Supplementary Figure Legends

MicroRNA let-7b regulates genomic balance by targeting Aurora B kinase

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Supplementary Figure A.1. Expression of let-7b-5p was increased upon let-7b-5p transfection of HeLa cells in comparison to miR-control transfected cells. (A) Schematic representation of premature let-7b loop showing the location of let-7b-5p (white circles) in the hairpin. The premature form of let-7b is further processed yielding let-7b-5p and let-7b-3p. (B) The graph shows quantification of let-7b expression levels in HeLa cells transfected with 20 nM control-miR or let-7b-5p 24 hours post-transfection. Data are from three separate experiments (mean ± SD). The asterisk denotes statistical significance (* $p<0.05$).

Supplementary Figure A.2. Excess let-7b decreases Aurora B mRNA and protein levels in breast cancer cells. MDA-MB-231 (A) and MDA-MB-231 SA (B) cells were transfected with 40 nM miR-control or let-7b and harvested 48 hours post-transfection for qRT-PCR and Western blot analysis. Data are from four (qRT-PCR) or three (Western blot) separate experiments (mean ± SD). (C) Micrographs of 40 nM let-7b or miR-control transfected MDA-MB-231 SA cells treated with 100

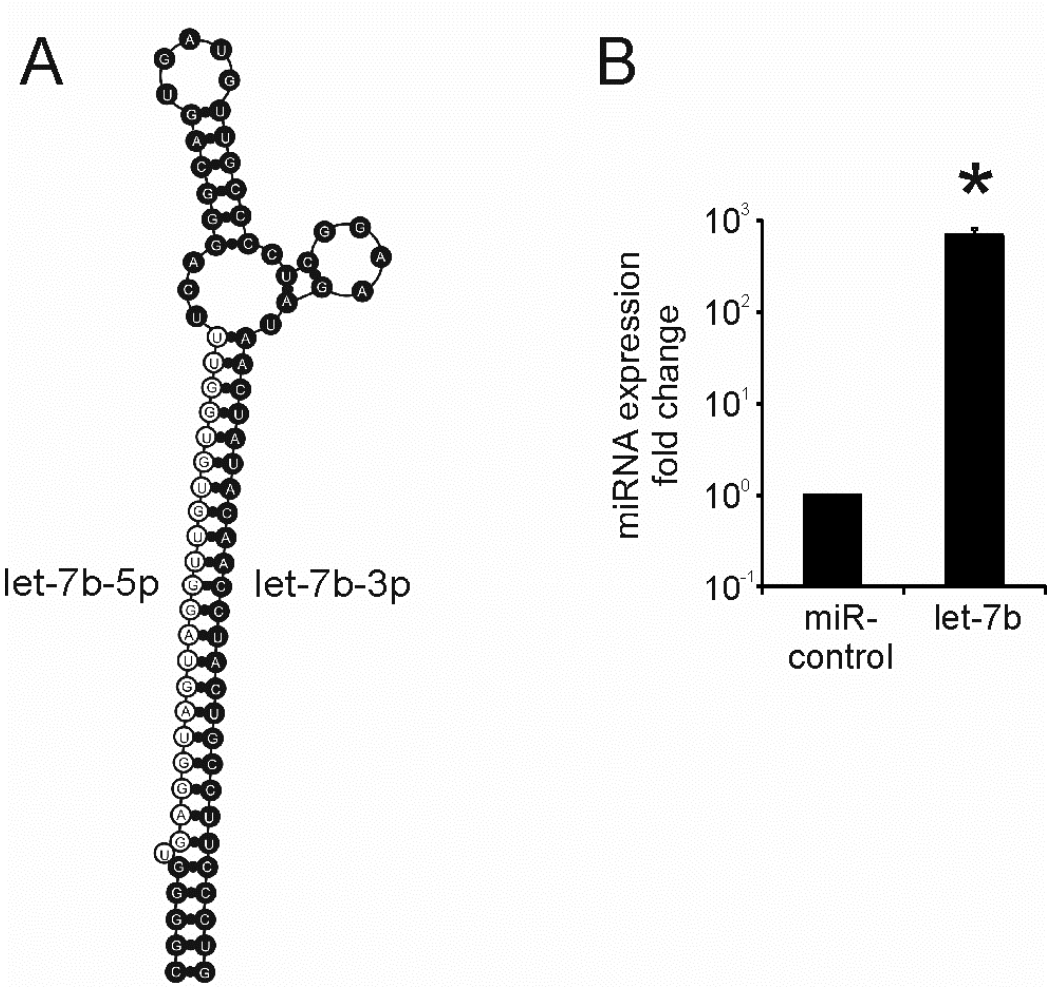
nM taxol 52 hours post-transfection for 12 hours. Cells were fixed and immunostained with antibodies against phosphorylated Cenp-A (pCenp-A) (Ser7) and centromere marker CREST. DNA was stained with DAPI. In merge, pCenpA (red), CREST (green) and DNA (blue) staining are combined. The graphs show quantification of centromeric pCenp-A signal intensities in mitotic cells normalized against CREST. Data are mean ± SD from 20 cells, 15 centromeres quantified per each cell. (D) Representative micrographs of interphase and mitotic cells transfected and treated like in C. The quantification of nuclear morphology based on DAPI staining is shown (n=156-168). Scale bars equal 10 µm. The asterisks denote statistical significance (* $p<0.05$, ** $p<0.01$, *** $p<0.001$).

Supplementary Figure A.3. The Aurora B inhibitor ZM447439 induces multipolar spindle formation. HeLa cells were incubated with 20 µM ZM447439 and 20 µM MG132 for 2 hours and 2.5 hours, respectively, prior to fixation and immunostaining with antibodies against pericentrin (red) and α-tubulin (green). DNA was stained with DAPI (blue). MG132 was used to prevent ZM447439 induced premature exit from M phase. For control, HeLa cells were transfected with 40 nM miR-control, fixed 48 hours post-transfection and processed as above. Scale bar equals 10 µm. The graph shows quantification of mitotic spindle morphology categorised into bipolar, multipolar and monopolar cells in the ZM447439 treated and miR-control transfected cell populations (n= 75–105 cells per treatment). Data are from two separate experiments (mean ± SD). The asterisks denote statistical significance (* $p<0.05$).

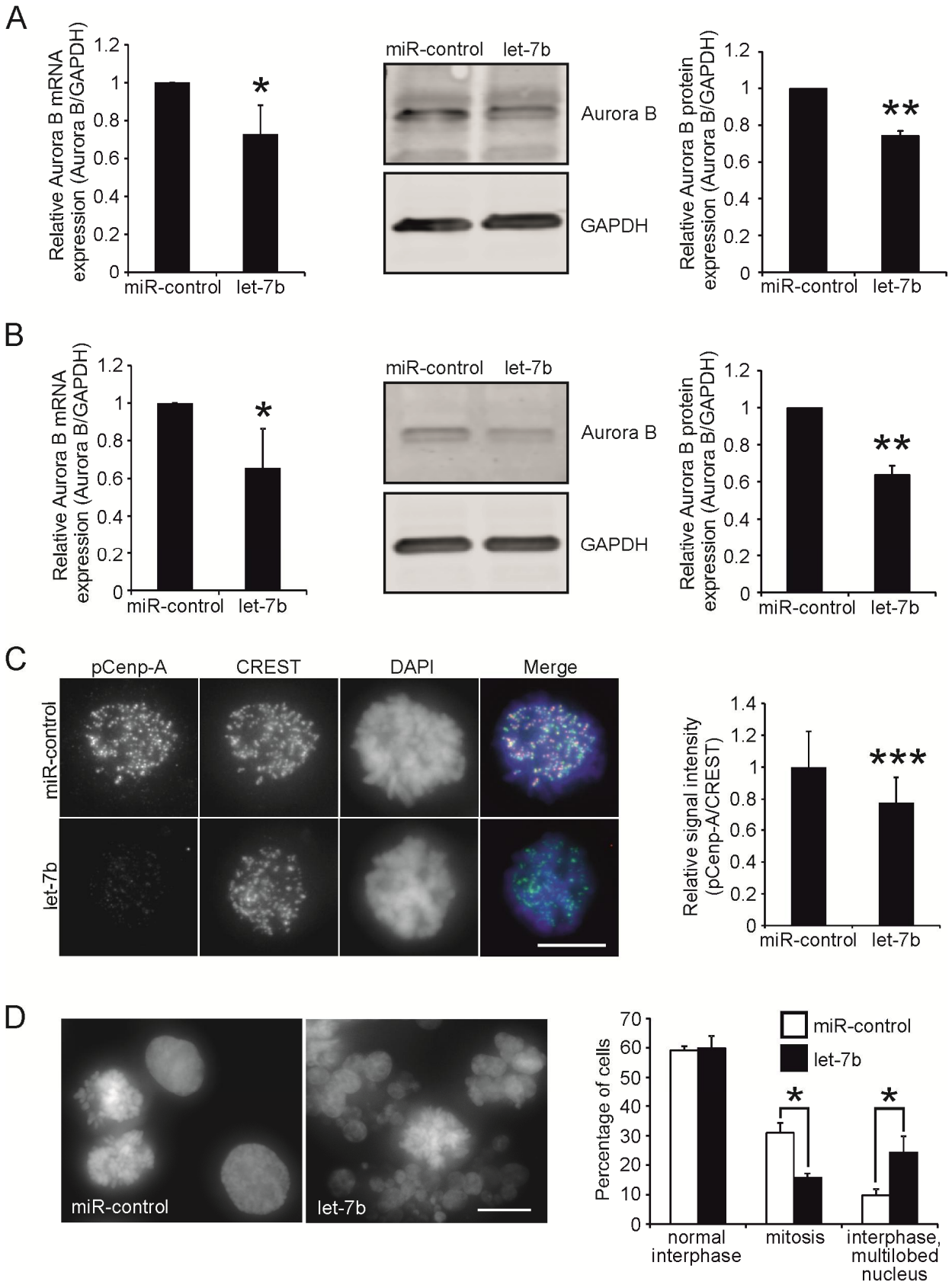
Supplementary Figure A.4. Let-7b expression and association to clinical parameters in the TCGA database. Let-7b expression data is obtained from TCGA for 395 patients (https://tcga-data.nci.nih.gov/docs/publications/brca_2012/). (A) Let-7b expression in the five molecular

subtypes of breast cancer (*LumA*: Luminal A; *LumB*: Luminal B). (B) Let-7b expression in HER2 negative and positive breast tumors. (C) Let-7b expression in ER negative and positive breast tumors. (D) Aurora B (AURKB) mRNA expression versus let-7b expression (Pearson correlation = -0.367). The regression line is shown. Each dot represents an individual breast tumor. The asterisks denote statistical significance (*** $p<0.001$). Round dots in panels A, B, and C represent outliers.

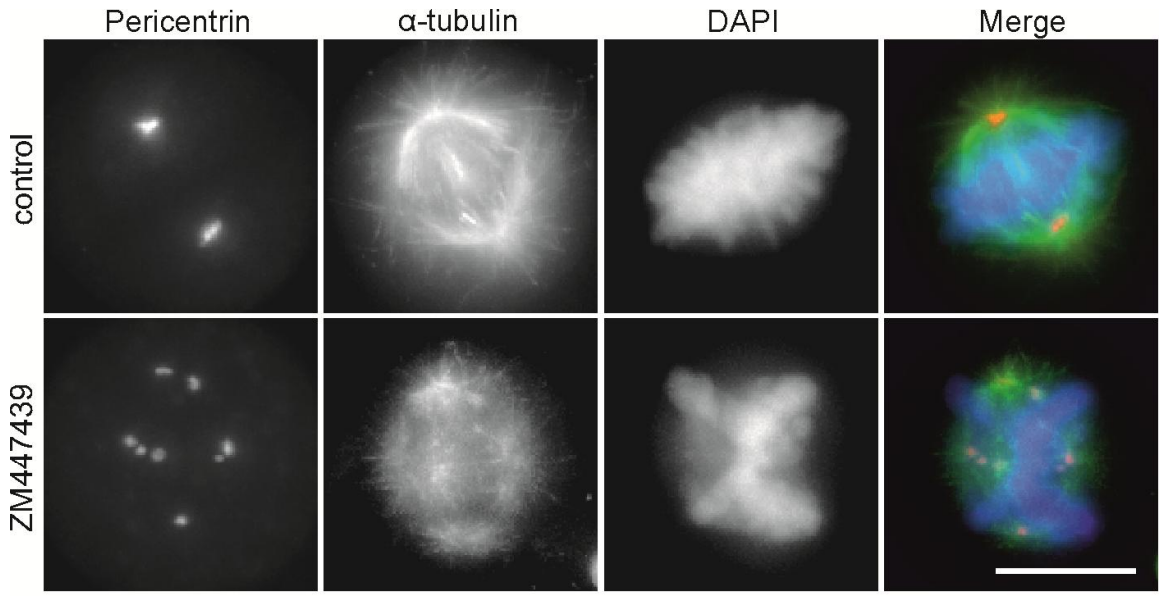
Supplementary Figure A.5. Expression of the let-7 family members and association to breast cancer tumor grades. Boxplots show log 2 expression of various let-7 family members detected in breast tumors of different grade (1, 2 and 3). ANOVA p-values are shown in parenthesis.

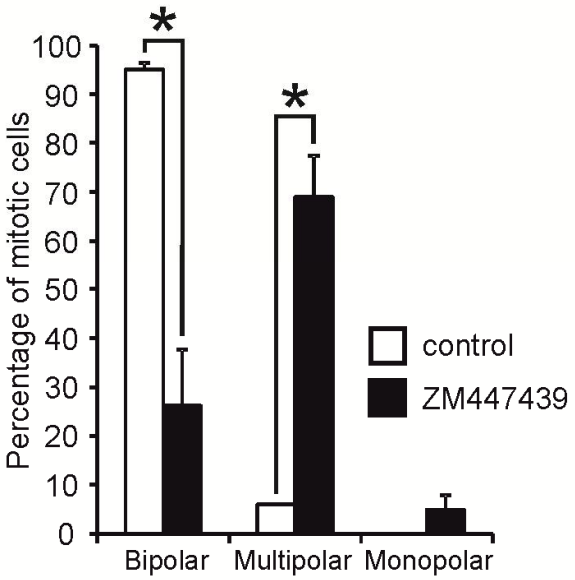


Supplementary Figure A.1. Mäki-Jouppila et al.

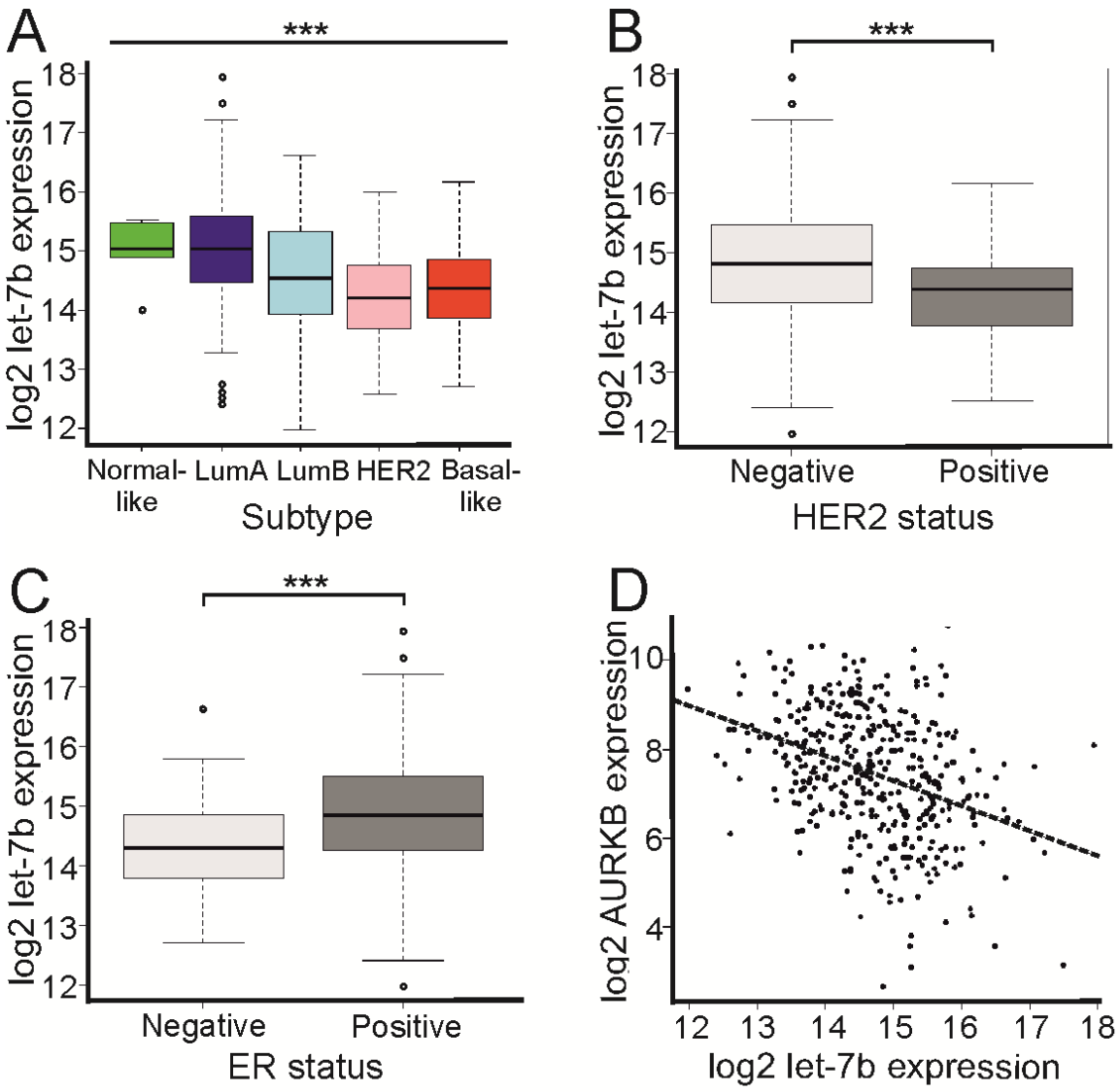


Supplementary Figure A.2. Mäki-Jouppila et al.

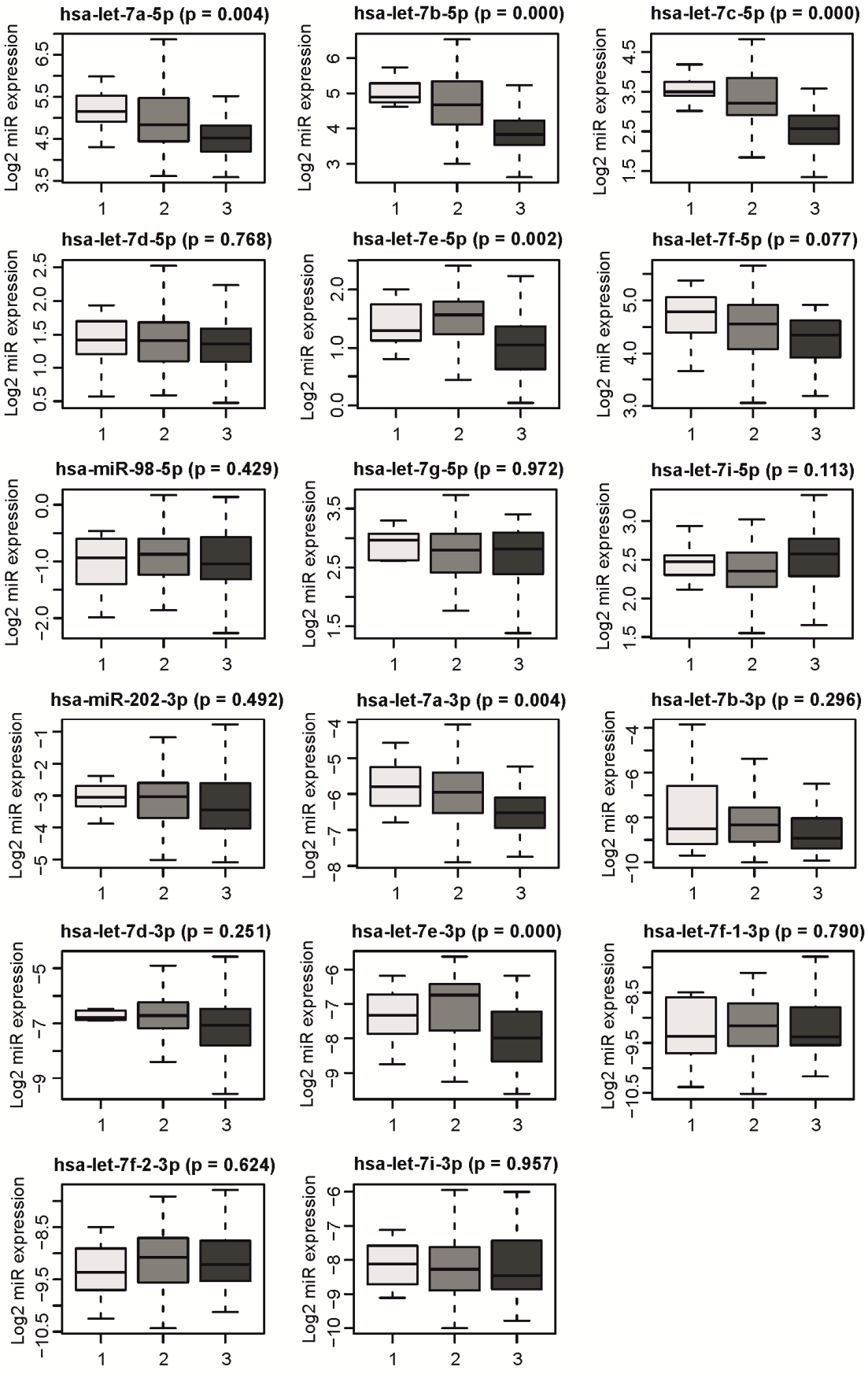




Supplementary Figure A.3. Mäki-Jouppila et al.



Supplementary Figure A.4. Mäki-Jouppila et al.



Supplementary Figure A.5. Mäki-Jouppila et al.

Supplementary Table A.1. The let-7 family members' association to clinical parameters in breast tumors. The table shows p-values to denote statistical significance of association between various let-7 family members and different tumor grades, the five molecular subtypes of breast cancer, HER2 status, ER status and *TP53* status. The p-values for grade and molecular subtype are calculated using the ANOVA test and the p-values for HER2, ER and *TP53* status are calculated using The Student's t-test.

Supplementary Movie A.1. HeLa H2B-GFP cells were transfected with miR-control and treated with 150 nM nocodazole 48 hours post-transfection. Cells arrest in mitosis and die without exit from M phase. Cells were filmed with 10 minutes frame capture intervals after addition of the drug. Numbers denote hours and minutes (h:min).

Supplementary Movie A.2. HeLa H2B-GFP cells were transfected with let-7b and treated with 150 nM nocodazole 48 hours post-transfection. Cells exhibit mitotic arrest followed by forced exit from M phase and cell death. Cells were filmed with 10 minutes frame capture intervals after addition of the drug. Numbers denote hours and minutes (h:min).