Supplementary Table 1. Clinical characteristics of 62 NSCLC patients with brain metastasis and 60 patients without brain metastasis.

| Characteristic                      | NSCLC with BM total 62 | NSCLC without BM total 60 |
|-------------------------------------|------------------------|---------------------------|
| Age (years), median (range)         | 58 (50-65)             | 60 (55-67)                |
| Gender                              |                        |                           |
| Male                                | 13 (21.0%)             | 37 (61.7%)                |
| Female                              | 49 (79.0%)             | 23 (38.3%)                |
| Tumor histology                     |                        |                           |
| Adenocarcinoma                      | 54 (87.1%)             | 41 (68.3%)                |
| Squamous cell carcinoma             | 8 (12.9%)              | 10 (16.7%)                |
| Carcinosarcoma                      | -                      | 2 (3.3%)                  |
| Large cell carcinoma                | -                      | 1 (1.7%)                  |
| Neuroendocrine carcinoma            | -                      | 6 (10.0%)                 |
| Disease stage at diagnose           |                        |                           |
| I                                   | -                      | 6 (10.0%)                 |
| II                                  | -                      | 12 (20.0%)                |
| III                                 | -                      | 11 (18.3%)                |
| IV                                  | 62 (100%)              | 31 (51.7%)                |
| Smoking history                     |                        |                           |
| Smoker                              | 18 (29.0%)             | 8 (13.3%)                 |
| Former smoker                       | 6 (9.7%)               | 22 (36.7%)                |
| Never                               | 38 (61.3%)             | 30 (50.0%)                |
| Lymph node metastatic status        |                        |                           |
| N0                                  | 4 (6.5%)               | 9 (15.0%)                 |
| N1                                  | 2 (3.2%)               | 7 (11.7%)                 |
| N2                                  | 22 (35.5%)             | 17 (28.3%)                |
| N3                                  | 34 (54.8%)             | 27 (45.0%)                |
| EGFR mutation status                |                        |                           |
| Mutant                              | 42 (67.7%)             | 32 (53.3%)                |
| Wild-type                           | 20 (32.3%)             | 28 (46.7%)                |
### Supplementary Table 2. Univariate analysis and Multivariate analysis of associations between clinical features and brain metastasis.

| Variable                          | Univariate analysis | Mutivariate analysis |
|-----------------------------------|---------------------|----------------------|
|                                   | OR      | 95% CI   | P        | OR      | 95% CI   | P        |
| **Gender**                        |         |          |          |         |          |          |
| Female vs Male                    | 2.84    | 1.55–5.21| 0.001    | 3.15    | 1.49–6.63| 0.003    |
| Age (year) ≥60 vs <60             | 3.45    | 0.16–0.52| < 0.001  | 4.54    | 0.11–0.46| <0.001   |
| **Smoking status**                |         |          |          |         |          |          |
| Former smoker vs Never            | 0.75    | 0.35–1.6 | 0.458    |         |          |          |
| Smoker vs Never                   | 1.38    | 0.62–3.08| 0.424    |         |          |          |
| **Tumor histology**               |         |          |          |         |          |          |
| Adnocarcinoma vs Other types      | 4.17    | 0.1–0.53 | 0.001    | 3.57    | 0.1–0.75 | 0.012    |
| **EGFR status**                   |         |          |          |         |          |          |
| 19 exon mutated vs Wildtype       | 3.28    | 1.13–9.56| 0.03     | 3.76    | 1.00–14.12| 0.05    |
| 21 exon mutated vs Wildtype       | 1.76    | 0.6–5.18 | 0.307    |         |          |          |
| **Lymph node metastatic status**  |         |          |          |         |          |          |
| N1 vs N0                          | 5       | 0.76–32.93| 0.094    | 6.14    | 0.8–47.19| 0.081    |
| N2 vs N0                          | 7.88    | 1.69–36.82| 0.009    | 8.23    | 1.57–43.01| 0.013   |
| N3 vs N0                          | 19.06   | 4.19–86.74| < 0.001  | 29.38   | 5.68–152.04| <0.001  |
| **Disease stage at diagnose**     |         |          |          |         |          |          |
| Stage III vs Stage I, II          | 1.89    | 0.01–2.56 | 0.177    |         |          |          |
| Stage IV vs Stage I, II           | 2.12    | 0.13–34.71| 0.599    |         |          |          |
| **PCR**                           |         |          |          |         |          |          |
| high expression vs low expression |         |          |          |         |          |          |
| miR-370                           | 1.167   | 0.302–4.512| 0.823    |         |          |          |
| miR-325                           | 0.435   | 0.147–1.289| 0.133    |         |          |          |
| miR-326                           | 0.318   | 0.086–1.182| 0.087    | 0.523   | 0.099–1.231| 0.032   |
| miR-330-3p                        | 0.159   | 0.048–0.531| 0.003    | 0.174   | 0.079–0.679| 0.001   |
| miR-350                           | 0.09    | 0.022–0.365| 0.001    |         |          |          |
| miR-328                           | 0.067   | 0.016–0.273| <0.001   | 0.073   | 0.023–0.281| 0.002   |
**Supplementary Table 3.** Univariate analysis of miRNA expression and brain metastasis.

| miRNA        | Sig. | 95% CI Lower | 95% CI Upper |
|--------------|------|--------------|--------------|
| miR-325      | 0.120| 2.323        | 5.793        |
| miR-328      | 0.048| 1.521        | 3.011        |
| miR-330-3p   | 0.023| 2.630        | 16.20        |
| miR-500-3p   | 0.087| 1.218        | 2.831        |
| miR-326      | 0.774| 1.718        | 2.956        |
| miR-370      | 0.384| 1.347        | 2.728        |

Sig., *p*-value; CI, confidence interval.

**Supplementary Table 4.** The sequence of predicted targets of miR-330-3p.

| Predicted targets                               | Paring of miRNA/targets                          |
|------------------------------------------------|--------------------------------------------------|
| Position 223-229 of GRIA3 3'UTR                 | 5'...UCAUUGAAACUUUUGCUUUUGC...3' AGAGACGUCCGCACACGAACG |
| miR-330-3p                                      | 3' AGAGACGUCCGCACACGAACG                         |
| Position 113-120 of SOSTDC1 3'UTR              | 5'...AAAGUAAUGCUUUUGCUUUUGA...3' AGAGACGUCCGCACACGAACG |
| miR-330-3p                                      | 3' AGAGACGUCCGCACACGAACG                         |
| Position 1484-1490 of BMI-1 3'UTR              | 5'...GAAGCACAUAUCUAUUGCUUUGU...3' AGAGACGUCCGCACACGAACG |
| miR-330-3p                                      | 3' AGAGACGUCCGCACACGAACG                         |
| Position 846-853 of AGTR2 3'UTR                | 5'...ACUUUUUGAUUGUCUUUGCUUUGA...3' AGAGACGUCCGCACACGAACG |
| miR-330-3p                                      | 3' AGAGACGUCCGCACACGAACG                         |

GRIA3, ionotropic glutamate receptors, AMPA3; SOSTDC1, sclerostin domain containing 1; BMI-1, B lymphoma Mo-MLV insertion region 1; AGTR2, Angiotensin Type-2 Receptor.

**Supplementary Table 5.** The primary antibodies for western blotting.

| Antibodies           | Accession                                      |
|----------------------|------------------------------------------------|
| cyclin D1            | ab6152, Abcam, Cambridge, MA, USA              |
| Bcl-2                | 15071, Cell Signaling Technology               |
| Bax                  | ab77566, Abcam                                 |
| VEGFA                | ab46154, Abcam                                 |
| GRIA3                | ab52896, Abcam                                 |
| GAPDH                | G9545, Sigma, St Louis, MO, USA                 |
| The EMT Antibody Sampler Kit | 9782, Cell Signaling Technology          |
| PARP                 | 13371-1-AP, Proteintech, Chicago, IL, USA      |
| Caspase3             | 19677-1-AP, Proteintech                        |
| p21                  | 10355-1-AP, Proteintech                        |
| p27                  | 25614-1-AP, Proteintech                        |
| CDK4                 | 11026-1-AP, Proteintech                        |
| CDK6                 | 14052-1-AP, Proteintech                        |
| VEGFC                | 22601-1-AP, Proteintech                        |
| Twist                | 25465-1-AP, Proteintech                        |
| Bak                  | A0204, ABclonal Biotech, Cambridge, MA         |
| PIGF                 | A13617, ABclonal Biotech                       |
| VEGFB                | A12689, ABclonal Biotech                       |
| VEGFD                | A13617, ABclonal Biotech                       |
| p-β-catenin          | 4176, Cell Signaling Technology                |