DNA repair.
1370973_at	BF285019	64155	sodium channel, voltage-gated, type VII, alpha	Scn7a	4.52	0.99998	NO	NO	Nav2, Nax. Central control of salt homeostasis. Local control of sodium levels. VSMC contractility. **Upregulated in retinal Müller cells in diabetes.**
1378047_at	AA901337	314711	Spi-C transcription factor (Spi-1/PU.1 related) (predicted)	Spic_predicted	0.36	0.99488	NO	YES	Transcription factor. Positive/negative transcriptional regulator of B-lymphocyte differentiation. Upregulated in pulmonary epithelial cells in lal-/- mice (lung pathology/emphysema model).
UNKNOWN FUNCTION									
1385064_at	BM384729	298483	L-amino acid oxidase 1 (predicted)	Lao1_predicted	0.40	0.99565	NO	YES	Aminoacid catabolism. No human homolog. In the mouse expressed in mammary epithelium. Specific function unknown.
1384831_at	AI233155	313089	solute carrier family 7, (cationic amino acid transporter, y+ system) member 13	Slc7a13	0.45	0.99400	YES	YES	Aspartate/glutamate transporter 1. Cationic amino acid transporter. Specific function unknown.
1393217_at	BF282804	289453	ATP-binding cassette, sub-family G (WHITE), member 3	Abcg3	2.45	0.99781	YES	NO	Member of the ATP-binding cassette (ABC) transporter. Specific function unknown.
1376287_at	BM389585	362701	calpain 13	Capn13	0.41	0.99328	YES	YES	Putative calpain large subunit protein. Function unknown.
1388659_at	BI295783	260416	calcium regulated heat stable protein 1	Carhsp1	2.17	0.98746	YES	NO	Substrate of calcineurin and of several kinases including p90RSK. Specific function unknown.
1387349_at	NM_013028	25546	short stature homeobox 2	Shox2	0.31	0.99358	YES	YES	Transcription factor of the homeo box family. Development. Function unknown.
1392677_at	AA924705	315882	Zic family member 4 (predicted)	Zic4_predicted	0.37	0.99888	NO	YES	Transcription factor of the ZIC family of C2H2-type. Development. Function unknown.
1372419_at	BG380296	361565	vaccinia related kinase 3	Vrk3	1.97	0.98600	YES	NO	Nuclear protein. Lacks phosphorylation activity but retains its substrate binding capability. Function unknown.
1385199_a_at	AI073196	307956	RNA binding motif protein 34	Rbm34	1.80	0.98871	YES	NO	Contains an RNA recognition motif. Function unknown. **NOTE: THIS PROBE SET IS UP IN DM AND DM+ASA WHILE IT IS DOWN IN DM+SORB**
1387995_a_at	BI285494	361673	interferon induced transmembrane protein 3	Ifitm3	2.79	0.99941	NO	NO	Fragilis. Germ cells development. Epithelial cell differentiation. Specific function unknown. **Upregulated in retinal Müller cells in diabetes.**
1394200_at	BF410146	60460	heat shock 70kDa protein 2	Hspa2	2.81	1.00000	NO	NO	Testis specific hst70. Constitutively expressed in most tissues with high levels in testis and skeletal muscle. Required for spermatogenesis. Specific function unknown.
1368840_at	NM_134390	171411	LR8 protein	Lr8	2.92	1.00000	NO	NO	TORID (tolerance-related and induced transcript). Function unknown
1382387_at	BF288508	309135	Transmembrane protein 16A (predicted)	Tmem16a_predicted	1.94	0.99712	YES	NO	Amplified in various cancers. Function unknown.
1387276_at	NM_021584		Ania4	Ania4	3.34	0.99995	NO	NO	Function unknown. **Upregulated in retinal Müller cells in diabetes.**
1372310_at	AI227941	364879	isochorismatase domain containing 1	Isoc1	2.11	0.99500	NO	YES	Down-regulated in nephrectomized rat kidney (gene #1). Function unknown

REA 230 20 Index	Representative Public ID	Entrez Gene	Gene Title	Gene Symbol	DM vs C fold change	DM vs C posterior probability	Changes corrected by sorbinil	Changes corrected by aspirin	Summary notes (from Entrez Gene and literature)
1388127_at	AI170346	266761	cytochrome P450-like protein	Loc266761	2.21	0.99704	YES	NO	Function unknown.
1370389_at	AB036421	192179	glycoprotein m6b	Gpm6b	2.10	0.99900	YES	NO	Function unknown.
1374693_at	BM388613	315760	poly (ADP-ribose) polymerase family, member 16	Parp16	2.24	0.99771	NO	NO	Function unknown
1370659_at	AF016179	286981	putative pheromone receptor (Go-VN2)	LOC286981	0.39	0.99266	NO	YES	Function unknown.
1396631_at	BF410419	362768	tetratricopeptide repeat domain 7B (predicted)	Ttc7b_predicted	0.47	0.99268	YES	YES	Function unknown
1371968_at	AI013781	362884	transmembrane BAX inhibitor motif containing 4	Tmbim4	2.02	0.99600	NO	YES	Function unknown
1373938_at	BF284753	360497	WD repeat domain 24	Wdr24	2.40	0.99536	YES	NO	Function unknown

Supplemental Table 9: Genes differentially expressed in diabetic retinal vessels: comparison to diabetic retinal Müller cells.

GeneChip REA230 2.0 probe set ID	Gene Title	Gene Symbol	Vessels DM vs C	GeneChip RGU34A probe set ID	Müller cells DM vs C	Functional Categories
1379586_at	A disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 19 (predicted)	Adamts19_predicted	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1368223_at	a disintegrin-like and metallopeptidse (reprolysin type) with thrombospondin type 1 motif, 1	Adamts1	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1385397_at	Ab1-219	LOC499991	Upregulated	not in RGU34A	---	inflammation/response to injury
1375944_at	acyl-CoA synthetase short-chain family member 2 (predicted)	Acss2_predicted	Upregulated	not in RGU34A	---	other/unknown function
1390383_at 1390850_at	Adipose differentiation related protein	Adfp	Upregulated	rc_AA893280_at rc_AA874941_at	not detected	other/unknown function
1367794_at	alpha-2-macroglobulin	A2m	Upregulated	M23566exon_s_at rc_AA900582_at	Upregulated	inflammation/response to injury
1377100_at	androgen-induced proliferation inhibitor (predicted)	Aprin_predicted	Upregulated	not in RGU34A	---	cell cycle
1387276_at	Ania4	Ania4	Upregulated	AF030089UTR#1_at	Upregulated	other/unknown function
1392250_at	Annexin A2	Anxa2	Downregulated	L13039_s_at	no change	matrix and vascular remodeling
1393217_at	ATP-binding cassette, sub-family G (WHITE), member 3	Abcg3	Upregulated	not in RGU34A	---	other/unknown function
1370913_at	Best5 protein	Best5	Upregulated	Y07704_g_at	Upregulated	inflammation/response to injury
1370907_at	Beta galactoside alpha 2,6 sialyltransferase 1	St6gal1	Upregulated	M83143_at M83143_g_at	no change	matrix and vascular remodeling, inflammation/response to injury
1367595_s_at	beta-2 microglobulin	B2m	Upregulated	rc_AI170268_at	no change	inflammation/response to injury
1371245_a_at	beta-globin	LOC689064	Upregulated	not in RGU34A	---	other/unknown function
1389095_at	biregional cell adhesion molecule-related/down-regulated by oncogenes (Cdon) binding protein (predicted)	Boc_predicted	Upregulated	rc_AI639199_at	not detected	matrix and vascular remodeling
1390398_at	Bone morphogenetic protein receptor, type 1A	Bmpr1a	Upregulated	S75359_s_at	no change	TGFbeta/BMPs pathway
1388659_at	calcium regulated heat stable protein 1	Carhsp1	Upregulated	not in RGU34A	---	other/unknown function
1376287_at	calpain 13	Capn13	Downregulated	not in RGU34A	---	other/unknown function
1379300_at	carbohydrate sulfotransferase 2 (predicted)	Chst2_predicted	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1374778_at	cathepsin C	Ctsc	Upregulated	D90404_at D90404_g_at	no change	matrix and vascular remodeling
1387005_at	cathepsin S	Ctss	Upregulated	L03201_at	no change	matrix and vascular remodeling, inflammation/response to injury, apoptosis
1368593_at	CD1d1 antigen	Cd1d1	Upregulated	D26439_at	no change	inflammation/response to injury
1368921_a_at	CD44 antigen	Cd44	Upregulated	M61875_s_at	no change	TGFbeta/BMPs pathway, matrix and vascular remodeling
1367679_at	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)	Cd74	Upregulated	X13044_at	Upregulated	inflammation/response to injury
1371499_at	CD9 antigen	Cd9	Upregulated	X76489cds_g_at	no change	matrix and vascular remodeling
1389791_at	ceroid-lipofuscinosis, neuronal 8	Cln8	Upregulated	not in RGU34A	---	other/unknown function
1368418_a_at 1368419_at 1368420_at	ceruloplasmin	Cp	Upregulated	L33869_at	Upregulated	inflammation/response to injury, oxidative stress
1392171_at	chitinase 3-like 1	Chi3l1	Upregulated	not in RGU34A	---	inflammation/response to injury, matrix and vascular remodeling
1387893_at	complement component 1, s subcomponent	C1s	Upregulated	D88250_at	Upregulated	inflammation/response to injury
1383391_a_at	complement component 2	C2	Upregulated	not in RGU34A	---	inflammation/response to injury

GeneChip REA230 2.0 probe set ID	Gene Title	Gene Symbol	Vessels DM vs C	GeneChip RGU34A probe set ID	Müller cells DM vs C	Functional Categories
1368000_at	complement component 3	C3	Upregulated	M29866_s_at X52477_at	Upregulated	inflammation/response to injury
1389470_at	Complement factor B	Cfb	Upregulated	rc_AI639117_s_at	Upregulated	inflammation/response to injury
1367631_at	connective tissue growth factor	Ctgf	Upregulated	not in RGU34A	---	TGFbeta/BMPs pathway, matrix and vascular remodeling
1369321_s_at	cytochrome c, testis	Cyct	Downregulated	M20623_at	not detected	oxidative stress
1387328_at	Cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase)	Cyp2c	Upregulated	J02657_s_at M18363cds_s_at	not detected	oxidative stress
1388127_at	cytochrome P450-like protein	Loc266761	Upregulated	not in RGU34A	---	other/unknown function
1375936_at	desmocollin 2	Dsc2	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1386979_at	developmentally regulated protein TPO1	Tpo1	Upregulated	rc_AI012275_at	no change	other/unknown function
1371430_at	dystroglycan 1	Dag1	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1389617_at	ELK3, member of ETS oncogene family (predicted)	Elk3_predicted	Upregulated	not in RGU34A	---	TGFbeta/BMPs pathway
1370048_at	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2	Edg2	Downregulated	rc_AA848831_at	not detected	apoptosis
1393067_at	endothelial-specific receptor tyrosine kinase	Tek	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1383641_at	endothelin receptor type A	Ednra	Upregulated	M60786_at	not detected	matrix and vascular remodeling
1373093_at	ERBB receptor feedback inhibitor 1	Errfi1	Upregulated	rc_AI169756_s_at	no change	matrix and vascular remodeling, apoptosis
1370256_at	frizzled homolog 1 (Drosophila)	Fzd1	Upregulated	L02529_at	no change	TGF-beta/BMPs pathway
1368353_at	glial fibrillary acidic protein	Gfap	Upregulated	AF028784mRNA#1_s_at	Upregulated	other/unknown function
1368951_at	glutamate receptor, ionotropic, N-methyl D-aspartate 2D	Grin2d	Upregulated	D13213_s_at U08260_at	not detected	other/unknown function
1383546_at	glycerophosphodiester phosphodiesterase domain containing 2 (predicted)	Gdpd2_predicted	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1379334_at	Glycine decarboxylase (predicted)	Gldc_predicted	Upregulated	not in RGU34A	---	other/unknown function
1388480_at	glycolipid transfer protein (predicted)	Gltp_predicted	Upregulated	not in RGU34A	---	other/unknown function
1370389_at	glycoprotein m6b	Gpm6b	Upregulated	not in RGU34A	---	other/unknown function
1392888_at	glypican 4	Gpc4	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1383413_at	Gup1, glycerol uptake/transporter homolog (yeast) (predicted)	Gup1_predicted	Downregulated	not in RGU34A	---	other/unknown function
1394200_at	heat shock 70kDa protein 2	Hspa2	Upregulated	X15705cds_at	no change	other/unknown function
1380442_at	homeo box C8	Hoxc8	Downregulated	M37568cds_at	not detected	TGFbeta/BMPs pathway
1374601_at	interferon gamma receptor 2 (predicted)	Ifngr2_predicted	Upregulated	not in RGU34A	---	TGF-beta/BMPs pathway, inflammation/response to injury
1387995_a_at	interferon induced transmembrane protein 3	Ifitm3	Upregulated	X61381cds_s_at	Upregulated	other/unknown function
1386987_at	interleukin 6 receptor, alpha	Il6ra	Upregulated	M58587_at	no change	inflammation/response to injury
1372310_at	isochorismatase domain containing 1	Isoc1	Upregulated	not in RGU34A	---	other/unknown function
1375426_a_at	KH-type splicing regulatory protein	Khsrp	Upregulated	not in RGU34A	---	other/unknown function
1391063_at	kinesin family member 23 (predicted)	Kif23_predicted	Downregulated	not in RGU34A	---	cell cycle
1391022_at	laminin, beta 3	Lamb3	Downregulated	not in RGU34A	---	matrix and vascular remodeling
1385064_at	L-amino acid oxidase 1 (predicted)	Lao1_predicted	Downregulated	not in RGU34A	---	other/unknown function
1386879_at	lectin, galactose binding, soluble 3	Lgals3	Upregulated	J02962_at	Upregulated	matrix and vascular remodeling, inflammation/response to injury
1387011_at	lipocalin 2	Lcn2	Upregulated	rc_AA946503_at	Upregulated	inflammation/response to injury, matrix and vascular remodeling
1370928_at	LPS-induced TN factor	Litaf	Upregulated	U53184_at	no change	apoptosis

GeneChip REA230 2.0 probe set ID	Gene Title	Gene Symbol	Vessels DM vs C	GeneChip RGU34A probe set ID	Müller cells DM vs C	Functional Categories
1368840_at	LR8 protein	Lr8	Upregulated	not in RGU34A	---	other/unknown function
1368963_at	Max interacting protein 1	Mxi1	Upregulated	AF003008_at	not detected	TGFbeta/BMPs pathway
1385433_at	metastasis suppressor 1 (predicted)	Mtss1_predicted	Downregulated	not in RGU34A	---	matrix and vascular remodeling
1392418_at	Mitogen-activated protein kinase 8	Mapk8	Upregulated	L27129_at	not detected	apoptosis
1377659_at	myeloid leukemia factor 1 (predicted)	Mlf1_predicted	Upregulated	rc_AA800632_at	not detected	apoptosis, cell cycle
1380048_at	Neuroligin 3	Nlgn3	Upregulated	U41663_at	not detected	other/unknown function
1385752_at	neuronal PAS domain protein 3 (predicted)	Npas3_predicted	Upregulated	not in RGU34A	---	other/unknown function
1374565_at	NIMA (never in mitosis gene a)-related expressed kinase 6	Nek6	Upregulated	not in RGU34A	---	cell cycle
1390426_at	Notch gene homolog 1 (Drosophila)	Notch1	Upregulated	X57405_at X57405_g_at	no change	TGFbeta/BMPs pathway, matrix and vascular remodeling, cell cycle
1380638_at	nuclear receptor coactivator 3	Ncoa3	Upregulated	not in RGU34A	---	TGFbeta/BMPs pathway
1387568_at	paired-Ig-like receptor B	Pirb	Downregulated	not in RGU34A	---	inflammation/response to injury, matrix and vascular remodeling
1373911_at	periostin, osteoblast specific factor (predicted)	Postn_predicted	Upregulated	rc_AA894092_at	no change	TGFbeta/BMPs pathway, matrix and vascular remodeling
1386913_at	podoplanin	Pdpn	Upregulated	U92081mRNA_s_at	no change	TGFbeta/BMPs pathway, matrix and vascular remodeling, inflammation/response to injury
1374693_at	poly (ADP-ribose) polymerase family, member 16	Parp16	Upregulated	not in RGU34A	---	other/unknown function
1397478_at	Prohibitin 2	Phb2	Upregulated	U75392_s_at	no change	apoptosis
1368259_at	prostaglandin-endoperoxide synthase 1	Ptgs1	Upregulated	U03388_s_at	not detected	TGF-beta/BMPs pathway, inflammation/response to injury
1367786_at	proteosome (prosome, macropain) subunit, beta type 8	Psmb8	Upregulated	D10729_s_at	no change	inflammation/response to injury
1370659_at	putative pheromone receptor (Go-VN2)	LOC286981	Downregulated	AF016179_at	not detected	other/unknown function
1392449_at	RAD18 homolog (S. cerevisiae) (predicted)	Rad18_predicted	Downregulated	not in RGU34A	---	other/unknown function
1385199_a_at	RNA binding motif protein 34	Rbm34	Upregulated	not in RGU34A	---	other/unknown function
1388071_x_at	RT1 class Ib, locus Aw2	RT1-Aw2	Upregulated	M31038_at	Upregulated	inflammation/response to injury
1388776_at	scotin	MGC94600	Upregulated	not in RGU34A	---	apoptosis
1381650_at	selenophosphate synthetase 1	Sephs1	Upregulated	not in RGU34A	---	oxidative stress, apoptosis
1368224_at	Serine (or cysteine) peptidase inhibitor, clade A, member 3N	Serpina3n	Upregulated	D00753_at	Upregulated	inflammation/response to injury
1372254_at	serine (or cysteine) peptidase inhibitor, clade G, member 1	Serping1	Upregulated	rc_AA800318_at	Upregulated	inflammation/response to injury
1371310_s_at	serine (or cysteine) proteinase inhibitor, clade H, member 1	Serpinh1	Upregulated	M69246_at	no change	TGFbeta/BMPs pathway, matrix and vascular remodeling
1383290_at	serine peptidase inhibitor, Kunitz type 1	Spint1	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1367725_at	serine/threonine-protein kinase pim-3	Pim3	Upregulated	AF086624_s_at	not detected	apoptosis
1387349_at	short stature homeobox 2	Shox2	Downregulated	AJ002259_at AJ002259_g_at	not detected	other/unknown function
1370224_at 1371781_at	signal transducer and activator of transcription 3	Stat3	Upregulated	rc_AI639141_at X91810_at	not detected	inflammation/response to injury
1372064_at	similar to chemokine (C-X-C motif) ligand 16	Cxcl16	Upregulated	not in RGU34A	---	inflammation/response to injury
1374904_at	sine oculis homeobox homolog 1 (Drosophila)	Six1	Downregulated	not in RGU34A	---	apoptosis
1370973_at	sodium channel, voltage-gated, type VII, alpha	Scn7a	Upregulated	rc_AA925248_at	Upregulated	other/unknown function
1390416_at	solute carrier family 25, member 30	Slc25a30	Upregulated	rc_AA892522_at	no change	oxidative stress

GeneChip REA230 2.0 probe set ID	Gene Title	Gene Symbol	Vessels DM vs C	GeneChip RGU34A probe set ID	Müller cells DM vs C	Functional Categories
1384831_at	solute carrier family 7, (cationic amino acid transporter, y+ system) member 13	Slc7a13	Downregulated	not in RGU34A	---	other/unknown function
1396268_at	SP110 nuclear body protein	Sp110	Upregulated	not in RGU34A	---	inflammation/response to injury
1371774_at	spermidine/spermine N1-acetyl transferase (mapped)	Sat	Upregulated	not in RGU34A	---	oxidative stress, apoptosis
1378047_at	Spi-C transcription factor (Spi-1/PU.1 related) (predicted)	Spic_predicted	Downregulated	not in RGU34A	---	other/unknown function
1392990_at	SRY-box containing gene 17 (predicted)	Sox17_predicted	Upregulated	rc_AA799800_at	not detected	matrix and vascular remodeling
1374976_a_at	Sterol O-acyltransferase 1	Soat1	Upregulated	D86373_s_at	not detected	TGFbeta/BMPs pathway
1382189_at	syndecan 2	Sdc2	Upregulated	M81687_at	no change	TGFbeta/BMPs pathway, matrix and vascular remodeling
1374621_at	TATA box binding protein (Tbp)-associated factor, RNA polymerase I, C	Taf1c	Upregulated	rc_AA892987_at	not detected	other/unknown function
1396631_at	tetratricopeptide repeat domain 7B (predicted)	Ttc7b_predicted	Downregulated	not in RGU34A	---	other/unknown function
1371131_a_at	Thioredoxin interacting protein	Txnip	Upregulated	rc_AI014169_at	no change	TGF-beta/BMPs pathway, oxidative stress, apoptosis
1367712_at	tissue inhibitor of metallopeptidase 1	Timp1	Upregulated	rc_AI169327_at rc_AI169327_g_at	Upregulated	TGFbeta/BMPs pathway, matrix and vascular remodeling
1369108_at	transformation related protein 63	Trp63	Downregulated	Y10258cds_at	not detected	apoptosis, cell cycle
1376636_at	transforming growth factor, beta receptor 1	Tgfbr1	Upregulated	L26110_at S81584_s_at	not detected	TGFbeta/BMPs pathway
1391374_at	transforming, acidic coiled-coil containing protein 3	Tacc3	Downregulated	not in RGU34A	---	apoptosis, cell cycle
1376102_at	transmembrane BAX inhibitor motif containing 1	Tmbim1	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1371968_at	transmembrane BAX inhibitor motif containing 4	Tmbim4	Upregulated	not in RGU34A	---	other/unknown function
1382387_at	Transmembrane protein 16A (predicted)	Tmem16a_predicted	Upregulated	not in RGU34A	---	other/unknown function
1370694_at	tribbles homolog 3	Trib3	Downregulated	rc_H31287_at rc_H31287_g_at	not detected	apoptosis
1370339_at	Tropomyosin 3, gamma	Tpm3	Upregulated	S82383_s_at	no change	matrix and vascular remodeling
1397221_s_at	Tumor necrosis factor receptor superfamily, member 6 (FAS, CD95)	Tnfrsf6	Upregulated	D26112_s_at	not detected	apoptosis, inflammation/response to injury
1396074_at	ubiquitin-conjugating enzyme E2I	Ube2i	Upregulated	U54632_g_at U54632_at	no change	TGFbeta/BMPs pathway
1372419_at	vaccinia related kinase 3	Vrk3	Upregulated	not in RGU34A	---	other/unknown function
1372564_at	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian) (mapped)	Ets2	Upregulated	not in RGU34A	---	apoptosis
1373938_at	WD repeat domain 24	Wdr24	Upregulated	not in RGU34A	---	other/unknown function
1376124_at	Wiskott-Aldrich syndrome-like (human)	Wasl	Upregulated	not in RGU34A	---	matrix and vascular remodeling
1392677_at	Zic family member 4 (predicted)	Zic4_predicted	Downregulated	not in RGU34A	---	other/unknown function
1369959_at	zinc finger protein 36, C3H type-like 1	Zfp36l1	Upregulated	rc_AI136891_at	no change	apoptosis

To determine whether the effect of diabetes on the gene expression profile of retinal vessels is specific to vascular cells, we compared the list of differentially expressed genes in diabetic retinal vessels with the list of genes differentially expressed in diabetic retinal Müller cells obtained in our previous study (Gerhardinger et al, *Invest. Ophthalmol. Vis. Sci.* 46:349-357). The gene expression profile of diabetic retinal Müller cells was obtained with the Affimetrix GeneChip RGU34A, an earlier and smaller array than the Affimetrix GeneChip REA230 2.0 used in the current study of retinal microvessels. Thus, we first compared the two arrays by probe set ID and by gene title (NetAffx, Affimetrix) to determine which of the genes identified as differentially expressed in diabetic retinal vessels (GeneChip REA230 2.0) were also represented in the GeneChip RGU34A; and then compared the data for the effect of diabetes on retinal vessels vs Müller cells.