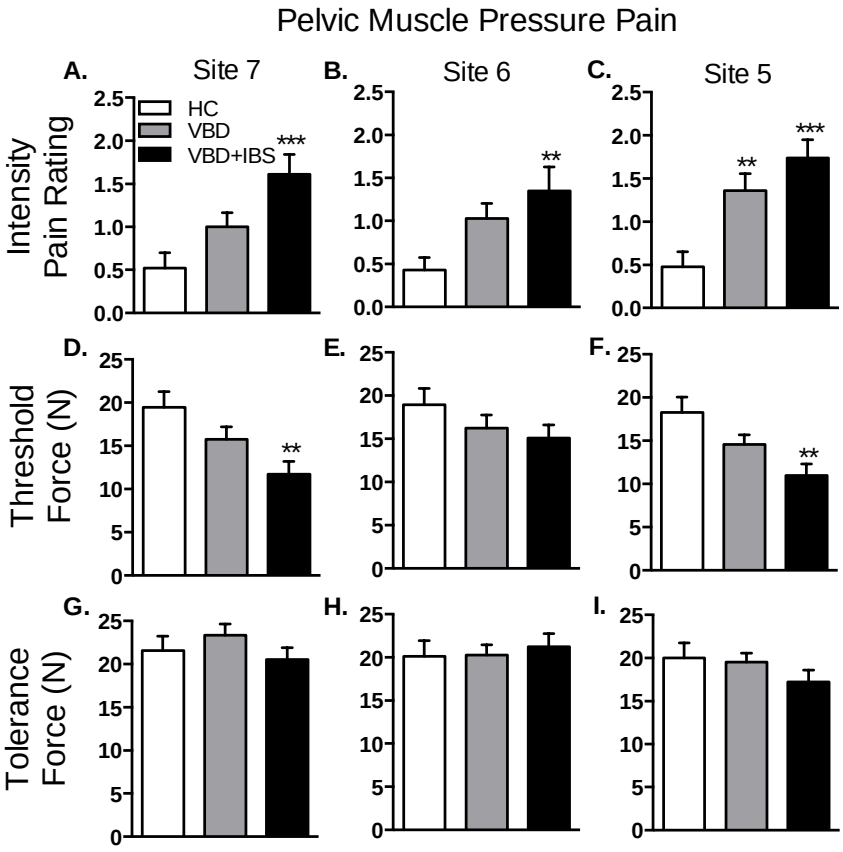
Supplemental Content

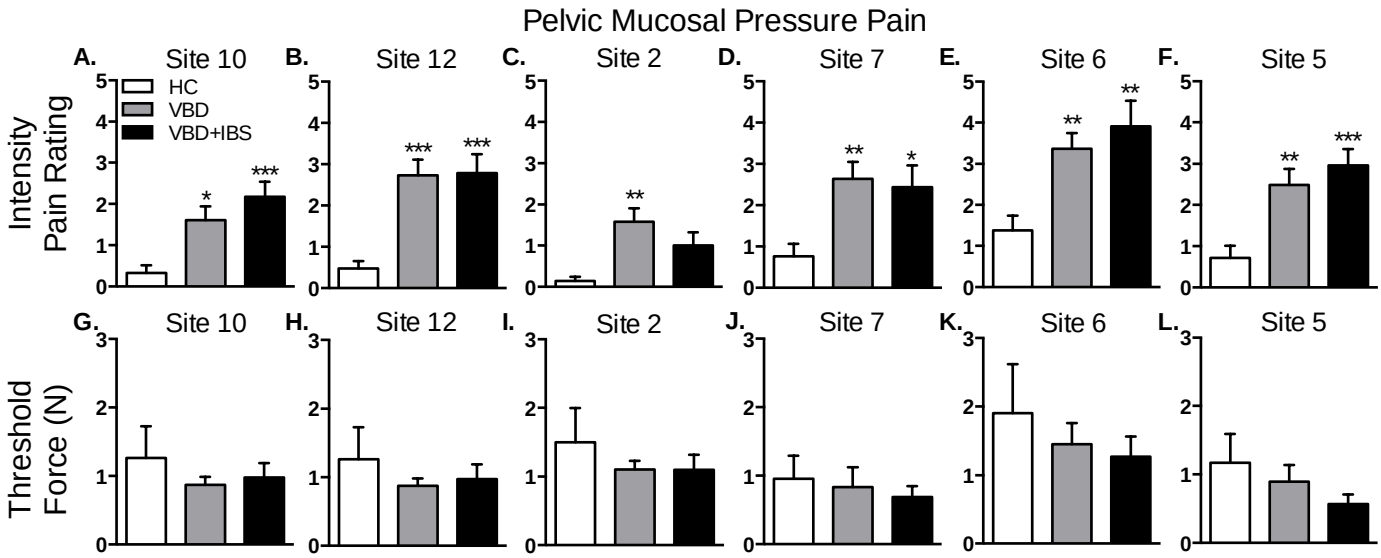
Ciszek BP, Khan AA, Dang H et al. MicroRNA expression profiles differentiate chronic pain condition subtypes

Supplemental Materials

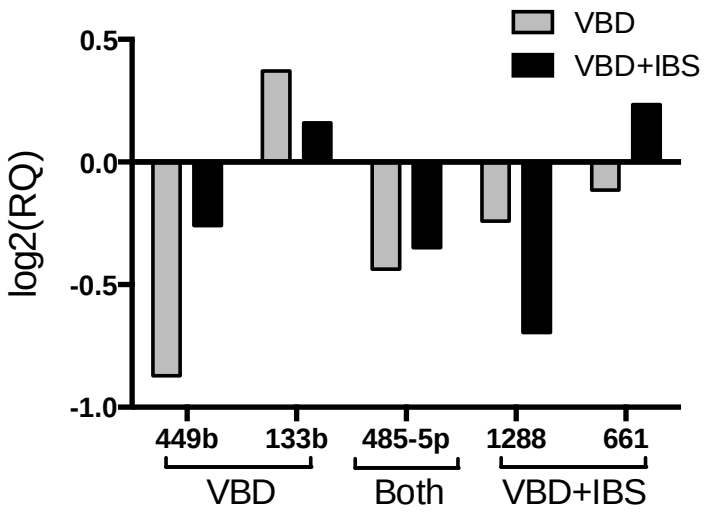
This supplementary material has been provided by the authors to give the readers additional information about their work.



Supplemental Figure 1. Pelvic muscle pressure pain is enhanced in patients with VBD and VBD + IBS. Patients with VBD alone exhibit modest increases in pain intensity **(A-C)** and decreases in mechanical threshold **(D-F)** at all 3 pelvic muscle sites, while those with VVS+IBS report dramatic increases in intensity and decreases in thresholds. No differences in tolerance were reported across groups **(G-I)**. Data are Mean ± SEM. *p<.05, **p<.01, ***p<.001 compared to HC.



Supplemental Figure 2. Pelvic mucosa pressure pain is enhanced in patients with VBD and VBD+IBS. VBD and VBD+IBS patients reported trends of enhanced pain intensity **(A-F)** and decreased pain thresholds **(G-L)** at all 6 pelvic mucosal sites. Data are Mean ± SEM.



Supplemental Figure 3. MicroRNA Signatures Are Altered in VBD and VBD+IBS. Consistent with our miRNA array results, women with VBD (N=5) have decreased miR-449b and increased miR-133b whereas women with VBD+IBS (N=5) have decreased miR-1288 and increased miR-661 as compared to HC (N=5). Women in both groups have decreased miR-485-5p as compared to HC.

Supplemental Table 1. MicroRNA expression is correlated with intermediate phenotype data

Intermediate Phenotype	miRNA	Correlation (r)	p-value
IL-1ra expression	miR-99b	-0.74	<0.0001
	miR-373	0.44	0.020
	miR-627	0.42	0.034
IL-8 expression	miR-125a-5p	-0.44	0.052
Stabbing Pain (MPQ)	miR-1305	0.56	<0.001
	miR-425#	-0.54	<0.001
	miR-30d	-0.54	<0.001
	miR-1255B	-0.52	<0.001
	miR-454#	-0.51	<0.001
	miR-302b	0.51	<0.001
	miR-15b#	-0.51	<0.001
	miR-320B	-0.49	<0.01
	miR-551b	0.43	0.015
	miR-570	0.42	0.023
	miR-1254	-0.41	0.027
	miR-487a	0.40	0.037
Affective Pain (MPQ)	miR-551b	0.49	0.015
Impact of Pain on Daily	miR-491-3p	0.48	0.029
Activity (CPSQ)	miR-10b	0.46	0.035
Remote Bodily Pressure	RNU44	-0.55	<0.001
Pain (Masseter)	miR-645	-0.47	0.010
	miR-1274A	-0.45	0.016
	miR-213	-0.42	0.036
	miR-543	-0.41	0.037
	RNU48	-0.41	0.037
	miR-192#	-0.40	0.041
	miR-1274B	-0.40	0.041
Remote Bodily Pressure	RNU44	-0.56	<0.001

Pain (Trapezius)	RNU48	-0.44	0.019
	miR-543	-0.44	0.019
	miR-645	-0.44	0.019
	miR-1274A	-0.43	0.019
	miR-1270	-0.43	0.019
	miR-1179	-0.43	0.019
	miR-589	-0.42	0.020
	miR-378	-0.42	0.022
	miR-213	-0.41	0.024
	miR-1180	-0.40	0.027

Abbreviations: Interleukin 1 receptor antagonist (IL-1ra), interleukin 8 (IL-8), McGill Pain Questionnaire (MPQ), Comprehensive Pain and Symptom Questionnaire (CPSQ).

Supplemental Table 2. MicroRNA Pathway Dysregulation in VBD+IBS

MiRNAs	Target Genes	ln(p-val)
	Wnt Signaling	
miR-34b miR-449b miR-503 miR-645 miR-200b miR-133b	CCND2, CTNNB1, DKK1, FZD4, FZD5, MAP3K7, VANGL2, DAAM1, LEF1, MYC, NFAT5, PLCB1, SMAD2, SMAD4, TP53, WNT1, BTRC, CCND2, CCND2, CCND3, FOSL1, MAP3K7, NKD1, PPP3CB, WNT3A, PPP3CB, CTBP2, EP300, FBXW11, JUN, MPAK9, PLCB4, PPP2R2C, PRKACB, PRKCA, RAC1, RHOA, SIAH1, WNT16, CTBP2, CXXC4, FBXW11, NFAT5, NFATC2, PLCB4, PPP2CA, PPP2CB, PSEN1, TBL1X, TCF7, WNT4	21.37
	Adherens Junction	
miR-34b miR-449b miR-503 miR-200b miR-133b	CTNNB1, MAP3K7, LEF1, MET, PTPRM, PVRL1, SMAD2, SMAD4, VCL, WASF1, IGF1R, MAP3K7, PVRL1, WASL, EP300, LMO7, PVRL1, PVRL4, RAC1, RHOA, WASF1, WASF3, EGFR, FGFR1, IGF1R, INSR, MLLT4, TCF7, TGFBR1, WASF2, YES1	18.76
	Colorectal Cancer	
miR-34b miR-449b miR-503 miR-200b miR-133b	CTNNB1, FZD4, FZD5, GRB2, PIK3R3, LEF1, MAP2K1, MET, MYC, PDGFRA, SMAD2, SMAD4, TP53, AKT3, BCL2, CCND1, CDD, IGF1R, MAP2K1, PIK3R1, RAF1, ACVR1C, APPL1, BCL2, JUN, KRAS, MAPK9, RAC1, SOS1, EGFR, IGF1R, TCF7, TGFBR1	18.33
	Prostate Cancer	
miR-34b miR-449b miR-503 miR-200b miR-133b	CREB1, CREB3, CREB3L1, CTNNB1, GRB2, PDGFA, PIK3R3, CREB1, CREB3L1, E2F3, LEF1, MAP2K1, PDGFRA, TP53, AKT3, BCL2, CCND1, CCNE1, CREB5, E2F3, IGF1R, IKBKB, MAP2K1, PIK3RI, RAF1, BCL2, CCNE2, CDK2, CDKN1B, CREB5, E2F3, EP300, IKBKB, KRAS, SOS1, CREB5, EGFR, FGFR1, IGF1R, TCF7	17.01
	Chronic Myeloid Leukemia	
miR-34b miR-449b miR-503 miR-200b miR-133b	GRB2, PIK3R3, E2F3, HDAC1, MAP2K1, MYC, SMAD4, TP53, AKT3, CCND1, E2F3, IKBKB, MAP2K1, PIK3R1, RAF1, ACVR1C, CBL, CDKNN1B, CRKL, CTBP2, E2F3, IKBKB, KRAS, PTPN11, SHC1, SOS1, BCL2L1, CRK, CTBP2, EVI1, TGFBR1	14.95
	Renal Cell Carcinoma	
miR-34b miR-449b miR-503 miR-	GRB2, PIK3R3, RAP1B, ARNT2, ETS1, MAP2K1, MET, AKT3, MAP2K1, PIK3R1, RAF1, VEGFA, CRKL, EGLN1, EP300, ETS1, GAB1, JUN, KRAS, PAK6, PAK7, PTPN11, RAC1, RAP1B, SOS1, TCEB1, VEGFA, CRK	14.35

miR-200b miR-133b		
	ErbB Signaling Pathway	
miR-34b miR-449b miR-503 miR-645 miR-200b miR-133b	ERBB4, GRB2, NCK2, PIK3R3, RPS6KB1, MAP2K1, MYC, RPS6KB1, AKT3, MAP2K1, PIK3R1, RAF1, HBEGF, CBL, CDKN1B, CRKL, GAB1, JUN, KRAS, MAPK9, PAK6, PAK7, PLCG1, PRKCA, RPS6KB1, SHC1, SOS1, CRK, EGFR, MAP2K4	12.44
	Melanogenesis	
miR-34b miR-449b miR-503 miR-200b miR-133b	CREB1, CREB3, CREB3L1, CTNNB1, FZD4, FZD5, CREB1, CREB3L1, KITLG, MAP2K1, MITF, PLCB1, WNT1, GNAI3, MAP2K1, RAF1, WNT3A, ADCY2, ADCY9, EP300, GNAI3, KRAS, PLCB4, PRKACB, PRKCA, WNT16, ADCY5, ADCY6, CALM1, PLCB4, TCF7, WNT4	10.51
	Focal Adhesion	
miR-34b miR-449b miR-503 miR-200b miR-133b	CCND2, CTNNB1, GRB2, ITGA2, PDGFA, PIK3R3, RAP1B, RELN, VAV3, MAP2K1, MET, PDGFRA, THBS1, VCL, AKT3, BCL2, CCND1, CCND2, CCND3, IGF1R, MAP2K1, MYLK, PIK3R1, RAF1, VEGFA, BCL2, CRKL, FLT1, FM1, JUN, KDR, LAMC1, MAPK9, MYLK, PAK6, PAK7, PRKCA, RAC1, RAP1B, RELN, RHOA, SHC1, SOS1, TLN2, VEGFA, XIAP, COL1A1, COL5A3, COL6A3, CRK, EGFR, IGF1R, TNR	10.21
	MAPK Signaling Pathway	
miR-34b miR-449b miR-503 miR-645 miR-200b miR-133b	CACNB2, GRB2, MAP3K1, MAP3K7, MAP3K7IP2, PDGFA, RAP1B, CACNB1, CACNB3, FGF23, HSPA1B, MAP2K1, MAP4K4, MYC, PDGFRA, RPS6KA4, RRAS, TAOK1, TP53, AKT3, FGF2, FGF7, IKBKB, MAP2K1, MAP3K7, MAPK8IP2, NF1, PPP3CB, PTPRR, RAF1, MEF2C, PPP3CB, ACVR1C, CACNA2D1, CACNB2, CRKL, DUSP1, IKBKB, JUN, KRAS, MAP2K5, MAP3K1, MAP3K5, MAP4K3, MAP4K4, MAPK9, NTF3, PRKACB, PRKCA, RAC1, RAP1B, RPS6KA3, SOS1, SRF, CRK, DUSP1, EGFR, EV1, FGF1, FGFR1, MAP2K4, MAP3K3, NFATC2, TGFBR1	10
	Regulation of Actin Cytoskeleton	
miR-34b miR-449b miR-503 miR-200b miR-133b	CFL2, ITGA2, NCKAP1, PDGFA, PIK3R3, PIP5K1B, PIP5K3, VAV3, FGF23, IQGAP2, MAP2K1, MYH9, PDGFRA, RDX, RRAS, VCL, WASF1, FGF2, FGF7, MAP2K1, MYH10, MYLK, PIK3R1, RAF1, WASL, CFL2, CRKL, FGD1, FN1, KRAS, LIMK1, MSN, MYLK, PAK6, PAK7, PIP4K2B, PIP5K3, PPP1R12B, RAC1, RHOA, SOS1, SSH2, WASF1, ARPC1A, ARPC5, CRK, DIAPH2, EGFR, FGF1, FGFR1, IQGAP2, MSN, MYH9, PFN2, PIP4K2B, PIP5K3, WASF2	9.67
	Pancreatic Cancer	
miR-34b miR-449b miR-503	PIK3R3, E2F3, MAP2K1, RALA, SMAD2, SMAD4, TP53, AKT3, CCND1, E2F3, IKBKB, MAP2K1, PIK3R1, RAF1, VEGFA, ACVR1C, BRCA2, E2F3, IKBKB, KRAS, MAPK9, RAC1, VEGFA, BCL2L1, EGFR, JAK1, TGFBR1	9.57

miR-200b miR-133b		
	Axon Guidance	
miR-34b miR-449b miR-503 miR-645 miR-200b miR-133b	CFL2, DPYSL2, EPHA7, NCK2, NTNG1, ABLIM3, EFNB1, MET, NFAT5, SEMA4C, SEMA4F, DCC, EFNB2, EPHA7, GNAI3, PPP3CB, SEMA3D, SEMA6D, PPP3CB, SEMA3F, SEMA6D, CFL2, EFNA1, EFNB2, GNA13, KRAS, LIMK1, PAK6, PAK7, PLXNA2, RAC1, RHOA, SEMA3F, SEMA6D, EFNA4, EPHA7, EPHB4, NFAT5, HFATC2, SRGAP2, SRGAP3	8.58
	Notch Signaling Pathway	
miR-449b miR-503 miR-200b miR-133b	APH1A, DLL1, HDAC1, JAG1, NCSTN, NOTCH2, NUMBL, NUMB, CTBP2, EP300, JAG2, KAT2B, NUMB, CTBP2, PSEN1, RBPJ	8.32
	Thyroid Cancer	
miR-34b miR-449b miR-503 miR-200b miR-133b	CCDC6, CTNNB1, LEF1, MAP2K1, MYC, RET, TP53, CCND1, MAP2K1, KRAS, TCF7, TFG	8.21
	Glioma	
miR-34b miR-449b miR-503 miR-200b miR-133b	GRB2, PDGFA, PIK3R3, E2F3, MAP2K1, PDGFRA, TP53, AKT3, CCND1, E2F3, IGF1R, MAP2K1, PIK3R1, RAF1, E2F3, KRAS, PLCG1, PRKCA, SHC1, SOS1, CALM1, EGFR, IGF1R	8.06
	TGF-Beta Signaling Pathway	
miR-34b miR-449b miR-503 miR-200b miR-133b	ACVR2A, ID2, RP26KB1, SMURF1, ACVR2B, E2F5, MYC, RPS6KB1, SMAD2, SMAD4, THBS1, ACVR2A, ACVR2B, BMPR1A, SMAD7, SMURF1, SMURF2, ACVR1C, ACVR2A, EP300, NOG, PPP2R2C, RHOA, RPS6KB1, SMURF2, ID4, LTBP1, PPP2CA, PPP2CB, SP1, TGFBR1	7.82
	Acute Myeloid Leukemia	
miR-34b miR-449b miR-503 miR-	GRB2, PIK3R3, RPS6KB1, LEF1, MAP2K1, MYC, RPS6KB1, AKT1, CCND1, IKBKB, MAP2K1, PIK3R1, RAF1, IKBKB, KRAS, PIM2, RPS6KB1, SOS1, JUP, PML, TCF7	7.67

200b **miR-133b**		
	Oxidative Phosphorylation	
miR-449b **miR-200b** **miR-133b**	SDHC, NDUFS4, NDUFS3	7.21
	Dorso-Ventral Axis Formation	
miR-34b **miR-449b** **miR-503** **miR-200b** **miR-133b**	ERBB4, GRB2, ETS1, MAP2K1, NOTCH2, MAP2K1, RAF1, ETS1, ETS2, KRAS, SOS1, EGFR	7.18

The top 20 pathways, as determined by the Diana Lab DNA Intelligent Analysis, affected by miRNA dysregulation in women with VBD are shown with the names and union –ln(p-value) of target genes affected in each pathway. Genes are linked to miRNAs by color.

Supplemental Table 3. MicroRNA Pathway Dysregulation in VBD+IBS

MiRNAs	Target Genes	ln(p-val)
MAPK Signaling Pathway		
miR-593 let-7f-2# miR-125a-3p miR-512-3p miR-661	PDGFA, PDGFB, PTPN5, PTPRR, RAP1B, RPS6KA1, TAOK3, TGFB2, ACVR1B, ACVR1C, CACNA1D, CASP3, DUSP16, DUSP1, DUSP4, DUSP9, FGF11, FGF5, FLNA, MAP3K1, MAP3K3, MAP3K7IP2, MAP4K3, MAP4K4, MAPK11, MAPK8, NGF, NLK, PAK1, PDGFB, PPP3CA, RPS6KA3, TGFBR1, TP53, IL1R1, NF1, NLK, RPS6KA3, AKT1, CRK, DUSP1, EVI1, FGF19, MAP3K14, MAP3K1, MAPK10, MEF2C, MKNK2, PAK2, PPP3CA, RPS6KA2, RPS6KA3, RPS6KA5, SOS1, TGFBR2, DUSP3, FLNA, MAP3K10, MAP3K3, PLA2G6	16.5
TGF-Beta Signaling Pathway		
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	ACVR1, BMPR2, NOG, SP1, TGFB2, ACVR1B, ACVR1C, ACVR2A, ACVR2B, CHRD, E2F5, GDF6, TGFBR1, THBS1, ZFYVE16, ACVR2B, BMPR2, CUL1, E2F5, INHBB, LEFTY1, LEFTY2, PITX2, RBL1, RBL2, SMAD2, TGFBR2, PPP2R1A	16.07
Chronic Myeloid Leukemia		
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	CDK6, CTBP2, SHC4, TGFB2, ACVR1B, ACVR1C, BCL2L1, CBL, CCND1, CDKN1A, RB1, TGFBR1, TP53, E2F3, ACVR1C, APPL1, BCL2, JUN, KRAS, MAPK9, RAC1, SOS1, EGFR, IGF1R, TCF7, TGFBR1	15.09
Colorectal Cancer		
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	CREB1, CREB3, CREB3L1, CTNNB1, GRB2, PDGFA, PIK3R3, CREB1, CREB3L1, E2F3, LEF1, MAP2K1, PDGFRA, TP53, AKT3, BCL2, CCND1, CCNE1, CREB5, E2F3, IGF1R, IKBKB, MAP2K1, PIK3RI, RAF1, AKT1, CCND1, CDK4, CRK, E2F3, EVI1, PIK3CA, RUNX1, SOS1, TGFBR2, CBL, CDK6	11.98
Focal Adhesion		
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	COL4A6, ITGA10, ITGA5, PDGFA, RAP1B, SHC4, CCND1, CCND2, COL11A1, COL1A1, COL1A2, COL3A1, COL4A1, COL4A6, COL5A2, FLNA, IGF1, IGF1R, ITGB3, MAPK8, PAK1, PDGFB, THBS1, VAV3, FYN, IGF1R, ITGB1, ACTG1, AKT1, CCND1, CCND2, CRK, FLT1, IGF1R, ITGB8, LAMA3, MAPK10, PAK2, PAK7, PIK3CA, SOS1, COL6A3, FLNA, ITGA10, KDR	11.35
Axon Guidance		
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	EPHB3, SRGAP3, EPHA4, EPHB1, LIMK2, PAK1, PPP3CA, SEMA4C, SEMA4F, SEMA4G, CFL2, DCC, FYN, ITGB1, SEMA5B, ABLIM1, CFL2, DPYSL5, EFNB2, EPHA2, EPHA8, NTN4, PAK2, PAK7, PLXNA1, PPP3CA, SEMA3C, GNAI2, SEMA4G, SLIT1, SRGAP3	10.33
Pancreatic Cancer		
miR-593 let-7f miR-125a-3p miR-512-3p	CDK6, TGFB2, ACVR1B, ACVR1C, BCL2L1, CCND1, MAPK8, RB1, TGFBR1, TP53, CASP9, E2F3, AKT1, CCND1, CDK4, E2F3, MAPK10, PIK3CA, SMAD2, TGFBR2, CDK6	8.91

miR-661		
	ECM Receptor Interaction	
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	COL4A6, FNDC1, ITGA10, ITGA5, COL11A1, COL1A1, COL1A2, COL3A1, COL4A1, COL4A6, COL5A2, FNDC3A, ITGB3, THBS1, ITGB1, CD44, FNDC3A, LAMA3, COL6A3, DAG1, ITGA10	8.61
	Oxidative Phosphorylation	
miR-512-3p	ATP5E	6.81
	Glioma	
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	CDK6, PDGFA, PDGFB, SHC4, CCND1, CDKN1A, IGF1, IGF1R, PDGFB, RB1, TP53, E2F3, IGF1R, AKT1, CCND1, CDK4, E2F3, IGF1R, PIK3CA, SOS1, CDK6	6.7
	Melanoma	
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	CDK6, PDGFA, CCND1, CDKN1A, FGF11, FGF5, IGF1, IGF1R, PDGFB, RB1, TP53, E2F3, IGF1R, AKT1, CCND1, CDK4, E2F3, FGF19, IGH1R, PIK3CA, CDK6	6.27
	Adherens Junction	
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	TCF7, ACVR1B, ACVR1C, IGF1R, INSR, NLK, TGFBR1, WASL, FYN, IGF1R, INSR, NLK, SNAI1, ACTG1, IGF1R, LEF1, SAMD2, SSX1P, TGFBR2, PVRL2, WASL	6.27
	Prostate Cancer	
miR-593 let-7f miR-125a-3p miR-512-3p	CREB3L1, PDGFA, TCF7, CCND1, CDKN1A, IGF1, IGF1R, INS, PDGFB, RB1, TP53, CASP9, E2F3, IGF1R, INS, AKT1, CCND1, CREB5, E2F3, IGF1R, LEF1, PIK3CA, SOS1	5.65
	Type II Diabetes	
let-7f miR-125a-3p miR-512-3p miR-661	CACNA1D, INSR, IRS2, MAPK8, SOCS1, SOCS4, INS, INSR, MAPK10, PIK3CA, SLC2A4, SOCS4	5.3
	mTOR Signaling Pathway	
miR-593 let-7f miR-125a-3p miR-512-3p miR-661	RPS6KA1, IGF1, INS, RICTOR, RP26KA3, TSC1, ULK2, INS, RPS6KA3, AKT1, PIK3CA, RPS6KA2, RPS6KA3, ULK1, ULK2	4.77
	Dentatorubropallidoluysian Atrophy (DRPLA)	
miR-593 let-7f miR-125a-	ITCH, CASP3, INSR, INS, INSR, MAGI1	4.75

3p **miR-512-3p**		
	Bladder Cancer	
let-7f **miR-125a-3p** **miR-512-3p**	CCND1, CDKN1A, IL8, RB1, THBS1, TP53, E2F3, CCND1, CDK4, DAPK2, E2F3, IL8, RPS6KA5	4.52
	Wnt Signaling Pathway	
miR-593 **let-7f** **miR-125a-3p** **miR-512-3p** **miR-661**	CTBP2, FOSL1, FXD7, NKD1, PRICKLE2, TCF7, VANGL1, VANGL2, CCND1, CCND2, FZD4, MAPK8, NKD1, NLK, PPP3CA, SENP2, TP53, VANGL1, VANGL2, WNT1, CSNK1E, NLK, CCND1, CCND2, CUL1, LEF1, MAPK10, PPP3CA, SMAD2, FZD4, FZD8, PPP2R1A	4.08
	ErbB Signaling Pathway	
miR-593 **let-7f** **miR-125a-3p** **miR-512-3p** **miR-661**	ERBB4, NRG3, SHC4, ABL2, CBL, CDKN1A, MAPK8, PAK1, NRG1, AKT1, CRK, MAPK10, PAK2, PAK7, PIK3CA, SOS1, CBL	3.75
	Regulation of Actin Cytoskeleton	
miR-593 **let-7f** **miR-125a-3p** **miR-512-3p** **miR-661**	ITGA10, ITGA5, ITGB1, PDGFA, SCIN, DIAPH2, FGF11, FGF5, ITGB3, LIMK2, PAK1, PDGFB, RDX, SSH1, VAV3, WASL, CFL2, INS, ITGB1, ACTG1, CFL2, CRK, FGF19, ITGB8, PAK2, PAK7, PFN2, PIK3CA, RDX, SOS1, SSH2, ARHGEF4, ITGA10, PIP4K2B, WASL	3.65

The top 20 pathways, as determined by the Diana Lab DNA Intelligent Analysis, affected by miRNA dysregulation in women with VBD+IBS are shown with the names and union –ln(p-value) of target genes affected in each pathway. Genes are linked to miRNAs by color.

Figure 4 Abbreviations

Abbreviations: insulin (INS), insulin receptor (INSR), extracellular signal-regulated kinases (ERK), insulin receptor substrate 2 (IRS2), phosphatidylinositol-4,5-Bisphosphate 3-Kinase, Catalytic Subunit Alpha (PIK3CA), brain-specific angiogenesis inhibitor 1-associated protein 2 (BAIAP2), dentatorubral-pallidoluysian atrophy (DRPLA), caspase 3 (CASP3), suppressor of cytokine signaling 1 (SOCS), alpha-1 type I collagen (COL1a1), laminin alpha-3 (LAMA3), fibronectin type III domain containing 1 (FNDC1), thrombospondin 1 (THBS1), integrin alpha-5 (ITGA5), integrin beta-1 (ITGB1), dystroglycan 1 (DAG1), extracellular matrix (ECM), transforming growth factor beta (TGF-B), TGF-B receptor 2 (TGFBR2), TGF-B receptor 1 (TGFBR1), death domain-associated protein (DAXX), RAC-alpha serine/threonine-protein kinase (AKT1), mitogen-activated protein kinase (MAPK), ribosomal protein S6 kinase 90kDa polypeptide 3 (RPS6KA3), cell division cycle 25B (CDC25B), MYC-associated factor X (MAX), myocyte enhancer factor 2C (MEF2C), protein phosphatase 2 regulatory subunit A beta (PPP2R1B), Rho-associated coiled-coil containing protein kinase 1 (ROCK1), E2F transcription factor 5 p130-binding (E2F5), cyclin-dependent kinase 4 inhibitor B (p15), inhibin beta B (INHBB), activin A receptor type II-like 1 (ACVRL1), wingless-type MMTV integration site family member 3A (WNT3A), frizzled class receptor 10 (FZD10), phospholipase C beta 4 (PLCB4), protein phosphatase 3 catalytic subunit alpha isozyme (PPP3CA), nuclear factor of activated T cells cytoplasmic calcineurin-dependent 2 (NFATC2), jun proto-oncogene (c-JUN), disheveled segment polarity protein 3 (DvI3), glycogen synthase kinase 3 beta (GSK-3B), beta-catenin (B-catenin), transcription factor 7- like 2 (TCF7L2), disheveled-associated activator of morphogenesis 1 (Daam1), ras homolog family member A (RhoA), VANGL Planar Cell Polarity Protein 1 (VANGL1), dual-specificity protein phosphatase (DUSP), platelet-derived growth factor alpha polypeptide (PDGFA), PDGF receptor alpha polypeptide (PDGFRA), growth factor receptor-bound protein 2 (GRB2), son of sevenless homolog 1 (SOS1), methyl ethyl ketone (MEK), MAPK interacting serine/threonine kinase 2 (MKNK2), cyclic adenosine monophosphate (cAMP), protein kinase cAMP-dependent catalytic beta (PRKACB), member of ras oncogene family (RAP1A), MAPK kinase 4 (MKK4), c-Jun N-terminal kinase (JNK), nuclear factor kappa beta (NFkB), Kirsten rat sarcoma viral oncogene homolog (KRAS), proto-oncogene c-RAF (RAF1), v-ets erythroblastosis virus E26 oncogene homolog (ETS), broad-complex (BR-C), gonadotropin-releasing hormone (GnRH), luteinizing hormone beta polypeptide (LHB), alpha gonadotropin (aGSU), follicle-stimulating hormone beta subunit (FSHB), heparin-binding EGF-like growth factor (HB-EGF), epidermal growth factor receptor (EGFR), proto-oncogene c-Src (Src), cell-division control protein 42 homolog (CDC42), v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 4 (ERBB4), protein kinase cGMP-dependent type I (PRKG1), protein kinase C alpha (PRKCA), PRK cAMP-dependent catalytic beta (PRKACB), adenylate cyclase 1 (ADCY1), G protein alpha inhibiting activity polypeptide 3 (GNAI3), guanylate cyclase 1 alpha 3 (GUCY1A3), inositol 1,4,5- trisphosphate receptor type 1 (ITPR1), phospholipase C beta 4 (PLCB4), lysophosphatidic acid receptor 1 (LPAR1), lipoprotein (LPA), serotonin receptor (HTR2).