Supplementary Materials for

Therapeutic targeting miR130b counteracts diffuse large B-cell lymphoma progression via OX40/OX40L-mediated interaction with Th17 cells

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| Characteristics                  | PFS             |       | OS             |       |
|---------------------------------|-----------------|-------|----------------|-------|
|                                 | HR (95% CI)     | P value | HR (95% CI)     | P value |
| Sex                             |                 |       |                |       |
| Female                          | 1.243           | 0.190 | 1.233          | 0.290 |
| Male                            |                 |       |                |       |
| Age                             |                 |       |                |       |
| > 60 years                      | 1.567           | 0.006 | 2.471          | <0.001|
| ≤ 60 years                      |                 |       |                |       |
| ECOG                            |                 |       |                |       |
| 0-1                             | 2.394           | <0.001| 2.413          | <0.001|
| 2                               |                 |       |                |       |
| Ann Arbor                       |                 |       |                |       |
| I-II                            | 3.406           | <0.001| 3.349          | <0.001|
| III-IV                          |                 |       |                |       |
| Extranodal involvement          |                 |       |                |       |
| No                              | 1.381           | 0.051 | 1.349          | 0.133 |
| Yes                             |                 |       |                |       |
| LDH                             |                 |       |                |       |
| Normal                          | 4.060           | <0.001| 3.686          | <0.001|
| Elevated                        |                 |       |                |       |
| International Prognostic Index (IPI) |           |       |                |       |
| 0-2                             | 3.397           | <0.001| 3.462          | <0.001|
| 3+5                             |                 |       |                |       |
| MiR130b                         |                 |       |                |       |
| Low                             | 3.232           | <0.001| 2.642          | <0.001|
| High                            |                 |       | 1.720-4.060    | <0.001|
| Variable | HR   | (95% CI)     | P value |
|----------|------|--------------|---------|
| PFS      |      |              |         |
| IPI      | 3.115| 2.236-4.339  | <0.001  |
| MiR130b  | 2.940| 2.024-4.272  | <0.001  |
| OS       |      |              |         |
| IPI      | 3.147| 2.104-4.707  | <0.001  |
| MiR130b  | 2.302| 1.494-3.548  | 0.008   |
Supplementary Fig. 1 Transfection efficiency of miR130b. a Real-time PCR analysis of miR130b expression in DB cells and OCI-ly10 cells. b Real-time PCR analysis of miR130b expression in DB cells transfected with control mimics or miR130b mimics, and OCI-ly10 cells
transfected with control inhibitor or miR130b inhibitor. c Real-time PCR analysis of IFNAR1, IFNAR2, STAT1, STAT2, STAT3 and OX40L on DB cells transfected with control mimics, miR130b mimics and OCI-ly10 cells transfected with control inhibitor, miR130b inhibitor. Data are summarized as mean ± SD (n=3). d Western blot analysis of IFNAR1, IFNAR2, p-STAT1, STAT1, p-STAT2, STAT2, p-STAT3, STAT3 and OX40L on DB cells transfected with control mimics, miR130b mimics and OCI-ly10 cells transfected with control inhibitor, miR130b inhibitor.
Supplementary Fig. 2 Representative flow cytometry images of miR130b modulated OX40/OX40L-mediated B-lymphoma cell interaction with Th17 cells via IFNAR1/p-STAT1 axis. a Representative flow cytometry images of OX40L expression on miR130b mimics
transfected DB co-culture system and miR130b inhibitor transfected OCI-ly10 co-culture system. 

b Representative flow cytometry images of OX40L expression in the IFNAR1-knockdown DB co-culture system and IFNAR1-overexpressing OCI-ly10 co-culture system. c Representative flow cytometry images of OX40 expression in the IFNAR1-knockdown DB co-culture system and IFNAR1-overexpressing OCI-ly10 co-culture system. d Representative flow cytometry images of OX40L expression in the STAT1-knockdown DB co-culture system and STAT1-overexpressing OCI-ly10 co-culture system. e Representative flow cytometry images of OX40 expression in the STAT1-knockdown DB co-culture system and STAT1-overexpressing OCI-ly10 co-culture system. f Representative flow cytometry images of OX40L expression in DB cells and OCI-ly10 cells upon treatment with p-STAT1 inhibitor. g Representative flow cytometry images of OX40L expression in the STAT1^{Y701F} DB cells and STAT1^{Y701F} OCI-ly10 cells. h Representative flow cytometry images of Th17 cell percentage in the OX40L-knockdown DB co-culture system and OX40L-overexpressing OCI-ly10 co-culture system.
Supplementary Fig. 3 MiR130b regulated immune checkpoint genes. a Flow cytometry analysis of immune checkpoint genes in the control mimics or miR130b mimics transfected DB co-culture system. Data are summarized as mean ± SD (n=3). b Flow cytometry analysis of immune checkpoint genes in the control inhibitor or miR130b inhibitor transfected OCI-ly10 co-culture system. Data are summarized as mean ± SD (n=3).
Supplementary Fig. 4 Intracellular distribution and transfection efficiency of Cy5.5/Fam-labeled LNPs-miR130b control and Cy5.5/Fam-labeled LNPs-miR130b. a The particle size distribution, hydrodynamic size and zeta potential of the LNPs, LNPs-miR130b control and LNPs-miR130b antagonim. b Transmission electron microscope images of the LNPs, LNPs-miR130b control and LNPs-miR130b antagonim (negatively stained by phosphotungstic acid). c Immunofluorescence assay of LNPs and nucleotide in DB cells (left panel) and OCI-ly10 cells (right panel) transfected with Cy5.5/Fam-labeled LNPs-miR130b control or Cy5.5/Fam-labeled LNPs-miR130b antagonim. d Real-time PCR analysis of miR130b expression in DB cells transfected with Cy5.5/Fam-labeled LNPs-miR130b control or Cy5.5/Fam-labeled LNPs-miR130b antagonim and OCI-ly10 cells transfected with Cy5.5/Fam-labeled LNPs-miR130b control or Cy5.5/Fam-labeled LNPs-miR130b antagonim. Data are summarized as mean ± SD (n=3).
Supplementary Fig. 5 MiR130b regulated immune cell accumulation and cytokine secretion

a Flow cytometry analysis of immune cell subsets in the control mimics or miR130b mimics transfected DB co-culture system upon treatment with LNP-s-miR130b control or LNP-s-miR130b...
antagomir. Data are summarized as mean ± SD (n=3). b Flow cytometry analysis of immune cell subsets in the control inhibitor or miR130b inhibitor transfected OCI-ly10 co-culture system upon treatment with LNPs-miR130b control or LNPs-miR130b antagonir. Data are summarized as mean ± SD (n=3). c ELISA analysis of related immunological cytokines in the control mimics or miR130b mimics transfected DB co-culture system upon treatment with LNPs-miR130b control or LNPs-miR130b antagonir. Data are summarized as mean ± SD (n=3). d ELISA analysis of related immunological cytokines in the control inhibitor or miR130b inhibitor transfected OCI-ly10 co-culture system upon treatment with LNPs-miR130b control and LNPs-miR130b antagonir. Data are summarized as mean ± SD (n=3).
**Supplementary Fig. 6 MiR130b mediated tumor apoptosis and cell cycle.**

**a** Flow cytometry analysis of DB cell apoptosis in the control mimics or miR130b mimics transfected DB co-culture system upon treatment with or without OX40 agonistic antibody.

**b** Flow cytometry analysis of OCI-ly10 cell apoptosis in the control inhibitor or miR130b inhibitor transfected OCI-ly10 co-culture system upon treatment with or without OX40 agonistic antibody.

**c** Flow cytometry analysis of DB cell cycle in the control mimics or miR130b mimics transfected DB co-culture system upon treatment with or without OX40 agonistic antibody.

**d** Flow cytometry analysis of OCI-ly10 cell cycle in the control inhibitor or miR130b inhibitor transfected OCI-ly10 co-culture system upon treatment with or without OX40 agonistic antibody.
Supplementary Fig. 7  IL17 inhibitor mediated tumor autophagy. a Cell growth in the control mimics or miR130b mimics transfected DB co-culture system upon treatment with or without IL17 inhibitor. MTT assay was adopted to measure cell viability. Data are summarized as mean ± SD (n=3). b Cell growth in the control inhibitor or miR130b inhibitor transfected OCI-ly10 co-culture system upon treatment with or without IL17 inhibitor. MTT assay was adopted to measure cell viability. Data are summarized as mean ± SD (n=3). c Transmission electron microscope showed typical autophagosomes in the control mimics or miR130b mimics transfected DB co-culture system and control inhibitor or miR130b inhibitor transfected OCI-ly10 co-culture system upon treatment with or without IL17 inhibitor. The cells were counted from five visions selected at random and subjected for statistical analysis. Data are summarized as mean ± SD (n=5).