Supplementary information

Table S1. Integrative analysis of KEGG signaling pathways involving miR-17~92, 105~25 and 99a~125b clusters by mirFOCUS.

| KEGG ID | | KEGG Pathway | Involved miRNAs |
|----------|------|--|---|
| hsa05219 | 4.62 | Bladder cancer | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-miR-99a,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa04350 | 4.57 | TGF-beta signaling pathway | hsa-miR-106b,hsa-miR-125b,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa05220 | 3.68 | Chronic myeloid leukemia | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-miR-99a,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa05212 | 3.68 | Pancreatic cancer | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa05214 | 3.65 | Glioma | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-miR-99a,hsa-let-7c,hsa-miR-19a |
| hsa04012 | 3.04 | ErbB signaling pathway | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-miR-99a,hsa-let-7c,hsa-miR-19a |
| hsa05218 | 2.65 | Melanoma | hsa-miR-125b |
| hsa00830 | 2.45 | Retinol metabolism | hsa-miR-125b |
| hsa00980 | 2.04 | Metabolism of xenobiotics by cytochrome P450 | hsa-miR-125b |
| hsa05223 | 2.03 | Non-small cell lung cancer | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-let-7c,hsa-miR-19a |
| hsa04144 | 1.93 | Endocytosis | hsa-miR-106b,hsa-miR-125b,hsa-miR-99a,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa00982 | 1.77 | Drug metabolism - cytochrome P450 | hsa-miR-125b |
| hsa05215 | 1.76 | Prostate cancer | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-miR-99a,hsa-let-7c,hsa-miR-19a |
| hsa04010 | 1.68 | MAPK signaling pathway | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-miR-99a,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa04115 | 1.52 | p53 signaling pathway | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa04110 | 1.52 | Cell cycle | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa05210 | 1.49 | Colorectal cancer | hsa-miR-106b,hsa-miR-25,hsa-miR-125b,hsa-miR-99a,hsa-let-7c,hsa-miR-19a,hsa-miR-92a |
| hsa00150 | 1.43 | Androgen and estrogen metabolism | hsa-miR-125b |
| hsa00040 | 1.43 | Pentose and glucuronate interconversions | hsa-miR-125b |
| hsa00860 | 1.43 | Porphyrin and chlorophyll metabolism | hsa-miR-125b |
| hsa00053 | 1.43 | Ascorbate and aldarate metabolism | hsa-miR-125b |

Table S2. Ingenuity analysis of predicted pathways for five key

mRNAs.

| Signaling pathway | RAC1 | NFĸB1 | MYC | JUN | CCND1 |
|---------------------|------|-------|-----|-----|-------|
| B cell receptor | + | + | | + | |
| Wnt | + | | + | + | + |
| Toll-like receptor | + | + | | + | |
| Neurotrophin M APK | + | + | | + | |
| ErbB | + | | + | + | + |
| Jak-STAT | | | + | + | |
| NOD-like receptor | | | + | | + |
| Chemokine | | + | | | |
| p53 | + | + | | | |
| Adipocytokine | | | | | + |
| RIG-I-like receptor | | + | | | |
| VEGF | | + | | | |
| Fc epsilon RI | + | | | | |
| TGF-beta | + | | | | |
| GnRH | | | + | | |
| | | | | + | |

| 5' UCCCUGAGACCCUAACUUGUGA 3' | miR-125b |
|--------------------------------|-----------------|
| 3' AGGGACTCTGGGATT GA ACACT 5' | antimiR-125b |
| 5' UCCCUGAGACCCUAACUUGUGA 3' | miR-125b |
| 3'AGGGACTC 5' | t-antimiR-125b |
| 5' AACCCGUAGAUCCGAUCUUGUG 3' | miR-99a |
| 3' TTGGGCAT 5' | t-antimiR-99a |
| 5'UGAGGUAGUAGGUUGUAUGGUU3' | miR-let-7 |
| 3'ACTCCATC 5' | t-antimiR-let-7 |

Figure S1.



Figure S2.



Figure S3.

Supplementary Legends

Figure S1. Sequences of anti-miR-125b, t-anti-miR-99a~125b cluster LNAs and seed sequences in the miR-99a~125b cluster.

Figure S2. Genes ranked by node numbers.

The mRNAs differentially regulated by BBR were integrated by R software with gplots package and the top 30 genes were ranked by node numbers.

Figure S3. Confocal localization and delivery of t-anti-mir-125b in comparison with anti-mir-125b.

Anti-mir-125b and t-anti-mir-125b were modified with FITC, and transfected into RPMI-8266 cells. (A) Representative optical sections of FAM-labeled anti-mir-125b immediately post-transfection. (B) Representative optical sections of FAM-labeled t-anti-mir-125b immediately post-transfection. (C) Flow cytometry showed that anti-mir-125b and t-anti-mir-125b-FITC-positive cells were 95.01% and 55.65% of the total, respectively, 24 h post-transfection. These results indicated that t-anti-mir-125b-FITC was detected at high levels and was located mainly in the cytoplasm, but rapidly degraded in comparison with anti-mir-125b-FITC.