MicroRNA in combination with HER2-targeting drugs reduces breast cancer cell viability *in vitro*

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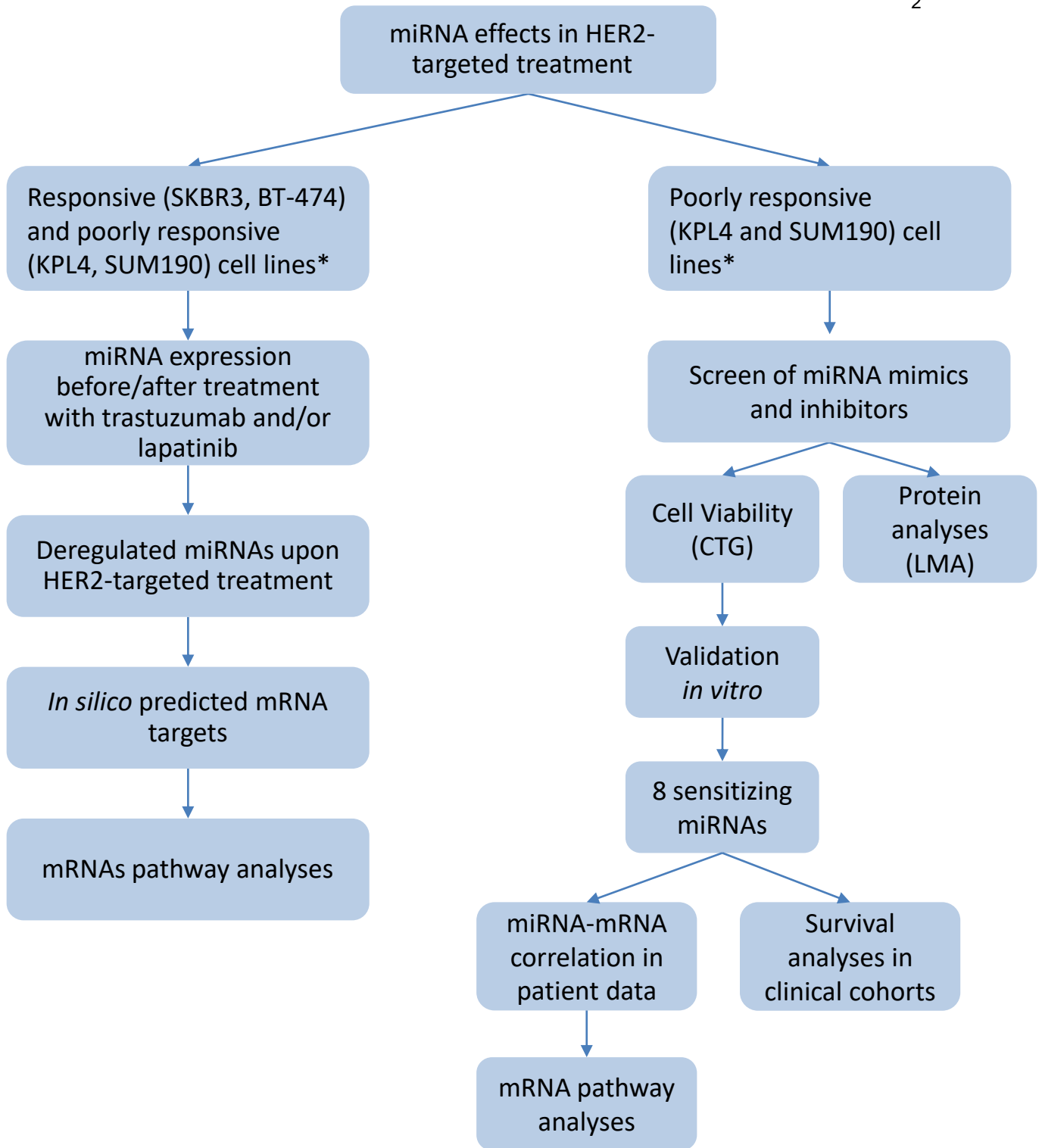[7]Institute for Medical Biology, Faculty of Health Sciences, UiT – The Arctic University of Norway.

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Supplementary Figure S1

*Response to targeted treatment (trastuzumab and lapatinib).
 CTG = CellTiter-Glo. LMA = Protein Lysate Microarray

Supplementary Figure S1: Flowchart illustrating the main topics covered in the paper.
On the left side, the effects of HER2-targeted treatment on endogenous miRNA expression levels in HER2+ breast cancer cells are studied. On the right side, the effects of combinatorial treatment with HER2-targeted drugs and transfection of miRNAs in poorly responsive cell lines are explored.

Supplementary Figure S2: miRNA expression before and after targeted treatment in four cell lines (SKBR3, BT-474, KPL4, SUM190PT)

a
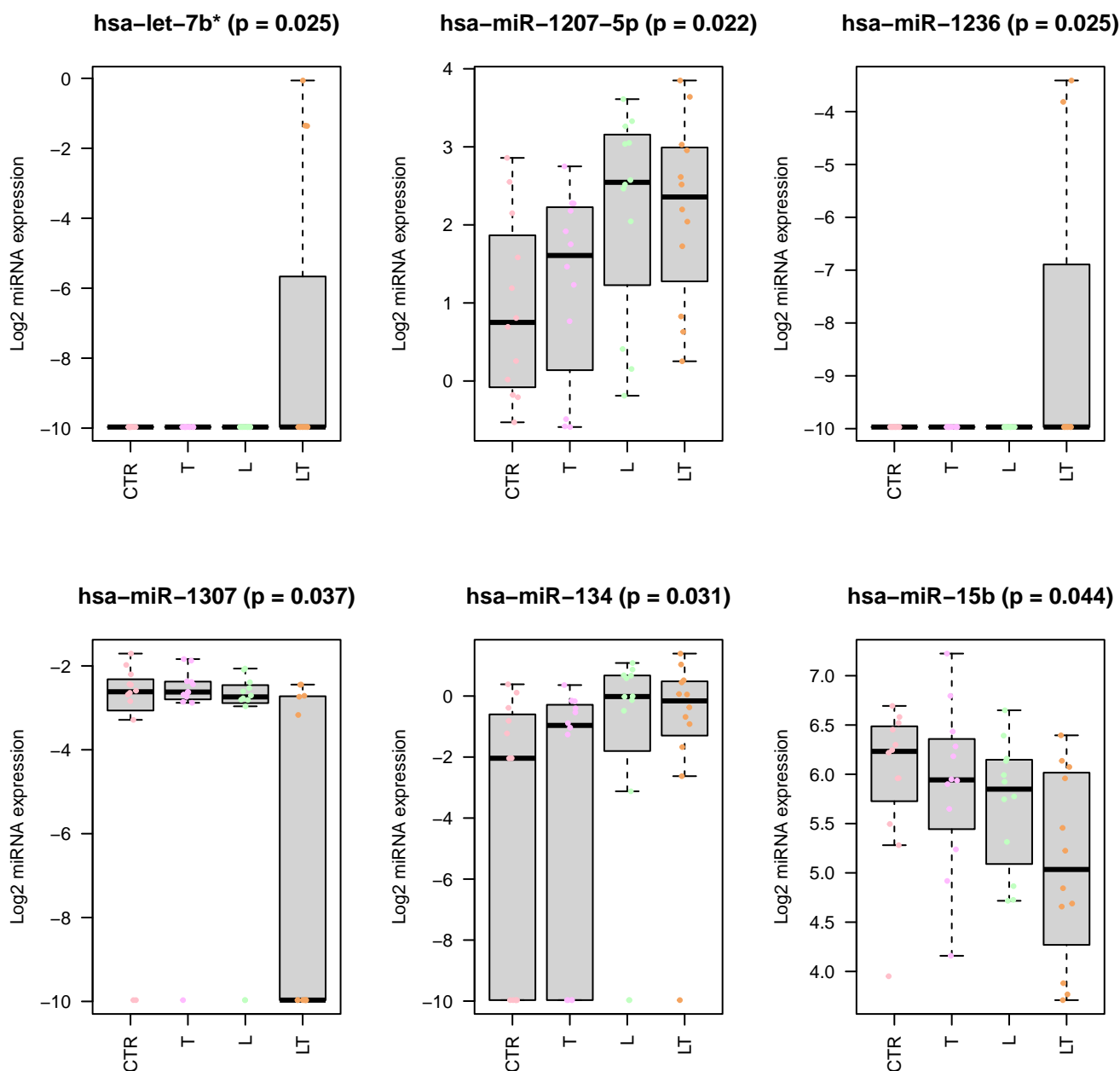
Supplementary Figure S2: miRNA expression after targeted treatment.
The cells were treated with trastuzumab (10 μg/mL) or lapatinib (100 nM) alone and in combination for 24 hours before total RNA was extracted, and miRNA levels were measured using a one-color microarray Human miRNA Microarray Kit and scanned on Agilent Scanner G2565B. miRNAs with significant (Kruskal-Wallis test p-value < 0.05) expression regulations between any treatment groups are presented. The plots are presented for a-b: four HER2+ cell lines pooled together (SKBR3, BT-474, KPL4, SUM190PT); c-h: cell lines responsive to trastuzumab and lapatinib (SKBR3 and BT-474); and i: poorly responsive cell lines (KPL4 and SUM190PT). T = trastuzumab, L = lapatinib, TL = trastuzumab and lapatinib.
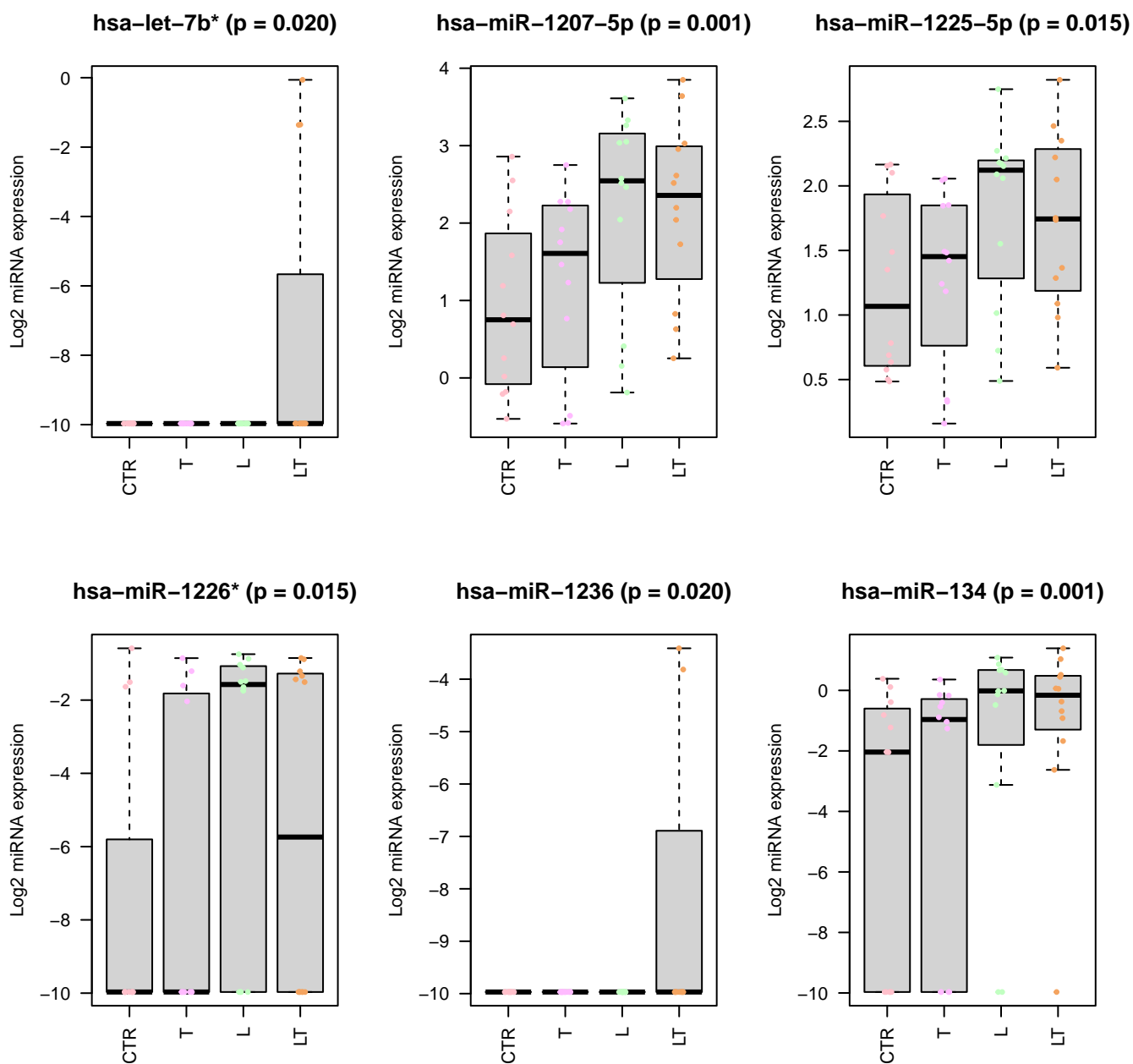
Supplementary Figure S2: miRNA expression before and after targeted treatment in four cell lines (SKBR3, BT-474, KPL4, SUM190PT)
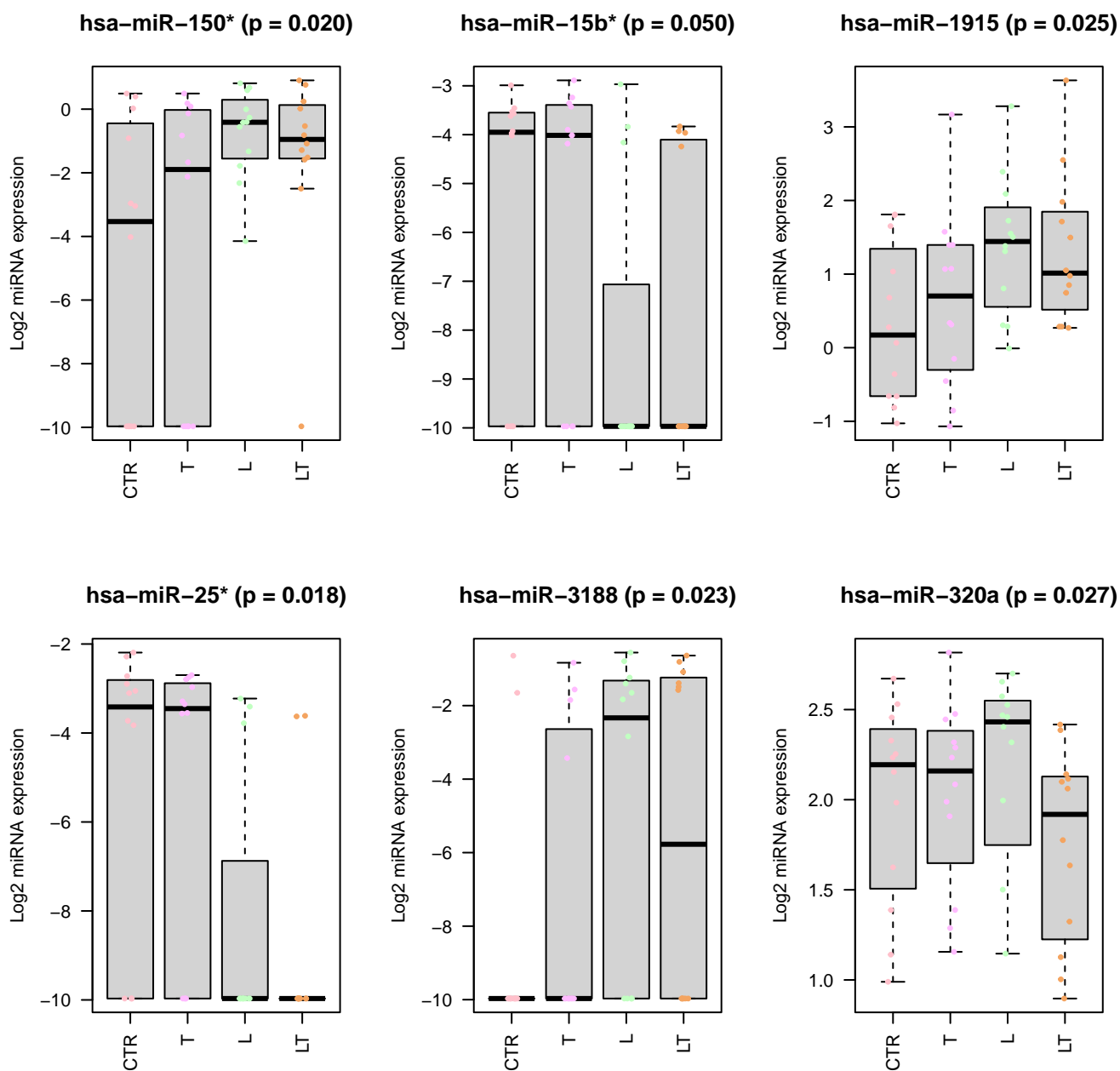
b
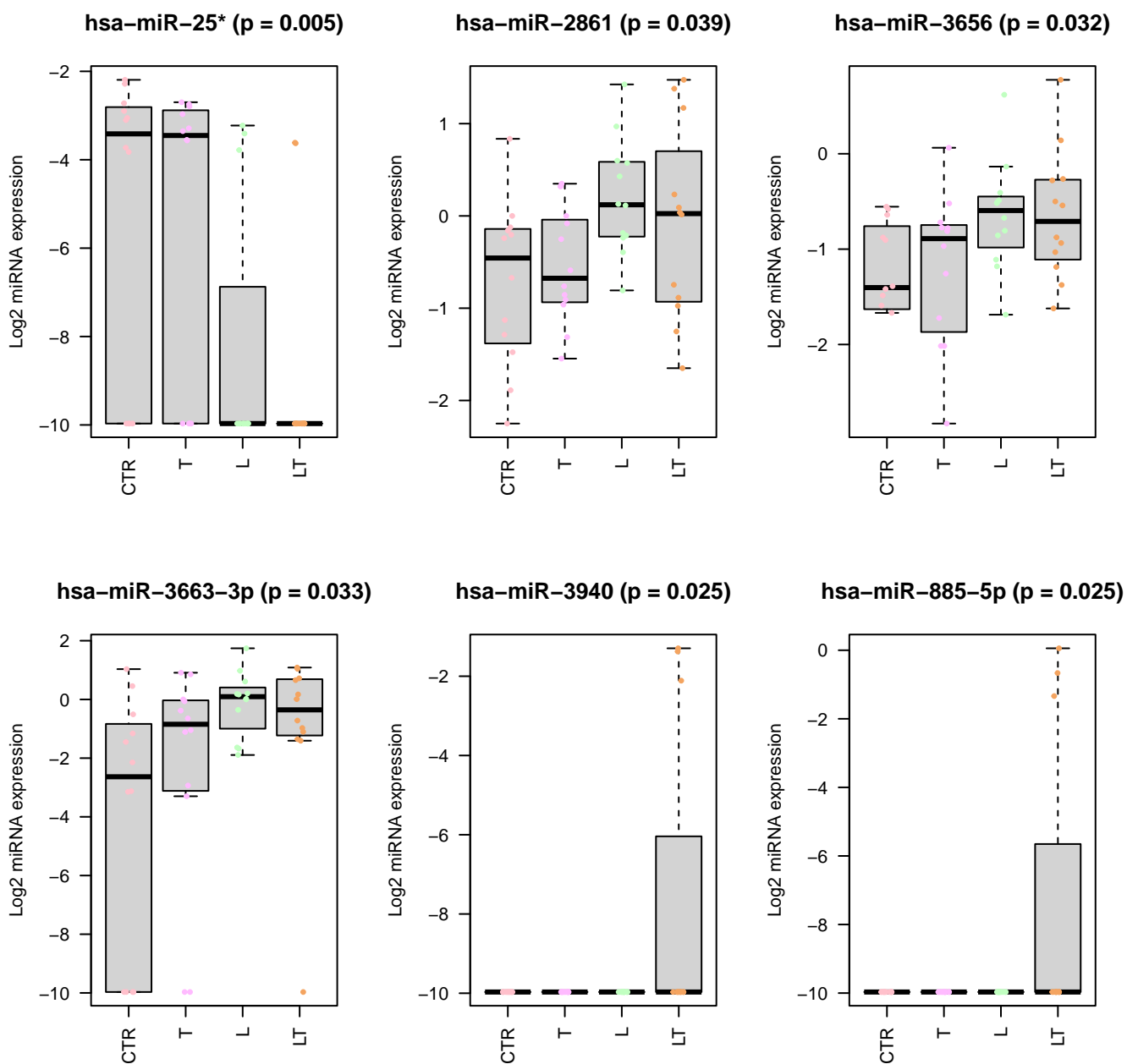
Supplementary Figure S2: miRNA expression before and after targeted treatment in responsive cell lines (SKBR3, BT-474)
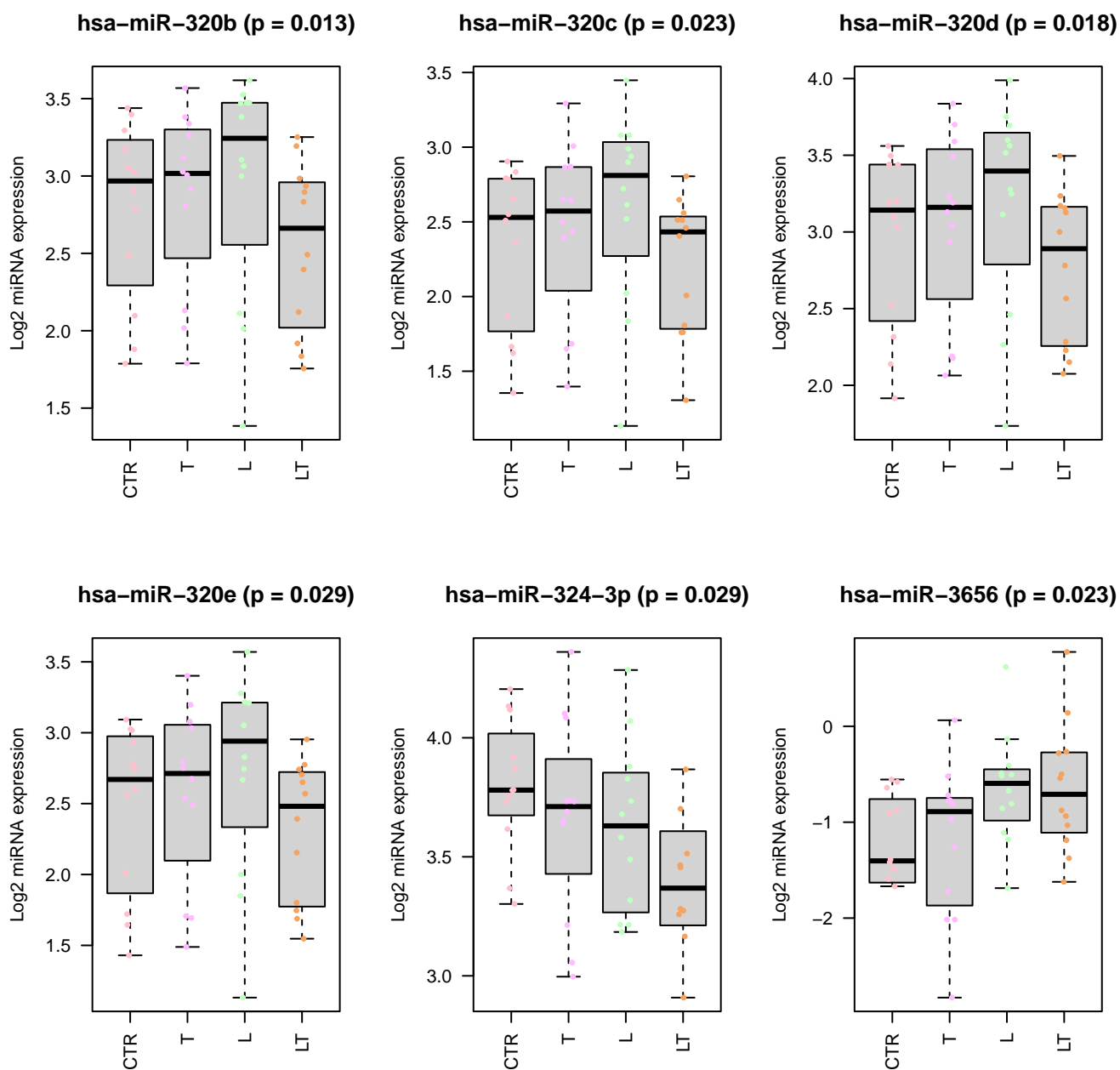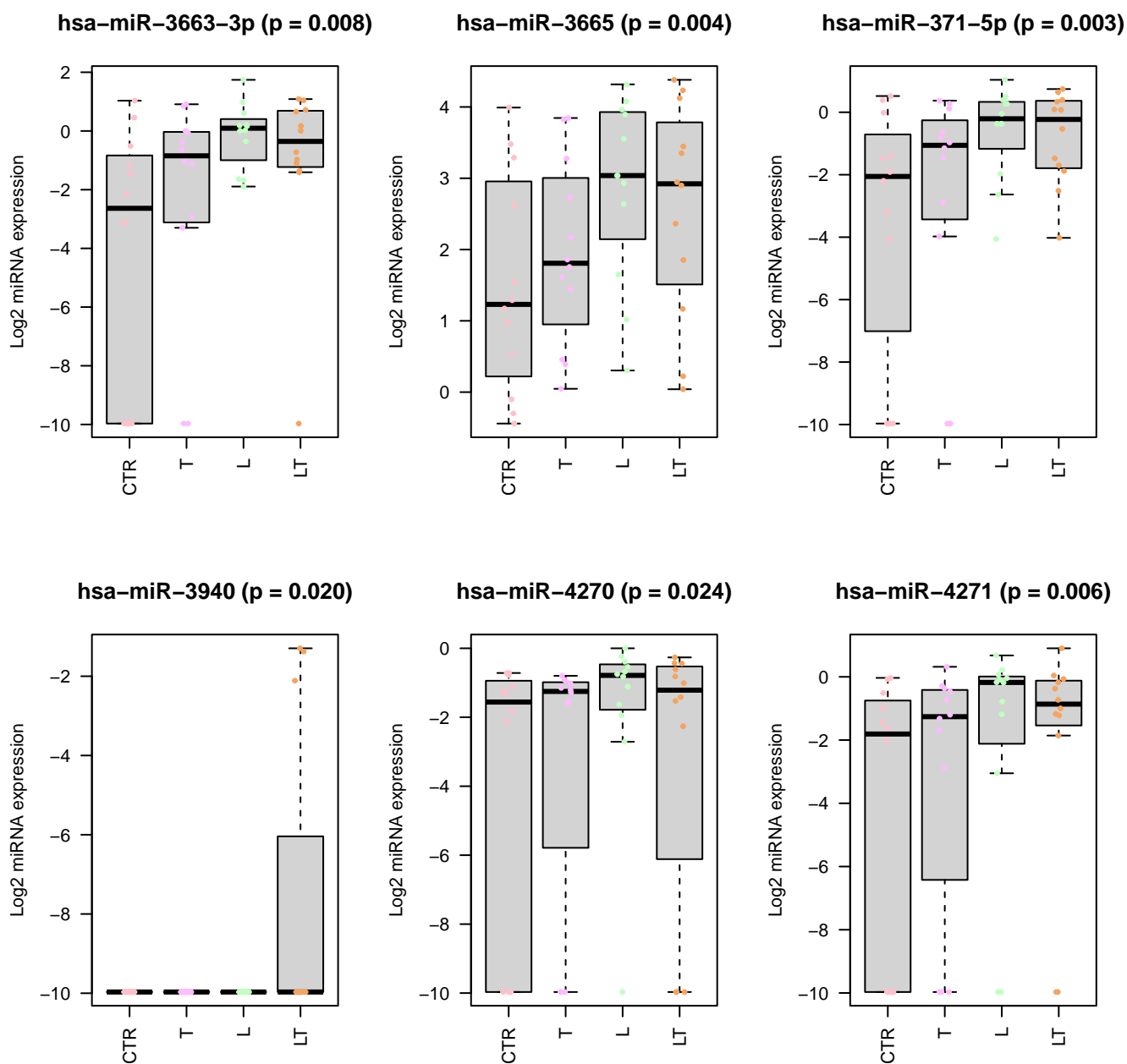
c

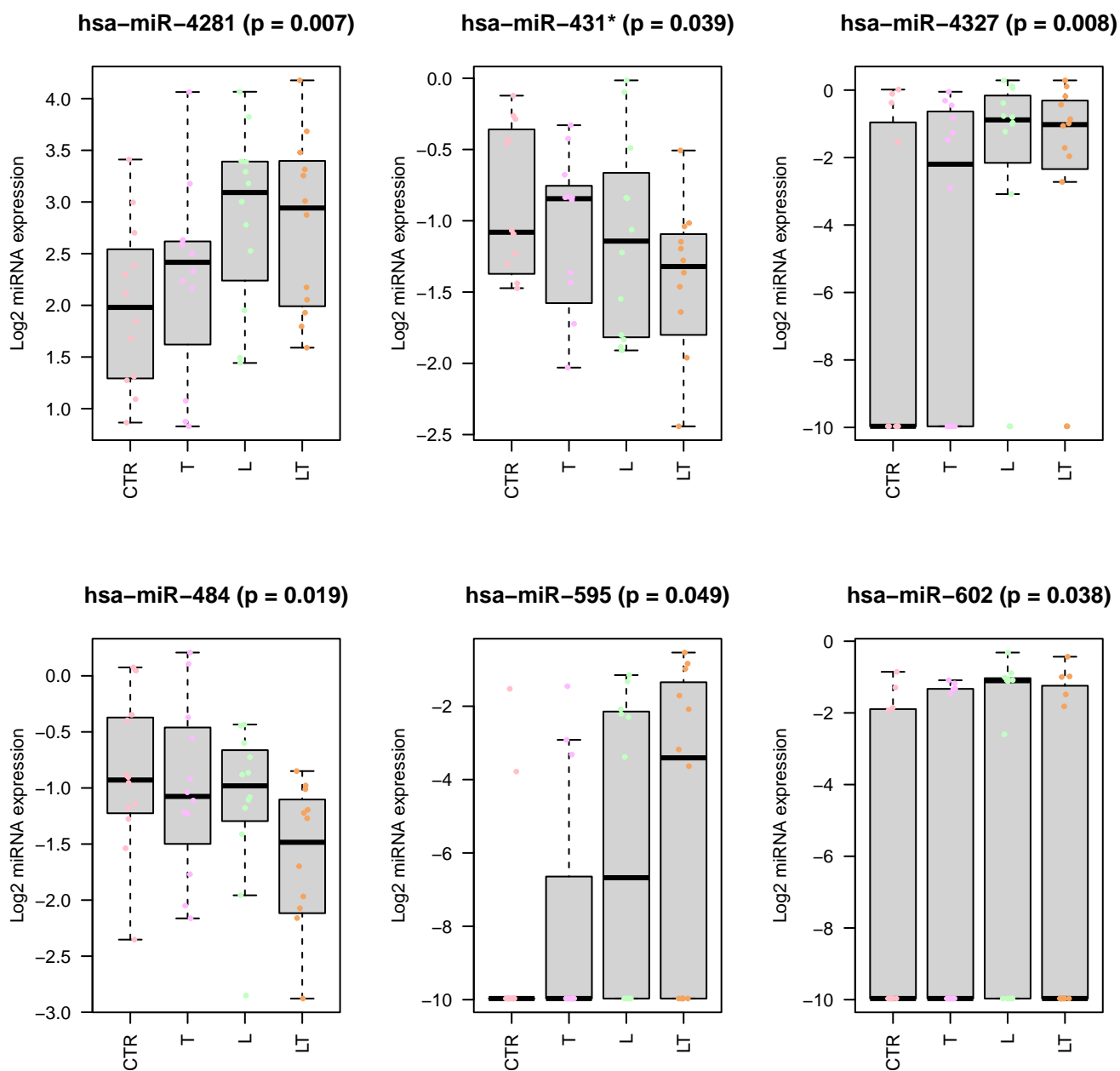Supplementary Figure S2: miRNA expression before and after targeted treatment in responsive cell lines (SKBR3, BT-474)
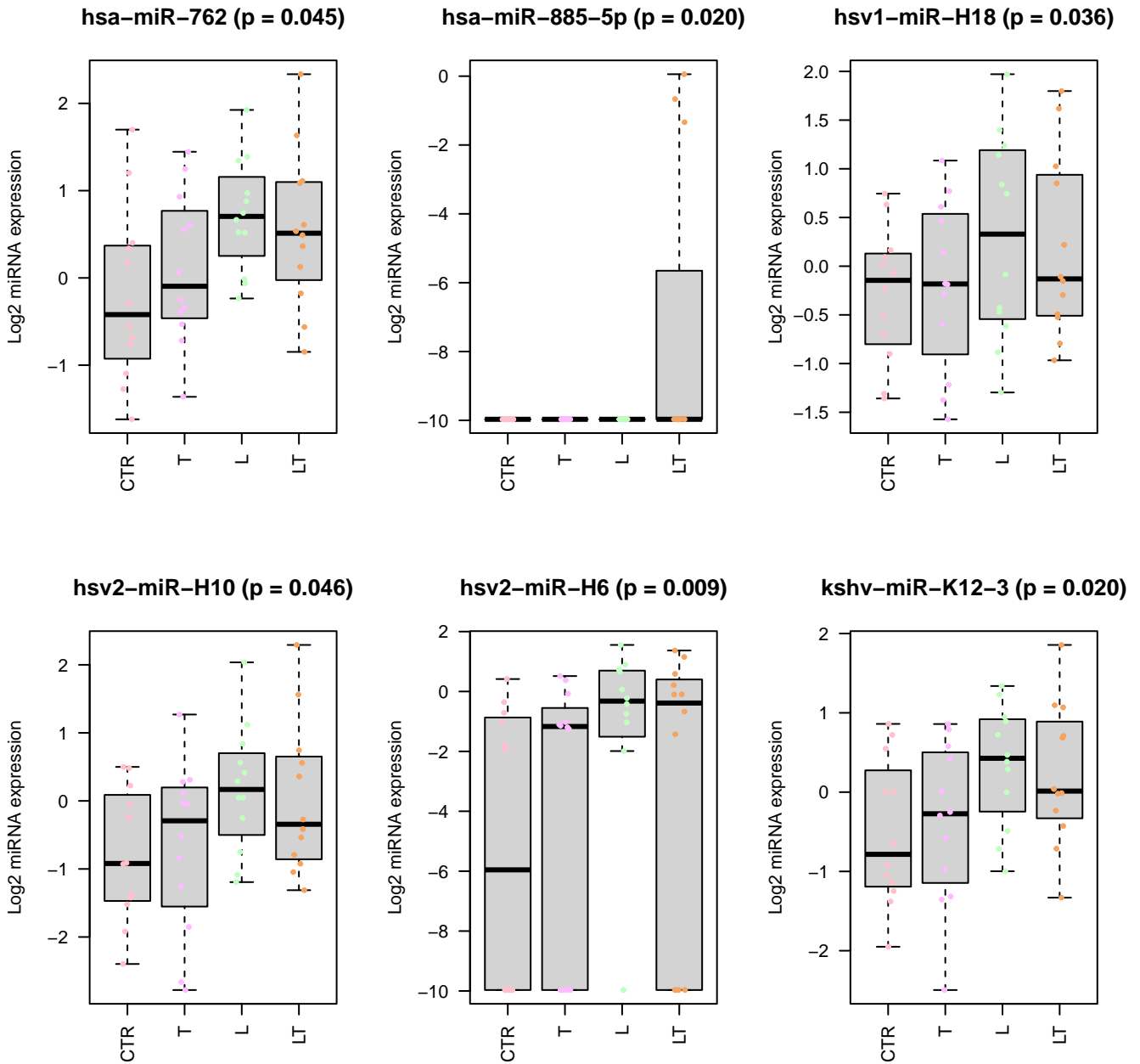
d

Supplementary Figure S2: miRNA expression before and after targeted treatment in responsive cell lines (SKBR3, BT-474)

e

Supplementary Figure S2: miRNA expression before and after targeted treatment in responsive cell lines (SKBR3, BT-474)

f

Supplementary Figure S2: miRNA expression before and after targeted
treatment in responsive cell lines (SKBR3, BT-474)

g

Supplementary Figure S2: miRNA expression before and after targeted treatment in responsive cell lines (SKBR3, BT-474)

h

hsa−miR−762 (p = 0.045)

hsa−miR−885−5p (p = 0.020)

hsv1−miR−H18 (p = 0.036)

hsv2−miR−H10 (p = 0.046)

hsv2−miR−H6 (p = 0.009)

kshv−miR−K12−3 (p = 0.020)

Supplementary Figure S2: miRNA expression before and after targeted treatment in poorly responsive cell lines (KPL4. SUM190PT)

i

hsa−miR−1268 (p=0.020)
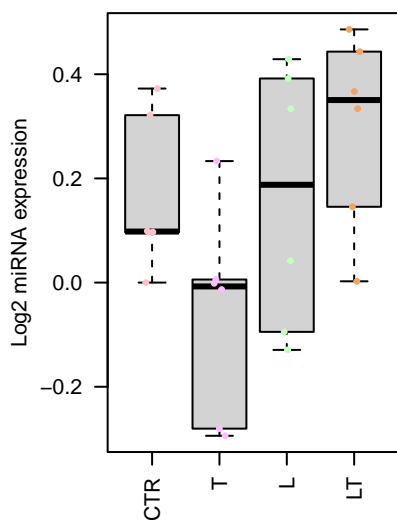
Supplementary Figure S3

a
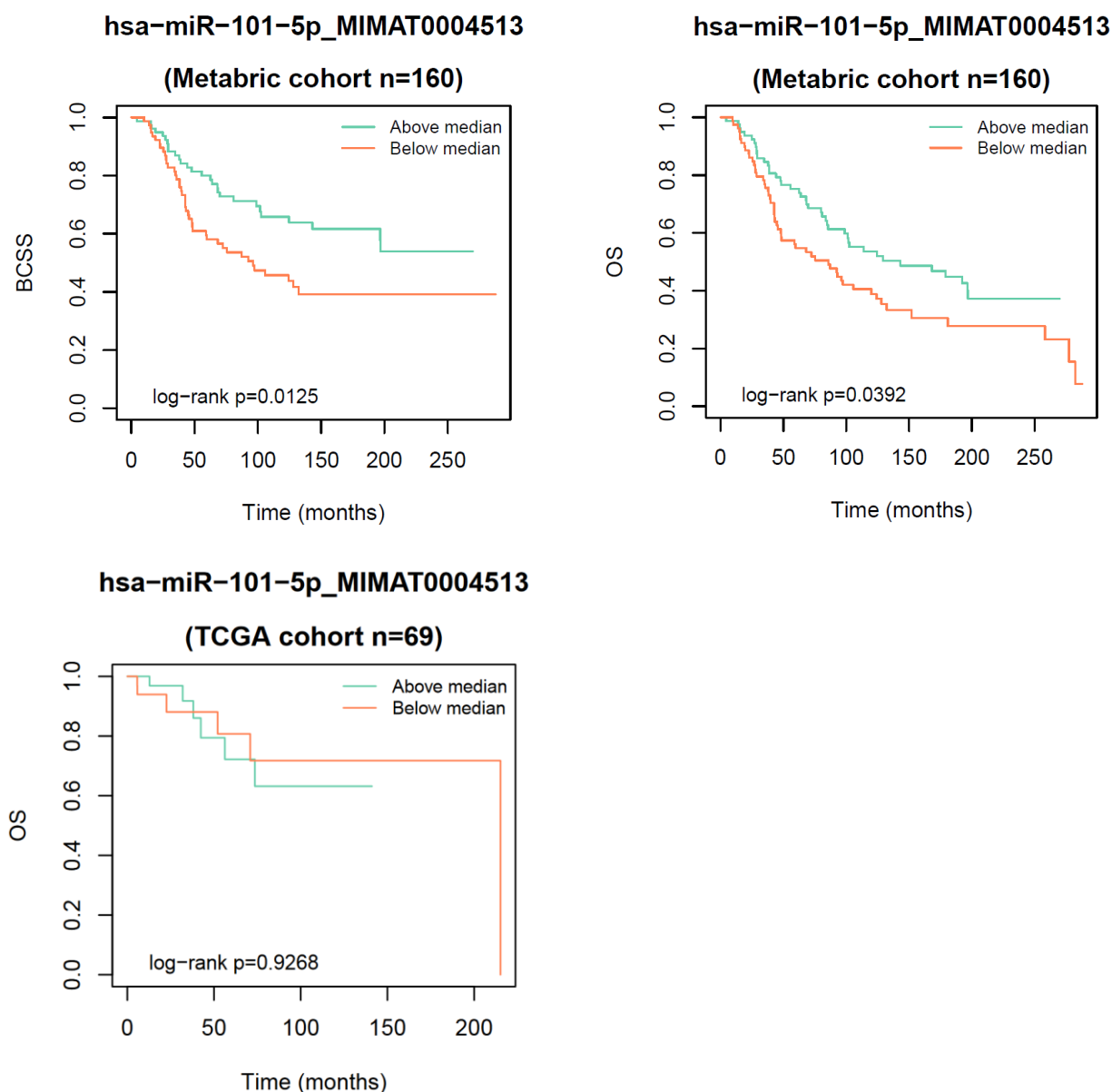
**Supplementary Figure S3: The clinical significance of sensitizing miRNAs in breast cancer patients**.

The survival curves are prepared for HER2+ breast cancer patients in the METABRIC ($n = 160$) and the TCGA($n = 69$) datasets. For the METABRIC data, breast cancer specific survival (BCSS) and overall survival (OS) of four miRNAs are presented (miR-101-5p (a), miR-29a-3p (b), miR29c-3p (c) and miR-744-3p (d)). For the TCGA data, OS for five miRNAs are presented (miR-101-5p (a), miR-29a-3p (b), miR29c-3p (c), miR-744-3p (d) and mir-106a-5p (e)). Log-rank p-values are significant ($p < 0.05$) only for miR-101-5p in the METABRIC dataset.
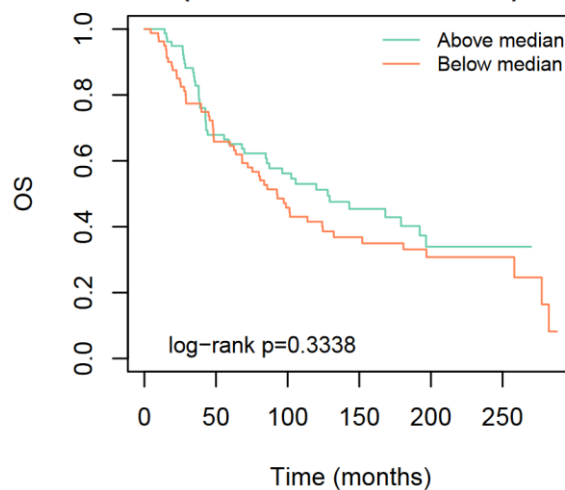
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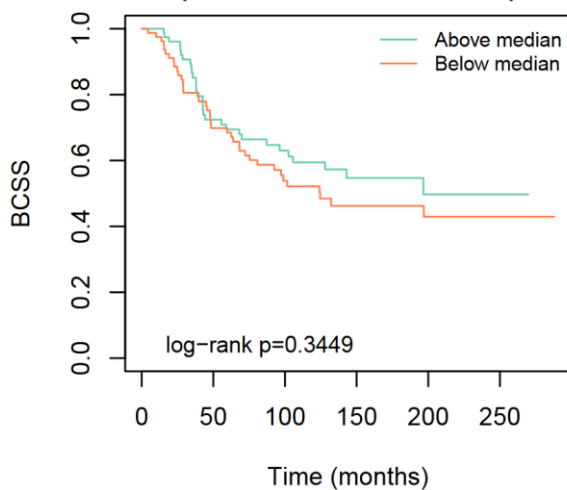
Supplementary Figure S3

c

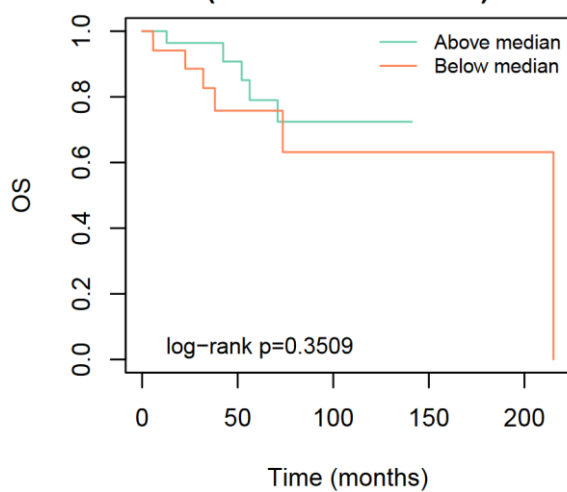hsa−miR−29c−3p _MIMAT0000681
(Metabric cohort n=160)
BCSS — Time (months)
Above median / Below median
log−rank p=0.5407

hsa−miR−29c−3p _MIMAT0000681
(Metabric cohort n=160)
OS — Time (months)
Above median / Below median
log−rank p=0.6978
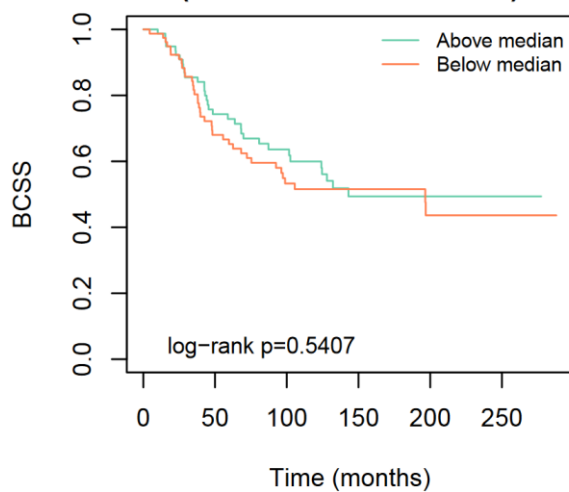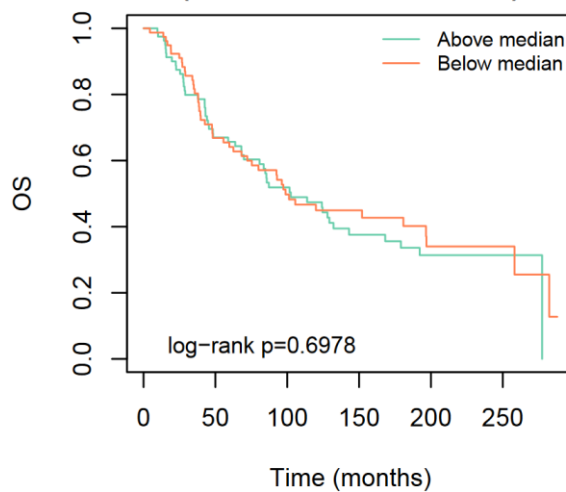
hsa−miR−29c−3p _MIMAT0000681
(TCGA cohort n=69)
OS — Time (months)
Above median / Below median
log−rank p=0.5991
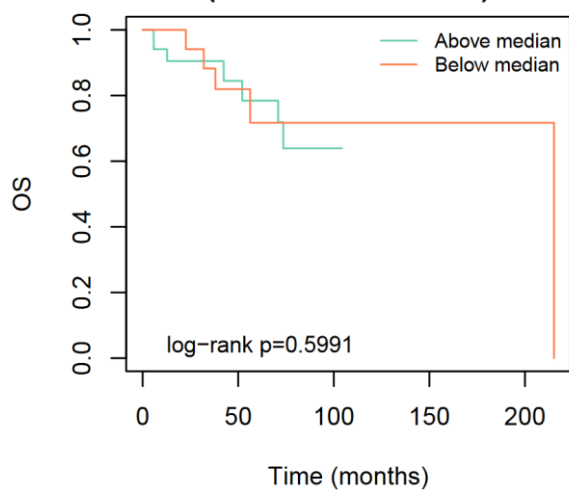
Supplementary Figure S3

d

hsa−miR−744−3p _MIMAT0004946
(Metabric cohort n=160)

log−rank p=0.6718

hsa−miR−744−3p _MIMAT0004946
(Metabric cohort n=160)

log−rank p=0.6268
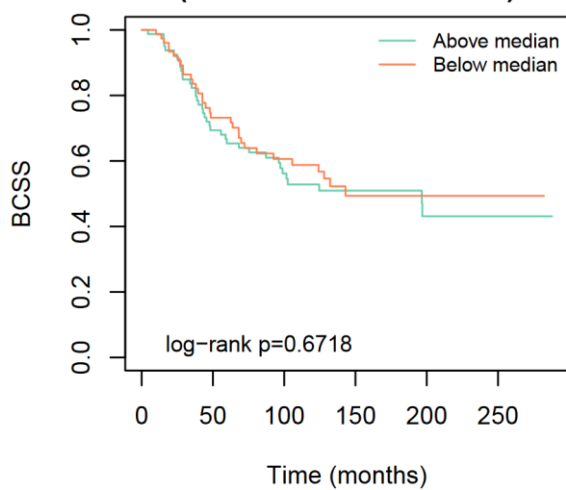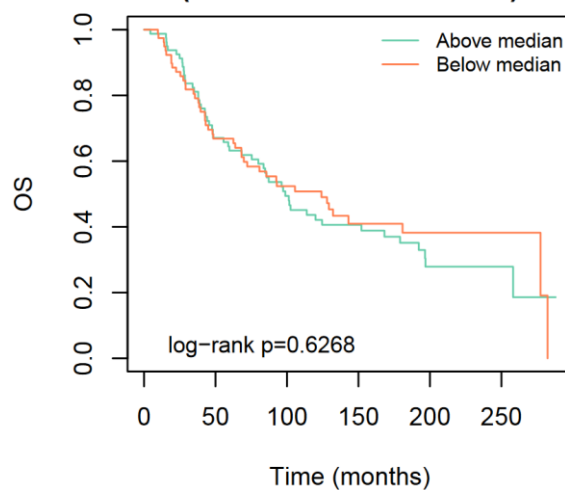
hsa−miR−744−3p _MIMAT0004946
(TCGA cohort n=69)

log−rank p=0.6039
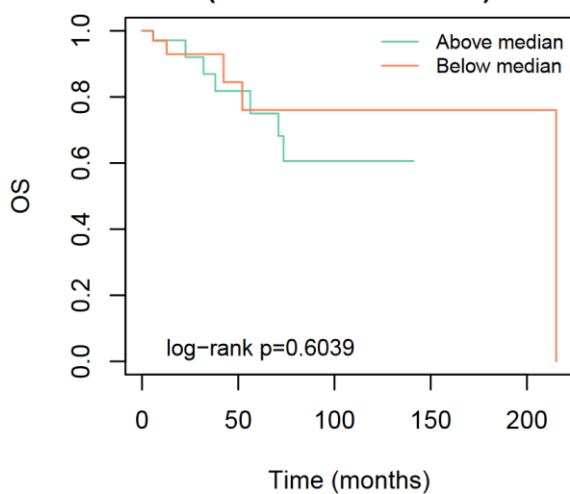
Supplementary Figure S3

e

hsa−miR−106a−5p_MIMAT0000103

(TCGA cohort n=69)