SUPPLEMENTARY INFORMATION

Supplemental Figure legends

Supplemental Figure 1. Correlation between *miR-124* levels and individual hypoxia/HIF signature targets. (a) Gene Set Enrichment Analysis showing a negative correlation between a hypoxia gene signature and *miR-124* levels. Red dots = *miR-124* levels for each individual TCGA patient (log scale). Heatmap shows individual levels of each patient sample. Orange = high level of mRNA expression. Blue = low level of mRNA expression. (b) Laser-Capture microdissection images before (left) and after the dissection (right). Red line indicates necrotic sample that was discarded as waste. Green line indicates perinecrotic area that was collected after disposal of necrotic sample.

This supplemental figure refers to Figure 1 in the manuscript.

Supplemental Figure 2. *miR-124* elicits increased cell death under stress. (a) U373-MG cells transfected with NT or *miR-124* mimics and grown in complete media, serum-free media, 0.5% O2, or a combination of serum-free media and 0.5% O_2 and imaged for viability. **(b)** Immunoblot showing increased levels of cleaved PARP upon *miR-124* + tunicamycin treatment.

This supplemental figure refers to Figure 2 in the manuscript.

Supplemental Figure 3. *miR-124* and target levels measured from individual patient samples. (a) *miR-124,* (**b)** *TEAD1*, **(c)** *SERP1* and **(d**) *MAPK14* expression analyzed by qRT-PCR from individual formalin-fixed, paraffin embedded patient samples. GBM sample number = 30. Normal brain sample number = 10.

This supplemental figure refers to Figure 4 in the manuscript.

Supplemental Figure 4. Role of *miR-124* and targets in modulating cellular proliferation *in vitro*. (a) Cell count of U87-MG cells expressing *miR-124* or a control scrambled miRNA. Cell count of U87-MG cells expressing control or **(b)** *TEAD1* shRNA, **(c)** *MAPK14* shRNA and **(d)** *SERP1* shRNA.

This supplemental figure refers to Figure 5 in the manuscript.

Supplemental Figure 5. Determination of lentiviral and doxycycline-inducible systems *in vitro*. (a) Flow cytometry analysis of Green Fluorescent Protein expression in Control-Dox expressing and 124-Dox expressing U87-MG cells. Time lapse of doxycycline administration up to 72 hours. FSC = Forward Scattering; Dox = Doxycycline. **(b)** qRT-PCR measuring *miR-124* levels upon doxycycline induction for a 72 hour time course. **(c)** GFP levels in control/pre-miR-124 transduced U87-MG cells, 48 hours after transduction.

This supplemental Figure refers to Figures 5 and 6 in the manuscript.

Table S1. Oligo primer sequences of seed regions of partial 3'UTRs for *TEAD1*, *SERP1* and *MAPK14*.

hSERP1 WT1 F

GGCACTAGTaggtttcttc atgagtcatt ccaagttttc tagtccatac cacagtgcct tgcaaaaaac accacatgaa taaagcaataAAGCTTGGC

hSERP1 WT1 R

GCCAAGCTTtattgctttattcatgtggtgttttttgcaaggcactgtggtatggactagaaaacttggaatgactcatgaagaaacctACTAGTGCC

hSERP1 MUT1 F

GGCACTAGTaggtttcttc atgagtcatt ccaagttttc tagtccatac caca GCCAGCA gcaaaaaac accacatgaa taaagcaataAAGCTTGGC

hSERP1 MUT1 R

GCCAAGCTTtattgctttattcatgtggtgttttttgcTGCTGGCtgtggtatggactagaaaacttggaatgactcatgaagaaacctACTAGTGCC

hSERP1 WT2 F

GGCACTAGTttaactaatt ctgttttatg gttgtgctaa attcatagca ggtgccttat tctttgcttt tagtcaaacc attccatatcAAGCTTGGC

hSERP1 WT2 R

GCCAAGCTTgatatggaatggtttgactaaaagcaaagaataaggcacctgctatgaatttagcacaaccataaaacagaattagttaaACTAGTGCC

hSERP1 MUT 2 F

GGCACTAGTttaactaatt ctgttttatg gttgtgctaa attcatagca g GCCAGCAGt tctttgcttt tagtcaaacc attccatatcAAGCTTGGC

hSERP1 MUT2 R

GCCAAGCTTgatatggaatggtttgactaaaagcaaagaaCTGCTGGCctgctatgaatttagcacaaccataaaacagaattagttaaACTA

GTGCC

hTEAD1 WT1 F

GGCACTAGTtgttcccgta agcagtgcct tagtaatacc ttagtcatgc cgccagcctt ttcttacaccAAGCTTGGC

hTEAD1 WT1 R

GCCAAGCTTggtgtaagaaaaggctggcggcatgactaaggtattactaaggcactgcttacgggaacaACTAGTGCC

hTEAD1 MUT1 F

GGCACTAGTtgttcccgta agcaGCCAGC AGgtaatacc ttagtcatgc cgccagcctt ttcttacaccAAGCTTGGC

hTEAD1 MUT1 R

GCCAAGCTTggtgtaagaaaaggctggcggcatgactaaggtattacCTGCTGGCtgcttacgggaacaACTAGTGCC

hTEAD1 WT2 F

GGCACTAGTttctgcactc tagcatgaaa gtgcctttgg tttgagattc cagcttagaa aagtgctgccAAGCTTGGC

hTEAD1 WT2 R

GCCAAGCTTggcagcacttttctaagctggaatctcaaaccaaaggcactttcatgctagagtgcagaaACTAGTGCC

hTEAD1 MUT2 F

GGCACTAGTttctgcactc tagcatgaaa GCCAGCAtgg tttgagattc cagcttagaa aagtgctgccAAGCTTGGC

hTEAD1 MUT2 R

GCCAAGCTTggcagcacttttctaagctggaatctcaaaccaTGCTGGCtttcatgctagagtgcagaaACTAGTGCC

hP38 WT1 F

GGCACTAGT tatggttctc agatcttgac agtatatttg aaactgtaaa tatgtttgtg ccttaaaagg agagaagaaa gtgtagatag

AAGCTTGGC

hP38 WT1 R

GCCAAGCTTctatctacactttcttctctccttttaaggcacaaacatatttacagtttcaaatatactgtcaagatctgagaaccataACTAGTGCC

hP38 MUT1 F

GGCACTAGT tatggttctc agatcttgac agtatatttg aaactgtaaa tatgtttGCC AGCAGaaagg agagaagaaa gtgtagatag

AAGCTTGGC

hP38 MUT1 R

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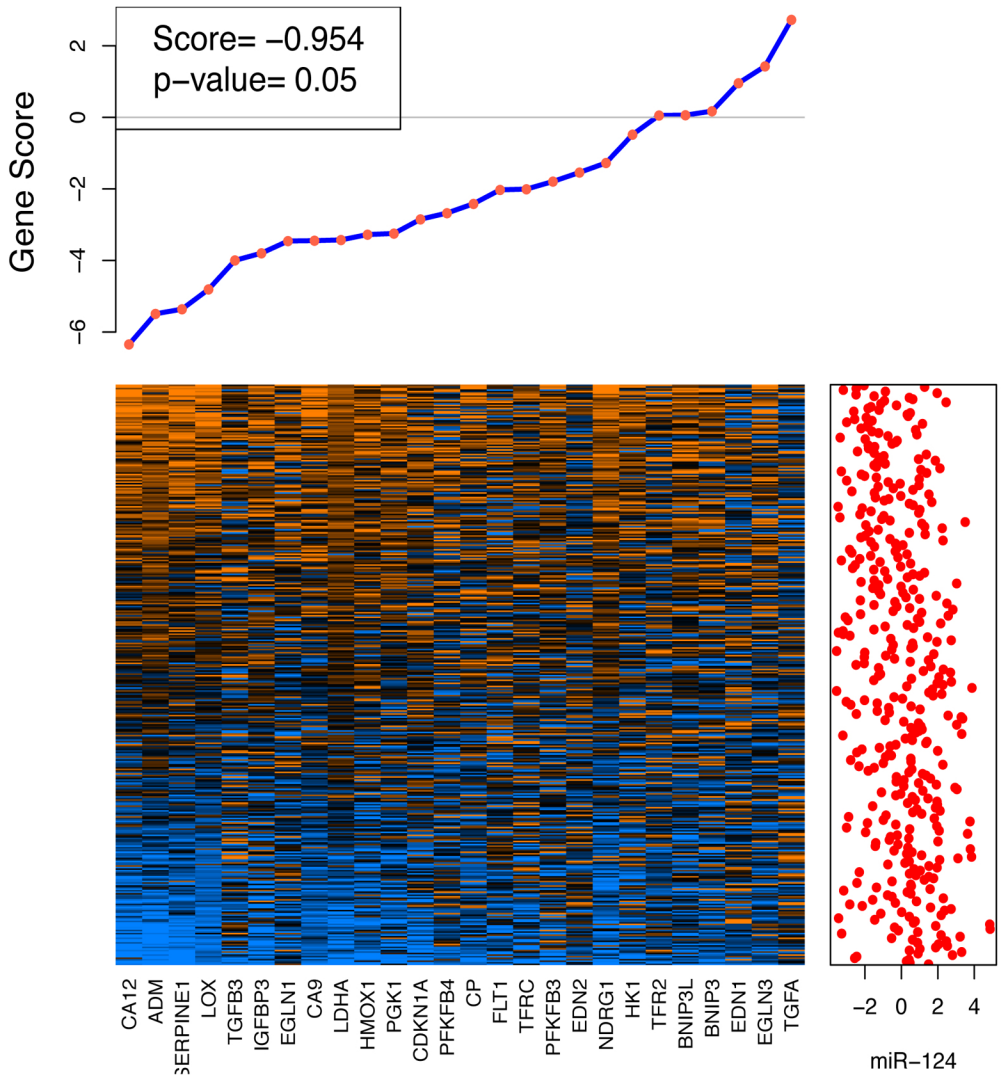
C

a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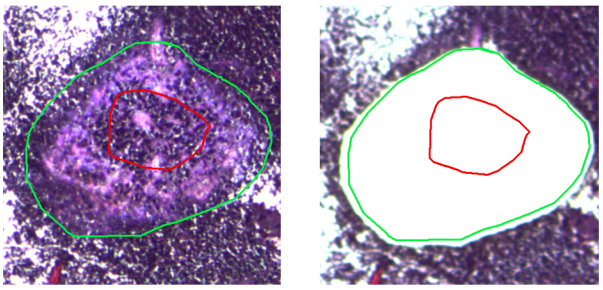
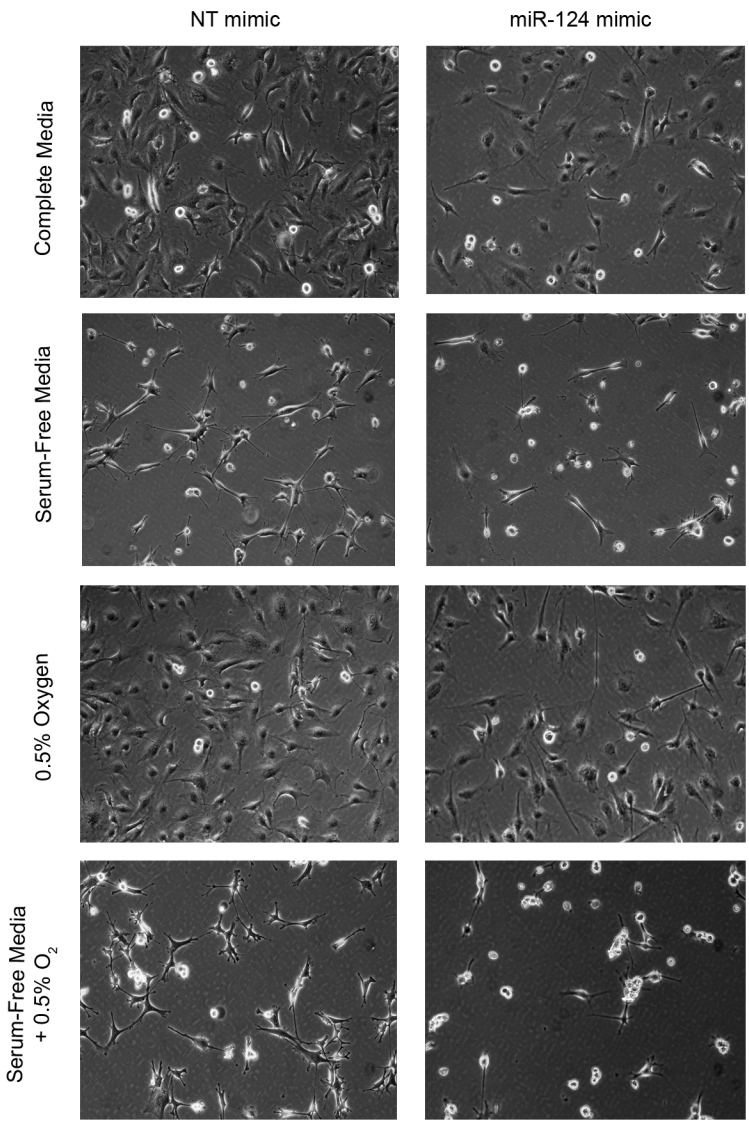
p−value= 0.05
Gene Score
2
0
−2
−4
−6
CA12
ADM
SERPINE1
LOX
TGFB3
IGFBP3
EGLN1
CA9
LDHA
HMOX1
PGK1
CDKN1A
PFKFB4
CP
FLT1
TFRC
PFKFB3
EDN2
NDRG1
HK1
TFR2
BNIP3L
BNIP3
EDN1
EGLN3
TGFA
−2
0
2
4
miR−124

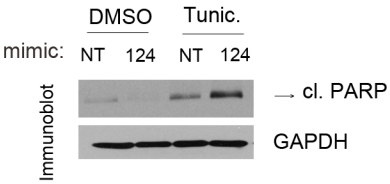
b



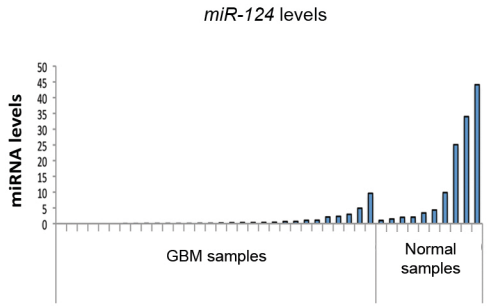
a


NT mimic
miR-124 mimic
Complete Media
Serum-Free Media
0.5% Oxygen
Serum-Free Media
+ 0.5% O2
U373 - MG cells

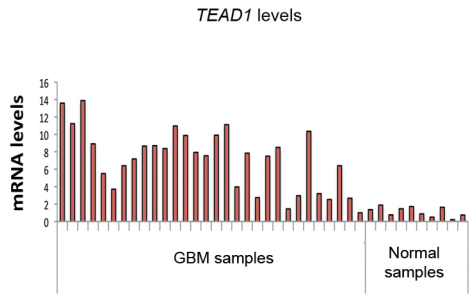
b


DMSO
Tunic.
mimic:
NT
124
NT
124
Immunoblot
cl. PARP
GAPDH

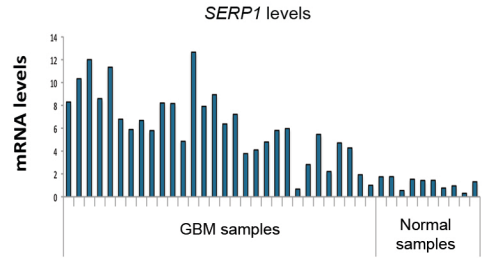
a


miR-124 levels
miRNA levels
50
45
40
35
30
25
20
15
10
5
0
GBM samples
Normal samples

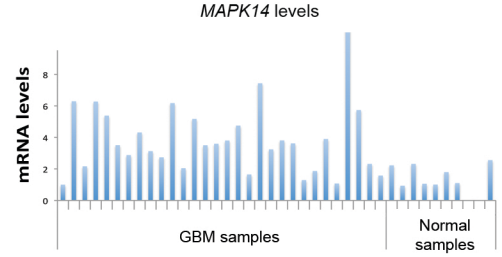
b

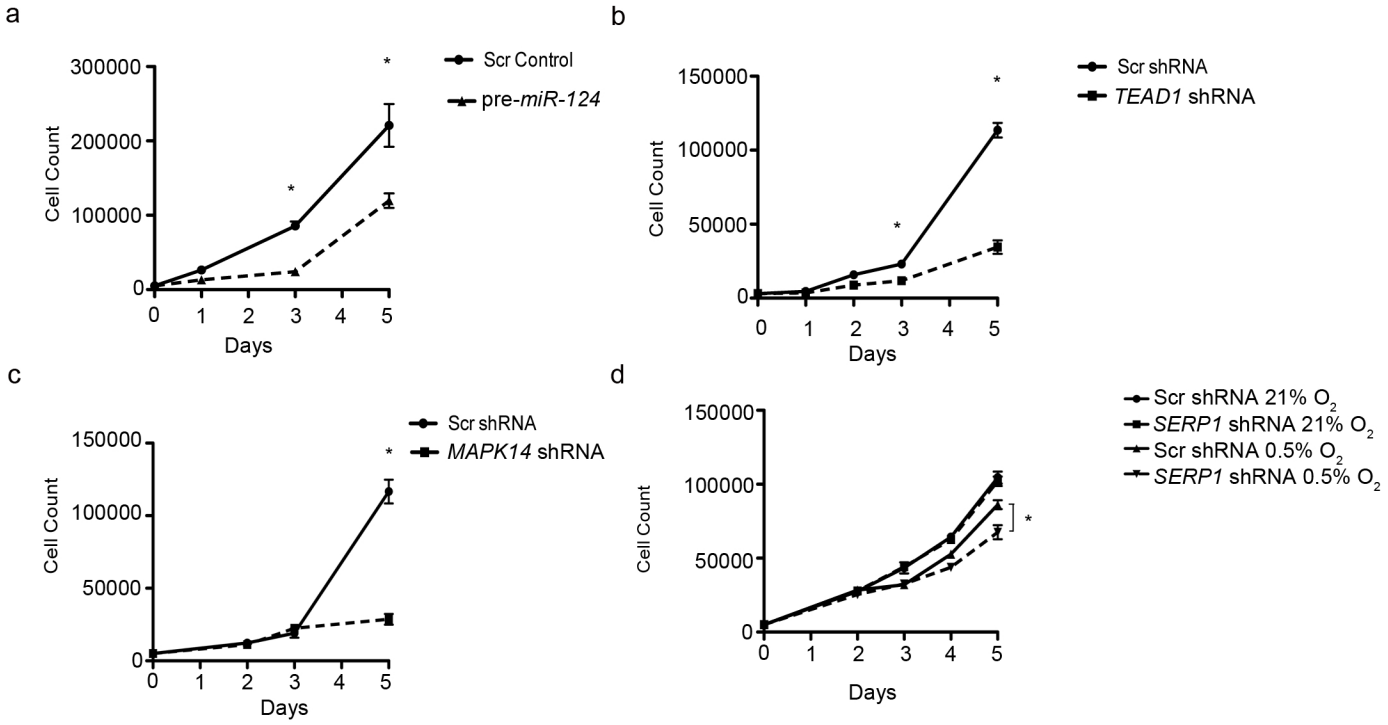

TEAD1 levels
mRNA levels
16
14
12
10
8
6
4
2
0
GBM samples
Normal samples

c

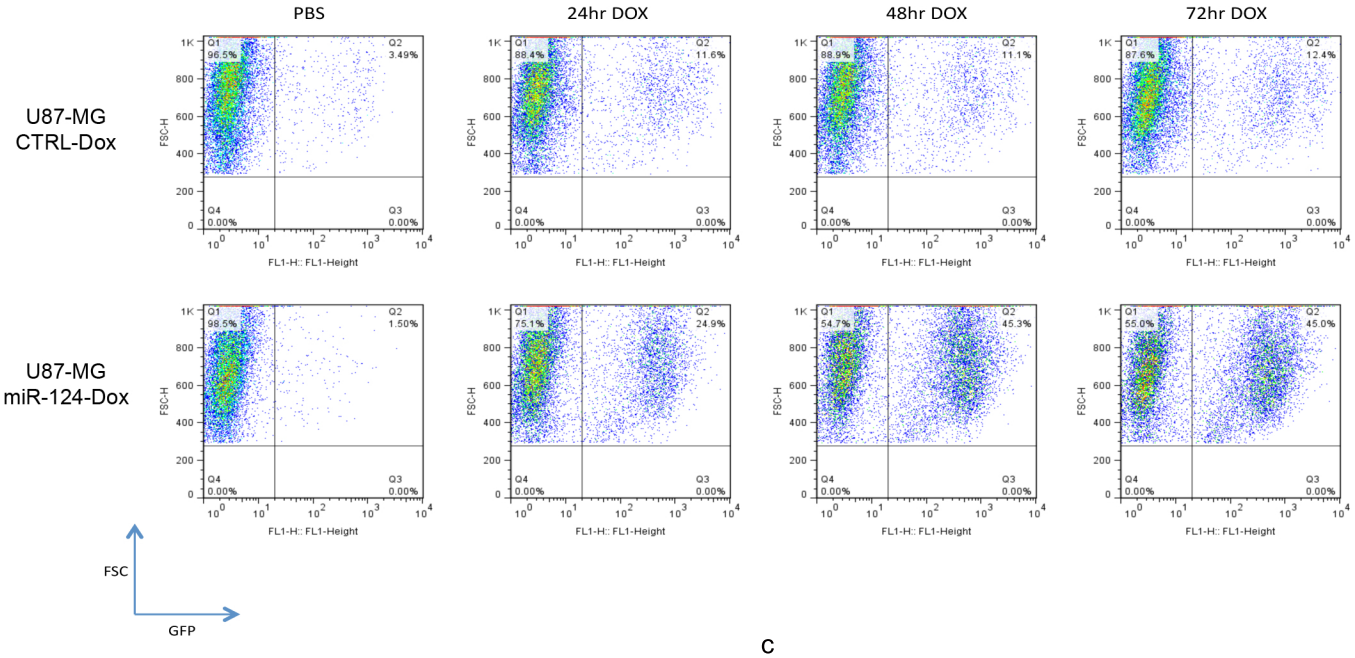

SERP1 levels
mRNA levels
14
12
10
8
6
4
2
0
GBM samples
Normal samples

d

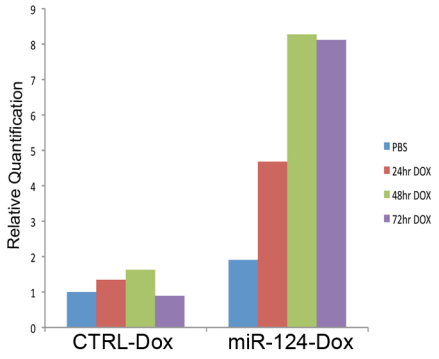

MAPK14 levels
mRNA levels
8
6
4
2
0
GBM samples
Normal samples


a
300000
200000
100000
0
Cell Count
0 1 2 3 4 5
Days
*
*
Scr Control
pre-miR-124
b
150000
100000
50000
0
Cell Count
0 1 2 3 4 5
Days
*
*
Scr shRNA
TEAD1 shRNA
c
150000
100000
50000
0
Cell Count
0 1 2 3 4 5
Days
*
Scr shRNA
MAPK14 shRNA
d
150000
100000
50000
0
Cell Count
0 1 2 3 4 5
Days
*
Scr shRNA 21% O2
SERP1 shRNA 21% O2
Scr shRNA 0.5% O2
SERP1 shRNA 0.5% O2

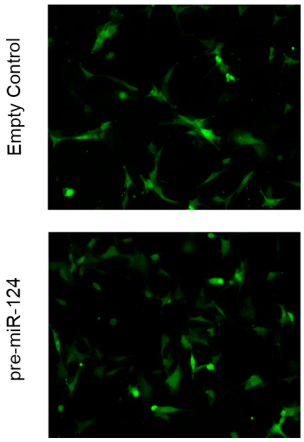
a


PBS
24hr DOX
48hr DOX
72hr DOX
U87-MG CTRL-Dox
U87-MG miR-124-Dox
Q1 96.5%
Q2 3.49%
Q4 0.00%
Q3 0.00%
Q1 88.4%
Q2 11.6%
Q1 88.9%
Q2 11.1%
Q1 87.6%
Q2 12.4%
Q1 98.5%
Q2 1.50%
Q1 75.1%
Q2 24.9%
Q1 54.7%
Q2 45.3%
Q1 55.0%
Q2 45.0%
FSC-H
FL1-H:: FL1-Height
FSC
GFP

b


Relative Quantification
PBS
24hr DOX
48hr DOX
72hr DOX
CTRL-Dox
miR-124-Dox

c


Empty Control
pre-miR-124