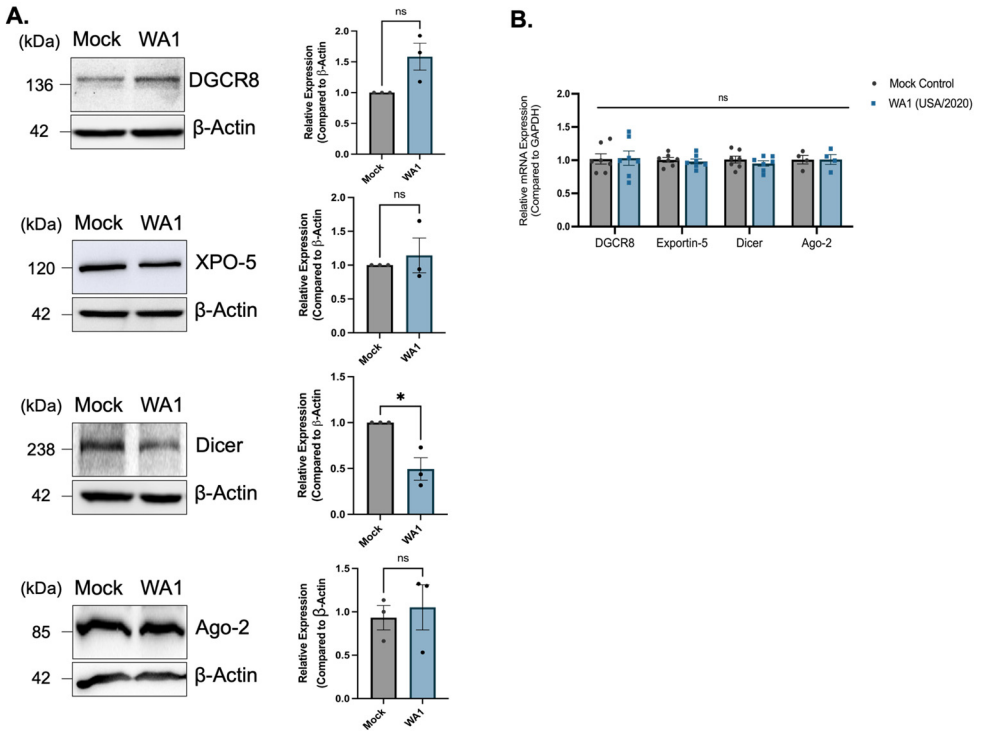
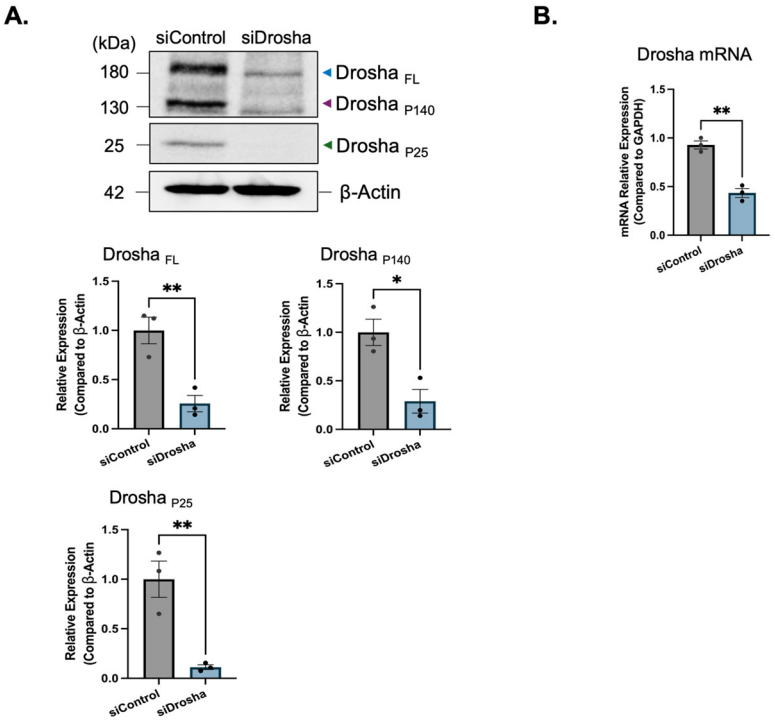



**Supplementary Figure S1.** The expression of key proteins within the miRNA biogenesis pathway, at the mRNA and protein level, following SARS-CoV-2 infection. (A) Western Blot of four proteins within the miRNA biogenesis pathway in mock and SARS-CoV-2-infected (MOI 1.0) NuLi-1 cells. Dicer expression is significantly decreased following infection. (B) qRT-PCR of the mRNA transcripts of four key proteins within the miRNA biogenesis pathway. Following infection there is no significant change in expression at the transcript level. Data are normalized to Beta-Actin or GAPDH and are presented as mean fold change ± SD from at least three independent experiments. The statistical significance between groups was determined using a two-tailed students T test, or two-way ANOVA followed by Tukey's post hoc test (ns, not significant; *$p < 0.05$).




**Supplementary Figure S2.** siRNA knockdown confirmation of Drosha p140 and p25 isoforms. (A) Western blot validation of Drosha isoforms by siRNA knockdown. NuLi-1 cells were transfected with 100pmol Drosha-specific siRNA (siDrosha) or a non-targeting control siRNA (siControl). Western blotting shows a marked reduction in both FL and cleavage product (P140 and P25) bands in siDrosha-treated cells, confirming their identity as Drosha-specific. (B) qRT-PCR quantification showed a significant reduction in Drosha mRNA expression. Data are normalized to Beta-Actin or GAPDH and are presented as mean fold change ± SD from at least three independent experiments. The statistical significance between groups was determined using a two-tailed students T test (*$p < 0.05$; **$p < 0.01$).

**Supplementary Table S1.** Cell lines used in this study.

| Cell Line | Cell Type | Sex | Modifications |
|---|---|---|---|
| NuLi-1 | Bronchial; *Homo sapiens* | Male | Normal; hTERT |
| VERO E6-hACE-2-hTMPRSS2 | Kidney; *Ceropithecus aethiops* | - | hACE-2/hTMPRSS-2 |
| MRC-5 | Lung fibroblast; *Homo sapiens* | Male | Normal; primary |
| HCT-116 (WT) | Colorectal Carcinoma; *Homo sapiens* | Male | Ras codon-13 mutation; |
| HCT-116 (Drosha KO) | Colorectal Carcinoma; *Homo sapiens* | Male | Mutated Ras; Drosha CRISPR |

**Supplementary Table S2.** Antibodies used in this study.

| Name of Antibody | Manufacturer; Catalogue # | Species; Clonality | Dilution; Application |
|---|---|---|---|
| Drosha Antibody #1 | CST; 3364S | Rabbit; Monoclonal | 1:1000 (WB) 1:50 (ICC) |
| Drosha Antibody #2 | Santa Cruz; SC-393591 | Mouse; Monoclonal | 1:1000 (WB) |
| Drosha Antibody #3 | Abcam; AB12286 | Rabbit Monoclonal | 1:1000 (WB) 1:50 (ICC) |
| Argonaute-2 | Sigma; SAB4200085 | Rat; Monoclonal | 1:1000 (WB) |
| DGCR8 | CST; D78E4 | Rabbit; Monoclonal | 1:1000 (WB) |
| Dicer | Santa Cruz; SC-136979 | Mouse Monoclonal | 1:1000 (WB) |
| Exportin-5 | Santa Cruz; SC-271036 | Mouse Monoclonal | 1:1000 (WB) |
| Beta Actin | Santa Cruz; SC-47778 | Mouse Monoclonal | 1:1000 (WB) |
| HRP-Linked Anti-Rabbit | CST; 5127S | Mouse Monoclonal | 1:1000 (WB) |
| HRP-Linked Anti-Mouse | CST; 58802 | Rabbit; Monoclonal | 1:1000 (WB) |
| HRP-Linked Anti-Rat | CST; 7077S | Goat; Monoclonal | 1:1000 (WB) |
| AlexaFluor 488 | CST; 4412S | Goat; Monoclonal | 1:1000 (ICC) |

**Supplementary Table S3.** q/RT-PCR primer sets used in this study.

| Primer Name | Sequence (5′ – 3′) |
|---|---|
| GAPDH FWD | CCACTCCTCCACCTTTGAC |
| GAPDH REV | ACCCTGTTGCTGTAGCCA |
| SARS-CoV-2 ORF1a FWD | TTCAGTTGACTTCGCAGTGG |
| SARS-CoV-2 ORF1a REV | GGACGGGTTTGAGTTTTTCA |
| SARS-CoV-2 N Gene FWD | ATGCTGCAATCGTGCTACAA |
| SARS-CoV-2 N Gene REV | GACTGCCGCCTCTGCTC |
| SARS-CoV-2 5′UTR FWD | ACTGTCGTTGACAGGACACG |
| SARS-CoV-2 5′UTR REV | AACACGGACGAAACCGTAAG |
| HCoV-229E N Gene FWD | TCAATCTCGGAATCCTTCAAGT |
| HCoV-229E N Gene REV | AGGCTTAGGAGTACCCGTTTTC |
| HCoV-229E 5′UTR FWD | CTTTGATGCTGGAGTCGTAGTG |
| HCoV-229E 5′UTR REV | GGCGTTTGTAGAATGGAATCTC |
| HCoV-OC43 N Gene FWD | AGGCTATTCCGACTAGGTTTCC |
| HCoV-OC43 N Gene REV | TACTACGCGATCCTGCACTAGA |
| SINV N Gene FWD | GGTTCCTACCACAGCGACGAT |
| SINV N Gene REV | TGATACTGGTGCTCGGAAAACA |
| IFN-β FWD | AAGCTCCTGTGGCAATTGAATG |
| IFN-β REV | TCTCATAGATGGTCAATGCGGC |
| CXCL10 FWD | GCTCTACTGAGGTGCTATGTTC |
| CXCL10 REV | GGAGGATGGCAGTGGAAGTC |
| Drosha AS27a FWD | TGTGCATCTTGATTTGCATCTG |
| Drosha AS27a REV | GGAGAAGTTTCAATAAGTTGTCG |
| Drosha AS32a FWD | TGGTGTTGAAAATGGCAAGAC |
| Drosha AS32a REV | TGGAAAGAAGCAGACATTCAT |
| Drosha FL (ORF) FWD | TCACGCCTTGGCCAAGATGAC |
| Drosha FL (ORF) REV | GCTGATTCTGAACAATGGCAG |
| Drosha (Exons 1-3) FWD | GAAGAGTTTTCCCTCCCTTGG |
| Drosha (Exons 1-3) REV | CACATCCCCGGGAAAAGC |
| Drosha (Exons 5-8) FWD | CGACAGGAGAAGACAAGACAGC |
| Drosha (Exons 5-8) REV | GTGCATCCAGCAGGTTCAGG |
| Drosha (Exons 31-35) FWD | CAGCGCTGTACATTGATAAGGA |
| Drosha (Exons 31-35) REV | ATCTGGCTCTCTCTCTTGATGC |
| Drosha Tile 1 (199-1447nt) FWD | GGGGATGTGAAGGATACAGAAA |
| Drosha Tile 1 (199-1447nt) REV | GCTCTCTTCTTCTCCCTACTTGG |
| Drosha Tile 2 (1137-2524nt) FWD | AGACAAGACAGCCGGTACAGAT |
| Drosha Tile 2 (1137-2524nt) REV | ATATTGGCAATCTCCTCCTCAG |
| Drosha Tile 3 (2161-3615nt) FWD | TTGAAGGATTTTCTATGTTTGCAC |
| Drosha Tile 3 (2161-3615nt) REV | GTGGGTGGAGAGGATAATTGAG |
| Drosha Tile 4 (2912-4460nt) FWD | CATCCGTTCTGATGTCTGTCA |
| Drosha Tile 4 (2912-4460nt) REV | ATCTGGCTCTCTCTCTTGATGC |
| DGCR8 FWD | GCCTCCTCATAGACCCGAAC |
| DGCR8 REV | CCACTGACAGGGCTAAGGAG |
| Exportin-5 FWD | CAACTCCACCCAGCGCTAC |
| Exportin-5 REV | TGACAACGTGTTCCAGGATCT |
| Argonaute-2 FWD | TTTTGAGACGATCCAGGCCC |
| Argonaute-2 REV | TTTTCCAGAGAGAAGGCCGG |
| Dicer FWD | TACCCGTGCAACCAACTACC |
| Dicer REV | GCATTACGGCCATCACAGGA |

**Supplementary Table S4.** Sequences of siRNAs used in this study.

| siRNA | Targeted Region | Strand | Strand | Sequence (3′ – 5′) |
|---|---|---|---|---|
| siDrosha | 3′UTR | Guide | Sense | C.A.U.U.A.G.A.A.U.A.G.G.A.G.A.G.A.A.A.U.U |
| | | Passenger | Antisense | U.U.U.C.U.C.U.C.C.U.A.U.U.C.U.A.A.U.G.U.U |