1 Supplementary figures



3 Figure S1.

- 4 A: Fibroblast activation markers expression in MRC5 treated by tumor cell-derived
- 5 conditioned medium. B: The survival rate of MRC5 treated by tumor cell-derived
- 6 conditioned medium determined by CCK-8. C: the quantity of TDE secreted by equal
- 7 quantity of LM3 cells were detected by nanoparticle tracking analysis.



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9 Figure S2.

10 A: PKH26-labelled tumor-derived exosomes were co-incubated with MRC5 cells. 11 The fluorescent photograph showed the exosomes intake ability of MRC5 cells. B. 12 The in vivo distribution of DIR-labelled tumor-derived exosomes at specific time 13 points after injection determined by living imaging system. C: Images taken from the 14 frozen section under fluorescence microscope. D: Schematic diagram of GW4869-15 mediated exosome blocking test. E: Immunofluorescence staining of FAP in the lungs 16 of mice treated with TDE. F: Immunohistochemical staining of POSTN in the lungs 17 of mice treated with TDE.

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22 Figure S3.

- 23 A: MDSC differentiation of mice monocytes cultured in TDE-treated WML2
- 24 conditioned medium was detected by flow cytometry. B: The level of
- 25 immunosuppressive factors expressed in mice monocytes which were cultured in
- 26 TDE-treated WML2 conditioned medium was determined by qRT-PCR. C: The tumor
- 27 stemness markers including SOX2, OCT4 and NANOG expressed in LM3 tumor cells

- treated with conditioned medium from educated MRC5 cells. D: Representative
- 29 panoramic paragraph of H&E-stained slides from pulmonary tissue of mice treated
- 30 with TDEs and injected i.v. with H22 tumor cells. E: The effect of miR-4508 on the
- 31 migration ability of MRC5 cells determined by transwell assay. **P<0.01.



33 Fig. S4.

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A: The effect of miR-4508 and hypoxia environment on the migration ability of LM3
tumor cells determined by transwell assay. B: The effect of miR-4508 and hypoxia
environment on the proliferation ability of LM3 tumor cells determined by CCK8
assay. **P<0.01.



- **39 Figure S5.**
- 40 Pathway analysis of downstream signals of miR-4508.

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