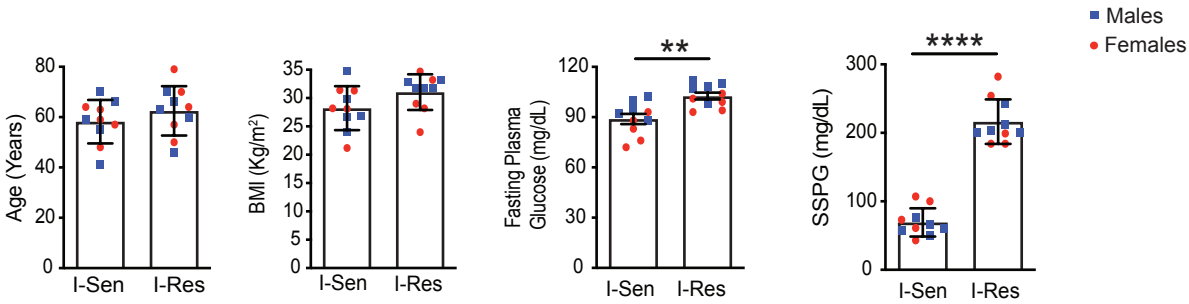
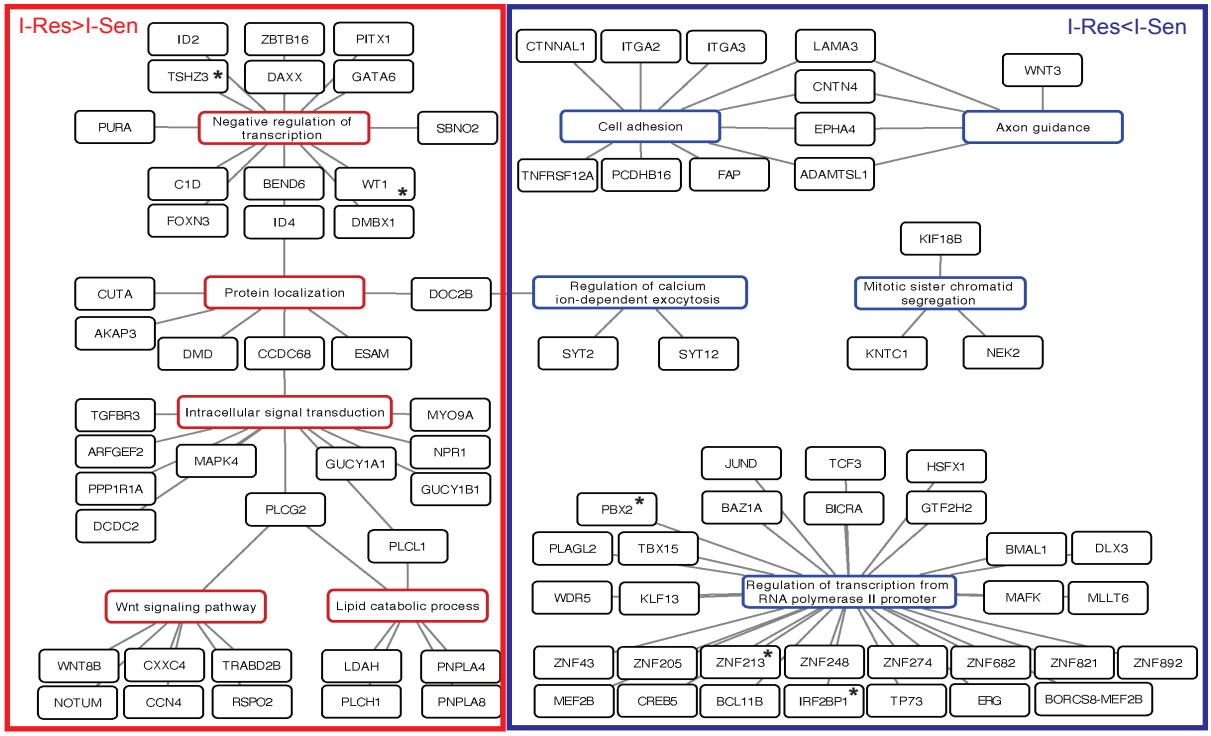
Supplemental Data Figure 1: Clinical characteristics (from (16))



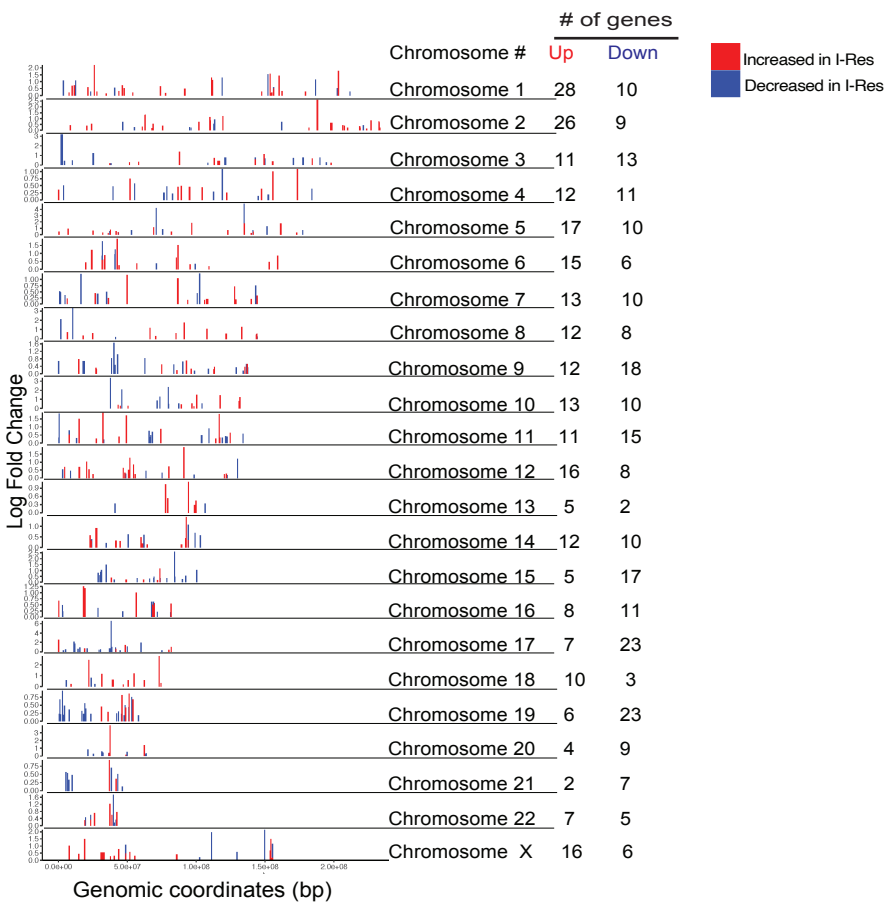
Supplemental Data Figure 2: Biological pathways and genomic distribution of the gene expression changes associated with insulin resistance

A.



* Genes associated with T2D

B.



Chromosome #	# of genes Up	Down
Chromosome 1	28	10
Chromosome 2	26	9
Chromosome 3	11	13
Chromosome 4	12	11
Chromosome 5	17	10
Chromosome 6	15	6
Chromosome 7	13	10
Chromosome 8	12	8
Chromosome 9	12	18
Chromosome 10	13	10
Chromosome 11	11	15
Chromosome 12	16	8
Chromosome 13	5	2
Chromosome 14	12	10
Chromosome 15	5	17
Chromosome 16	8	11
Chromosome 17	7	23
Chromosome 18	10	3
Chromosome 19	6	23
Chromosome 20	4	9
Chromosome 21	2	7
Chromosome 22	7	5
Chromosome X	16	6

Increased in I-Res
Decreased in I-Res

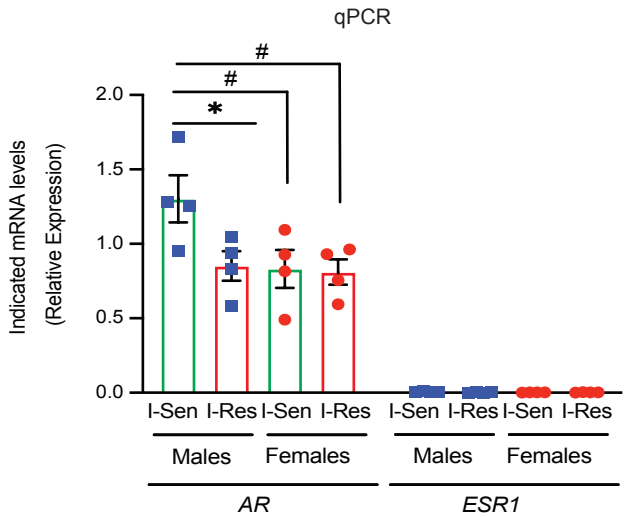
Supplemental Data Figure 3: T2D SNP associations in I-Res iMyos

Gene	Altered in I-Res iMyos	Function and T2D association	Chromosome
SOAT1	Increased	Catalyzes the formation of fatty acid-cholesterol esters, SOAT1 inhibition reduces podocyte injury in diabetic kidney disease [1]	Chr 1
ACP6	Increased	Lysophosphatidic acid phosphatase activity, increased in skeletal muscle biopsies of people with T2D family history [2]	Chr 1
TRIM63	Increased	Muscle E3 ubiquitin ligase, increased in muscle of T1D mice [3]	Chr 1
KCNJ13	Increased	Inward rectifier potassium channel activity, Up in T1D human islets [4]	Chr 2
LSAMP	Increased	Post-translational modification: synthesis of GPI-anchored proteins, levels positively correlates with HOMA-IR [5]	Chr 3
ABHD6	Increased	Enables acylglycerol lipase activity, ABHD6 KO mice are protected from obesity and T2D [6]	Chr 3
FBXW7	Decreased	Ubiquitin protein ligase binding, decreased in muscle of T2D rats [7]	Chr 4
LRRC66	Increased	Cell adhesion, cellular trafficking, and hormone-receptor interactions, altered in rat islets of intrauterine growth retardation, which is associated with development of T2D [8]	Chr 4
ANKDD1B	Decreased	Signal transduction, predicted loss of function SNP in T2D [9]	Chr 5
NADK2	Increased	Mitochondrial kinase that catalyzes yield of NADP, NAD+ precursor treatment is associated with muscle insulin resistance in humans [10]	Chr 5
HLA-B	Decreased	Peptide antigen binding, HLA-B polymorphisms are present in T2D [11]	Chr 6
PBX2	Decreased	DNA-binding transcription factor activity, polymorphism associated with vascular complications in diabetes [12]	Chr 6
LSM2	Decreased	RNA binding and small GTPase binding, altered in T1D patients [13]	Chr 6
SYNGAP1	Increased	Ras GTPase activating protein	Chr 6
RGS17	Increased	GTPase activator activity, associated with diabetes in GWAS [14]	Chr 6
DDAH2	Increased	Regulation of nitric oxide generation, involved in myocardial fibrosis in diabetic cardiomyopathy [15]	Chr 6
STK19	Increased	Protein serine/threonine kinase activity, associated with diabetes in GWAS [14]	Chr 6
HLA-DQA1	Increased	Peptide antigen binding and MHC class II receptor activity, associated with diabetes in GWAS [14]	Chr 6
TRIM26	Increased	E3 ubiquitin-protein ligase which regulates the IFN-beta production, contains T1D associated SNP [16]	Chr 6
TONSL	Decreased	Negative regulator of NF-kappa-B mediated transcription, polymorphisms associated with T2D [17]	Chr 8
GINS4	Decreased	Initiation and progression of DNA replication, associated with β cell dysfunction [18]	Chr 8
ASAH1	Increased	A member of the acid ceramidase family of proteins, associated with T2D in obese population [19]	Chr 8
WT1	Increased	Nucleic acid binding and sequence-specific DNA binding, negative regulator of IGF1 receptor in Wilms tumor biology [20]	Chr 11
RPUSD2	Decreased	Involved in mRNA pseudouridine synthesis	Chr 15
VPS13C	Increased	Mitochondrial function and maintenance, T2D associated gene in β cells [21]	Chr 15
CMIP	Decreased	T cell signaling pathway, polymorphisms associated with T2D [22]	Chr 16
ZNF213	Decreased	DNA-binding transcription factor activity	Chr 16
IRF2BP1	Decreased	Involved in protein polyubiquitination, altered in T2D muscles [23]	Chr 19

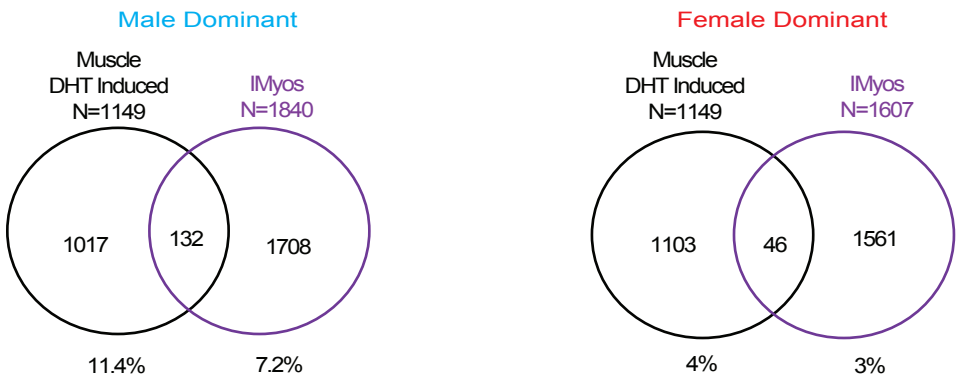
TSHZ3	Increased	Transcriptional regulator involved in developmental processes, *Tshz3* haploinsufficiency leads to abnormalities in mouse kidney [24]	Chr 19
PCSK1N	Decreased	Endopeptidase inhibitor activity, involved in proinsulin processing [25]	Chr X
TIMM17B	Increased	Facilitates the transport of mitochondrial proteins, related to diabetic retinopathy [26]	Chr X
KCND1	Increased	Monoatomic ion channel activity, associated with T2D [27]	Chr X

Supplemental Data Figure 4: Autosomal sex-specific gene expression changes are independent of the androgen receptor action

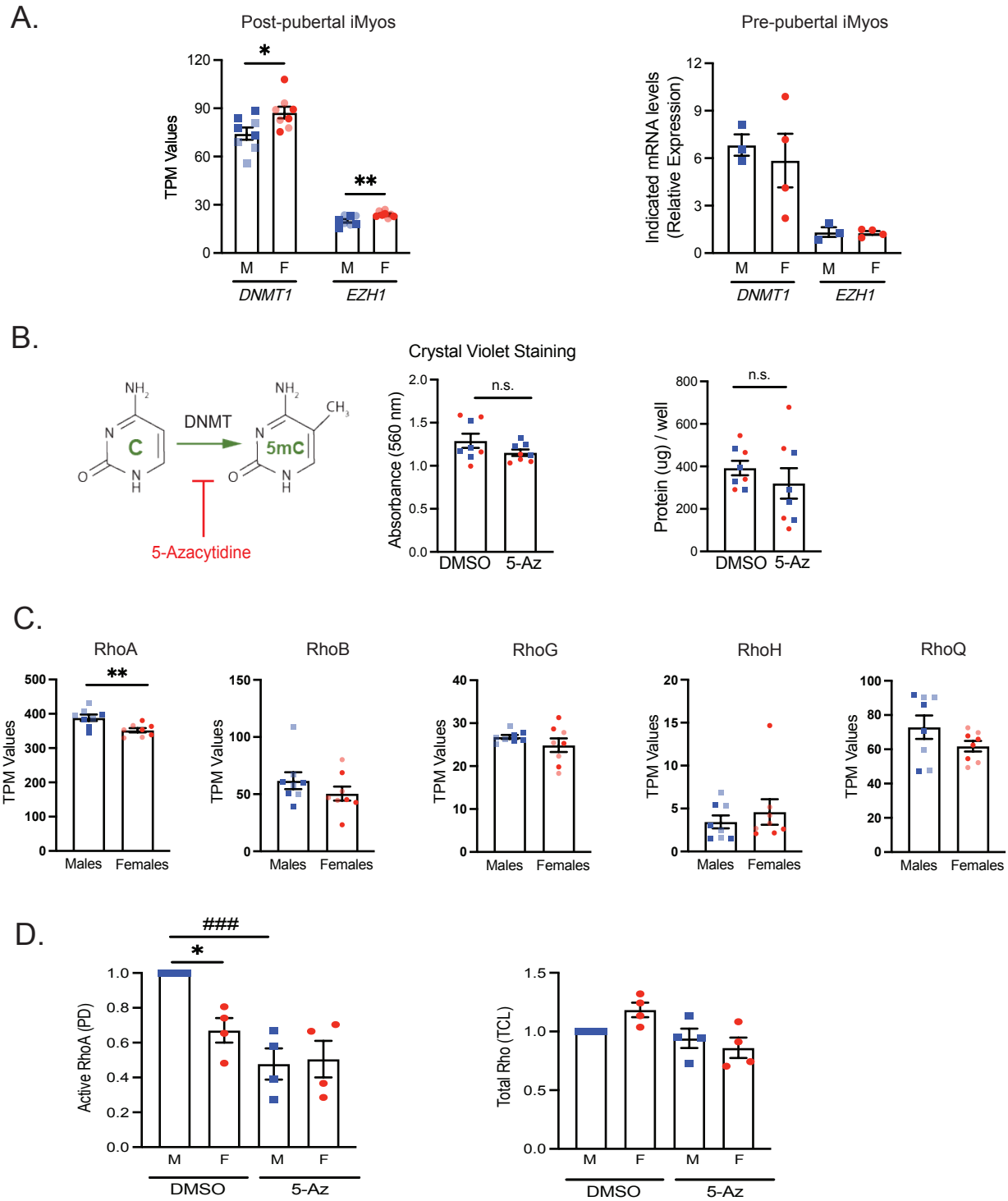
A.



B.



Supplemental Data Figure 5: Sex-specific regulation of epigenetic genes and RhoA isoform and activation



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