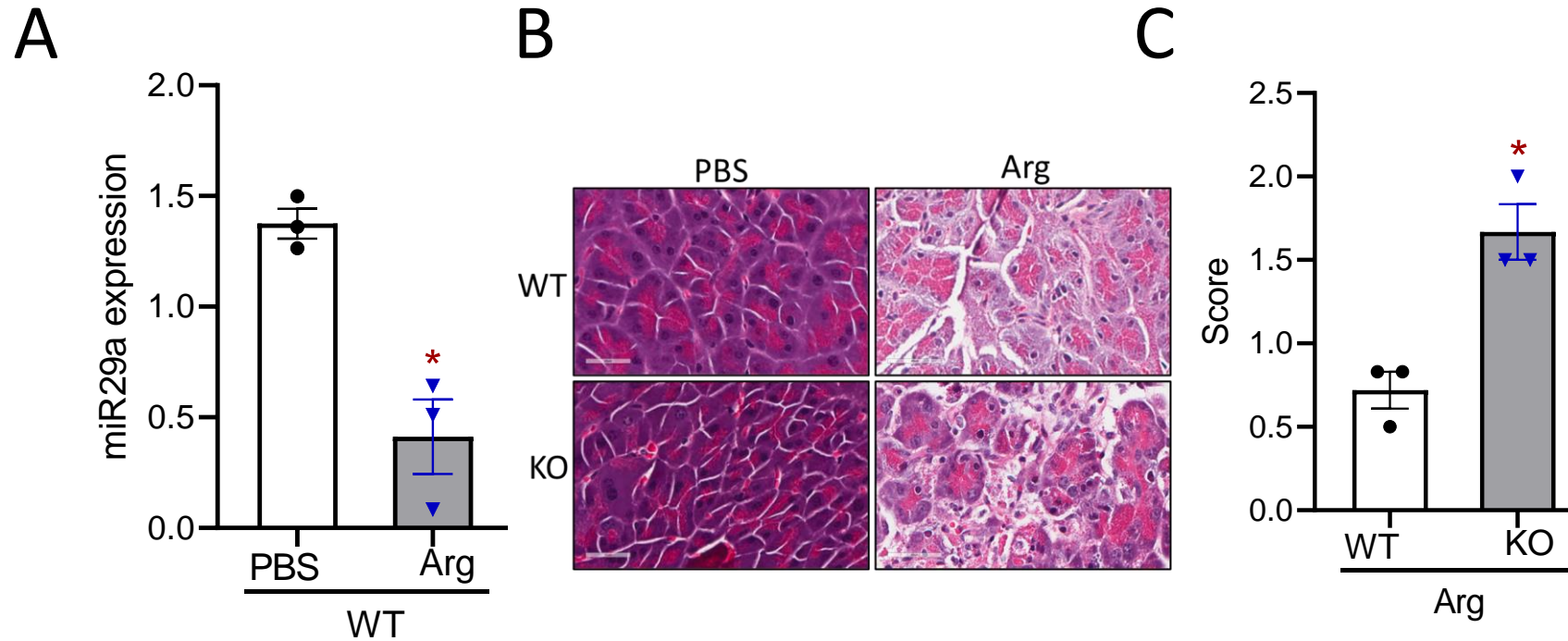
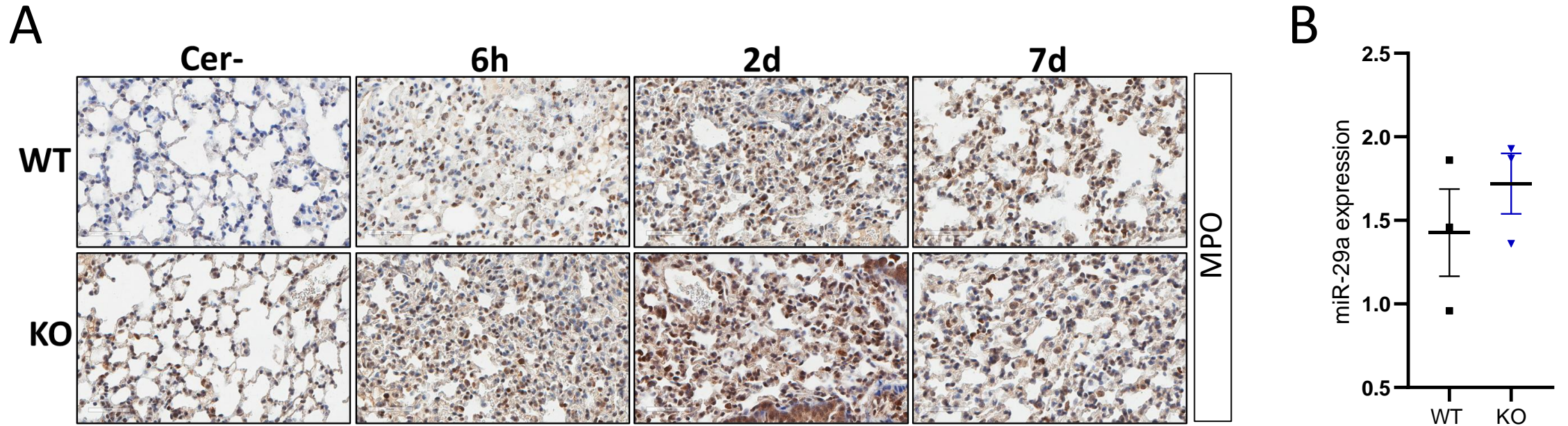


Supplemental Figure 1. Pancreatic sections of WT and KO mice at 1, 3 and 12 months of age immunostained with antibodies against **(A)** amylase (green)/ counterstained with DAPI (blue), **(B)** insulin (green)/counterstained with DAPI (blue), and **(C)** CK19 (green), photographed at 40X objective (scale bar= 62.2 μm).



Supplemental Figure 2. (A) qPCR analysis of miR-29a expression in pancreata of WT mice 72h post final L-arginine injection. **(B)** Representative H&E images of pancreatic sections of WT and KO mice treated with PBS or L-arginine at 72h post L-arginine administration (scale bars = 40 μ m). **(C)** Quantification of inflammatory cell infiltration from H&E-stained pancreatic sections of L-arginine dosed WT and miR-29a/b1 KO mice 72hrs post final injection. Graphs represent Mean \pm SEM; n=3 mice/group/timepoint, * p < 0.05, 2-tailed Student's t test.



Supplemental Figure 3. (A) Representative images for MPO staining in the lungs of saline (Cer-) or caerulein dosed WT and KO mice at the indicated time-points (Scale bars = 50 μ m). **(B)** miR-29a expression in the lungs of WT and miR-29a KO mice assessed by qPCR analysis. Results represent Mean \pm SEM; n= 3mice/group/timepoint, 2-tailed Student's *t* test.

Supplemental Table 1. Summary of clinical characteristics of human subjects.¹

	Normal	Chronic Pancreatitis (CP)
Pancreas		
Normal	4	0
Pancreatitis	0	4
Sex		
Male	2	3
Female	2	1
Average age at procedure	68.75	66.75
Age Range	61-77	56-76
Race		
Non-Hispanic, White	4	4

¹ Source: Indiana University Simon Cancer Center Tissue Bank and Department of Pathology

Supplemental Table 2. Demographic and clinical characteristics of normal and human chronic pancreatitis patients.¹

ID	Sex	Birth Year	Ethnicity	Race	Procedure Year	Histological Characteristics of pancreas
NP-1	F	1932	Non-Hispanic	White	2006	100% normal pancreas
NP-2	M	1947	Non-Hispanic	White	2010	100% normal pancreas
NP-3	F	1951	Non-Hispanic	White	2012	100% normal pancreas
NP-4	M	1936	Non-Hispanic	White	2013	100% normal pancreas
CP-1	M	1961	Non-Hispanic	White	2010	100% pancreatitis
CP-2	M	1949	Non-Hispanic	White	2010	100% pancreatitis
CP-3	M	1955	Non-Hispanic	White	2011	100% pancreatitis
CP-4	F	1935	Non-Hispanic	White	2011	100% pancreatitis

¹ Source: Indiana University Simon Cancer Center Tissue Bank and Department of Pathology

Supplemental Table 3. miR-29a/b1 KO Strategy using CRISPR/CAS9.

Long ssODN with offset homology:

Color codes: Blue: 5'-homology; Green: loxP; Purple: EcoR1; Black: Floxed miR-29a/b1 genomic region; Red: 3'-homology.

```

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Genomic sequence of miR-29a/b1 (yellow highlight)

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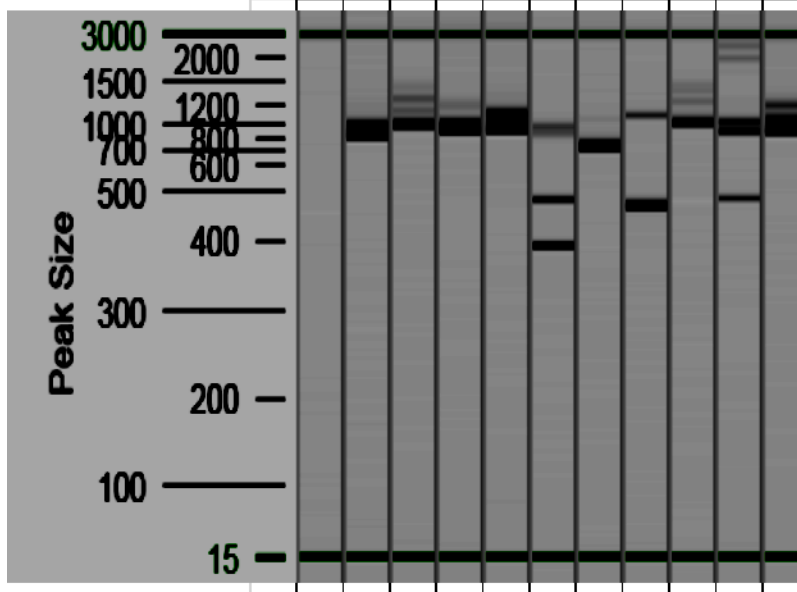
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Cut

Supplemental Table 4. PCR confirmation of founder line with expected deletion.

Sample	Exdel	Seq candidate
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CR1646-2	NO	
CR1646-3	NO	
CR1646-4	YES	
CR1646-5	NO	
CR1646-6	YES	YES
CR1646-7	NO	
CR1646-8	YES	
CR1646-9	NO	

Sample ID	Assay	Well
NTC	Mir29a/Mir29b-1	A:1
WT	5529	A:2
CR1646-1	5F/3R	A:3
CR1646-2		A:4
CR1646-3		A:5
CR1646-4		A:6
CR1646-5		A:7
CR1646-6		A:8
CR1646-7		A:9
CR1646-8		A:10
CR1646-9		A:11



Supplemental Table 5. Sequence confirmation of founder line with expected homologous recombination.

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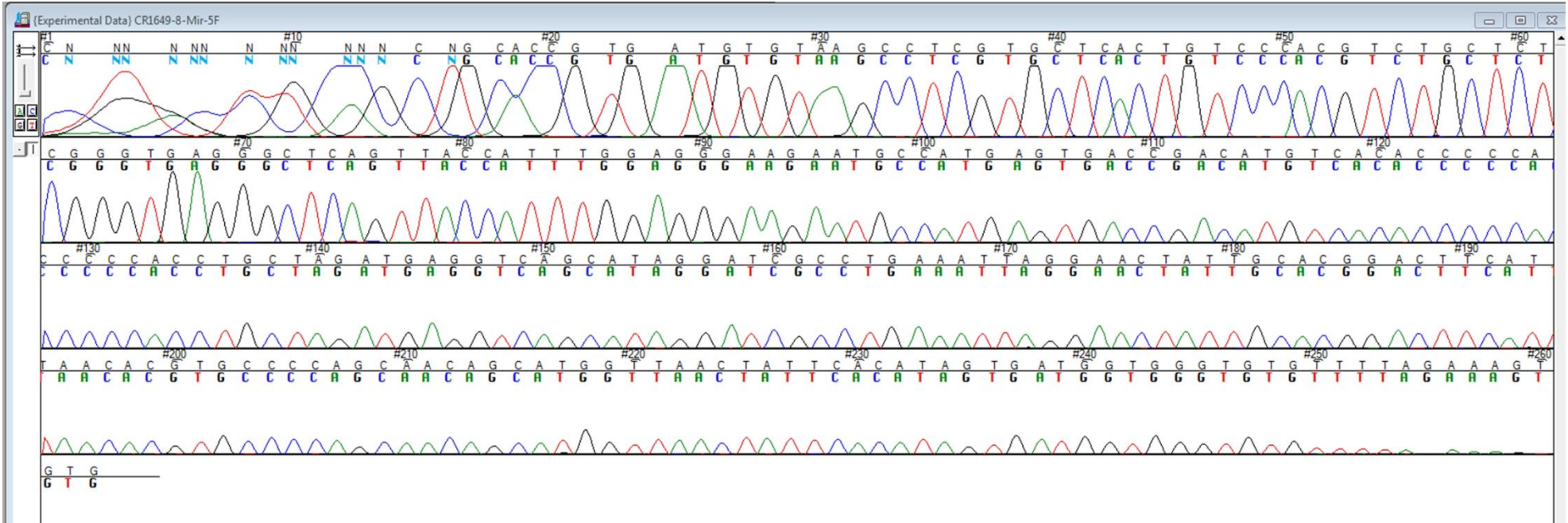
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CR1649-8

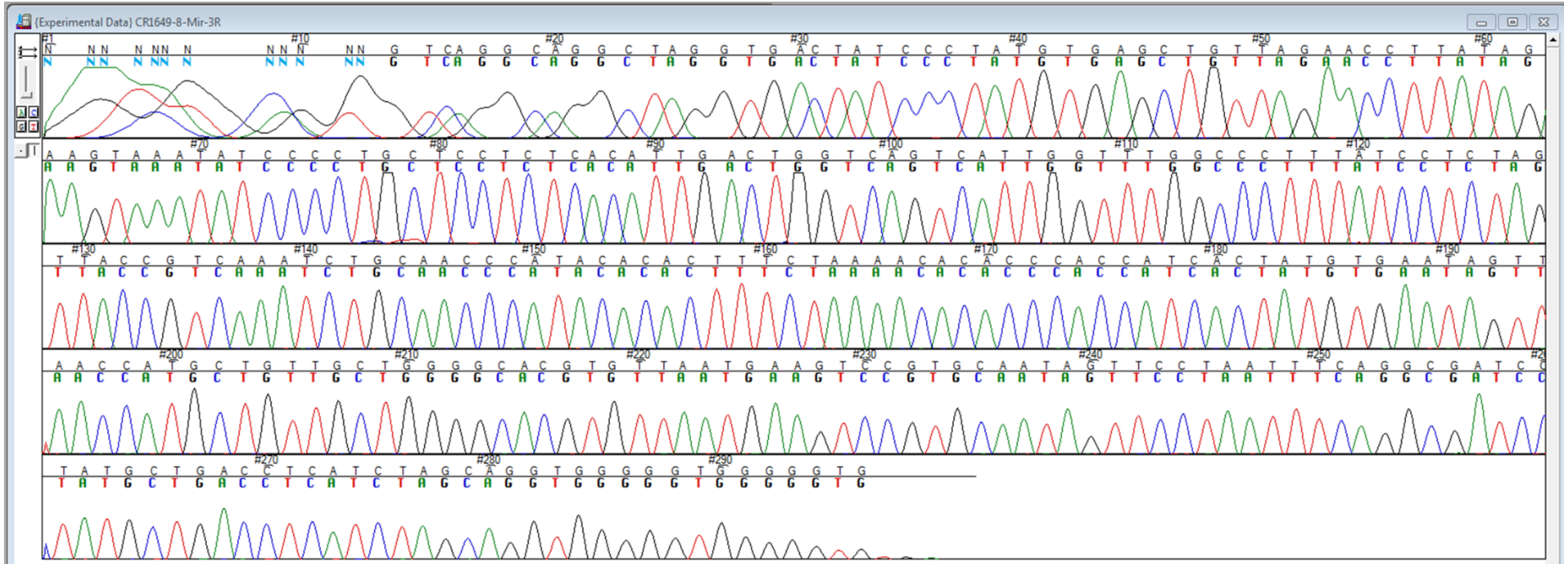
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Reverse:

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