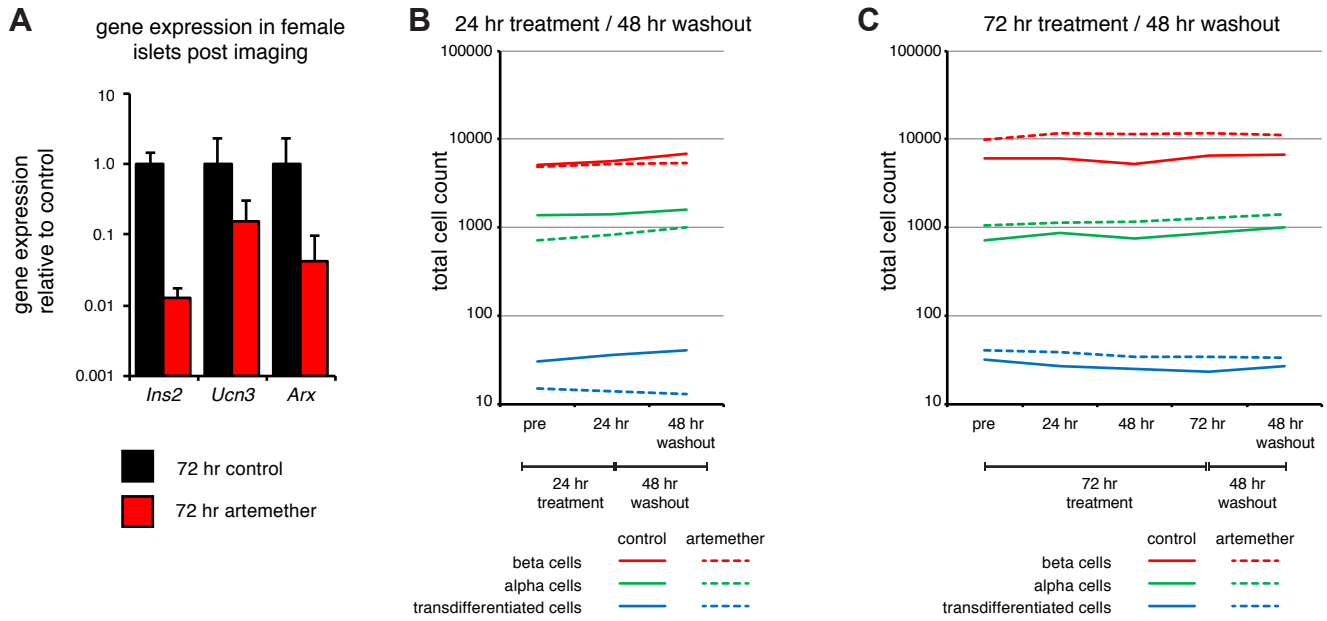


Figure S1. Confirmation of gene expression change in imaged islets and washout of artemether does not facilitate alpha to beta cell transdifferentiation. Related to Figure 1



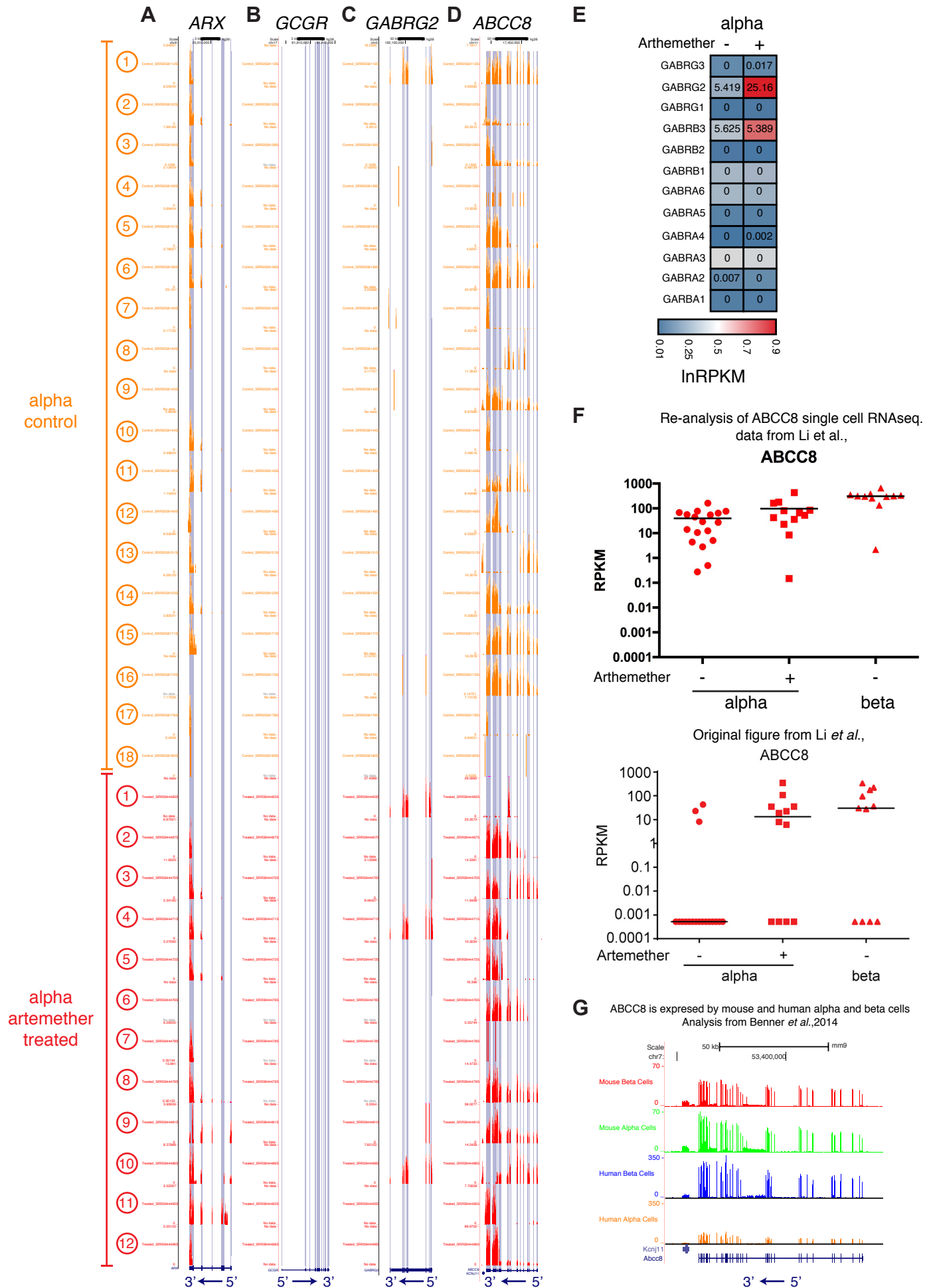
**Figure S1. Confirmation of gene expression change in imaged islets and washout of artemether does not facilitate alpha to beta cell transdifferentiation. Related to Figure 1**

(A) Confirmation of gene expression changes in the islets of 2 female mice at the conclusion of the image acquisition in Figure 1B-F.

(B) Quantification of the total number of alpha, beta, and alpha-to-beta transdifferentiated cells. The same islets were imaged, stimulated with 10  $\mu$ M artemether as indicated. Artemether was then washed out via media changes and the same islets were imaged 48 hr after the end of artemether stimulation. >10 islets for each treatment from a single *mIns1*-H2b-mCherry x *Gcg*-Cre x *Rosa26*-STOP-YFP triple transgenic mouse.

(C) Quantification of the total number of alpha, beta, and alpha-to-beta transdifferentiated cells. The same islets were imaged repeatedly in 3D at 24 hr intervals under stimulation with 10  $\mu$ M artemether as indicated. Artemether was then washed out media changes and the same islets were imaged 48 hr after the end of artemether stimulation. >10 islets for each treatment from two *mIns1*-H2b-mCherry x *Gcg*-Cre x *Rosa26*-STOP-YFP triple transgenic mice.

Figure S2. Re-analysis of single cell RNAseq data from Li et al., 2017. Related to Figure 1.



**Figure S2. Re-analysis of single cell RNAseq data from Li et al., 2017. Related to Figure 1.**

(A) Browser plots of *ARX* expression of the 18 single control alpha cells and 12 artemether-treated alpha cells reveal no evidence for artemether-induced inhibition of *ARX*. Note the 3' bias in all alpha cells where *ARX* is detected. RNAseq data from GEO: GSE73727 and GSE84714.

(B) Browser plots illustrate that none of the alpha cells in their study demonstrates detectable *GCGR* expression.

(C) Browser plots illustrate that *GABRG2* is detected in only 1 of 18 control and 3 of 12 artemether-treated cells.

(D) Browser plots illustrate that *ABCC8* is readily detected in most single alpha cells regardless of treatment. Note that sequence coverage tends to span the entire gene model (indicated by the blue columns).

(E) Modification of the heat map of human GABA receptor subunit genes. The original color coding by Li et al. is overlaid with the actual number of reads per kilobase of gene model per million reads sequenced (RPKM). Note that we are unable to detect any reads for the majority of GABA receptor genes. For *GABRG2*, which has the highest differential expression following artemether treatment, this expression is concentrated in a minority of single alpha cells. See also (C).

(F) Expression plot indicating *ABCC8* expression based on reanalysis of the single alpha cell RNAseq data by Li et al., There is no difference in *ABCC8* expression between control and artemether-treated single alpha cells. The original graph of these data by Li et al. is included for reference.

(G) Browser plots of bulk RNAseq data to indicate that *ABCC8* is robustly expressed by human and mouse alpha and beta cells. Analysis by Benner et al., 2012.

Table S1: Primers used for quantitative PCR. Related to Figure 2.

RefSeq ID	Gene	Oligonucleotide	Sequence	amplicon length (bp)
NM_007492	<i>Arx</i>	qmARX.fwu1	TTCCAGAAGACGCACTACCC	68
		qmARX.rvu1	TCTGTCCAGGTCAGCCTCAT	
NM_007522	<i>Bad</i>	qmBAD.fwu1	CCACCAACAGTCATCATGGA	121
		qmBAD.rvu1b	CGTCCTCGAAAAGGGCTAA	
XM_006540584	<i>Bax</i>	qmBAX.fwu2	AGTGTCTCCGGCGAATTG	69
		qmBAX.rvu2	CCACGTCAGCAATCATCCT	
NM_009741	<i>Bcl2</i>	qmBCL2.fwu2	GTACCTGAACCGGCATCTG	76
		qmBCL2.rvu2	GGGGCCATATAGTTCCACAA	
NM_001289716	<i>Bclxl</i>	qmBCLXL.fwu1	TGACCACCTAGAGCCTTGGGA	68
		qmBCLXL.rvu1	TGTTCCCGTAGAGATCCACAA	
NM_001163434	<i>Bip</i>	Bip.fwu1	GGAGACTGCTGAGGCGTATT	105
		Bip.rvu1	GTGCCAGCATCTTTGGTTG	
NM_008100	<i>Gcg</i>	qrodGcg.fwu1	TCACAGGGCACATTCACCAG	121
		qrodGcg.rvu1	CATCATGACGTTTGGCAATGTT	
NM_008245	<i>Hhex</i>	qmHhex.fwu1	CTACACGCACGCCCTACTC	76
		qmHhex.rvu1	CAGAGGTCGCTGGAGGAA	
NM_013556	<i>Hprt</i>	qmHPRT.fwu	TCCTCCTCAGACCGCTTTT	90
		qmHPRT.rvu	CCTGGTTCATCATCGCTAATC	
NM_008386	<i>Ins1</i>	qmINS1.fwu1	CAGAGAGGAGGTACTTTGGACTATAAA	113
		qmINS1.rvu1	GCCATGTTGAAACAATGACCT	
NM_001185084	<i>Ins2</i>	qrodINS2.fw1	GCTCTCTACCTGGTGTGTGGG	128
		qrodINS2.rv1	CAAGGTCTGAAGGTCACCTGC	
NM_010573	<i>Irx1</i>	qmlrx1.fwu1	GCCCCACAACAGTTAAAGTC	111
		qmlrx1.rvu1	CCCCTTAATCAGGCAGACG	
NM_194350	<i>MafA</i>	qmMAFA.fwu1	CTCCAGAGCCAGGTGGAG	66
		qmMAFA.rvu1	GTACAGGTCCCGCTCCTTG	
NM_010658	<i>Mafb</i>	qmMAFB.fwu1	GCAGGTATAAACGCGTCCAG	61
		qmMAFB.rvu1	TGAATGAGCTGCGTCTTCTC	
NM_008814	<i>Pdx1</i>	qmPdx1.fwu1	GAAATCCACCAAAGCTCACG	65
		qmPdx1.rvu1	CGGGTTCGCTGTGTAAG	
NM_031197	<i>Slc2a2</i>	qmGLUT2.fwu2	GGGCCATCAACATGATCTTC	86
		qmGLUT2.rvu2	AATCATCCCGGTTAGGAACA	
NM_009215	<i>Sst</i>	qrodSS.fw1	GACCCAGACTCCGTGAGTTT	112
		qrodSS.rv1	TCTCTGTCTGGTTGGGCTCG	
NM_001009935	<i>Txnip</i>	Txnip.fwu1	CTTGCGCTATGAAGACACACTT	75
		Txnip.rvu1	GGCCTCATGATCACCATCTC	
NM_031250	<i>Ucn3</i>	qmUcn 3.fwu1	GCTGTGCCCTCGACCT	71
		qmUcn 3.rvu1	TGGGCATCAGCATCGCT	