

Supplementary Fig. 1 Related to Fig. 1

Human PBMCs derived macrophages were treated with HCC827-MPs at the ratio 1: 20 (macrophages: MPs). 12 h later, *IL-12*, *iNOS* and *TNF-* α expression was analyzed by real-time PCR. Error bars indicate mean ± SEM; n=3 independent experiments. **P* < 0.05, *****P* < 0.0001.



Supplementary Fig. 2 Related to Fig. 1

Human PBMCs derived macrophages were treated with HCC827-MPs at the ratio 1: 20 (macrophages: MPs). 24 h later, mean fluorescence intensity of CD163 and CD206 expression was analyzed by flow cytometry. Error bars indicate mean \pm SEM; n=3 independent experiments. ****P* < 0.001.



Supplementary Fig. 3 Related to Fig. 1

Human PBMCs derived macrophages were treated with 100ng/ml LPS for 12 h and then incubated with HCC827-MPs at the ratio 1: 20 (macrophages: MPs). Another 12 h later, *IL-10*, *VEGF* and *arginase-1* expression were analyzed by real-time PCR. Error bars indicate mean \pm SEM; n=3 independent experiments. **P < 0.01, ****P < 0.0001.



Supplementary Fig. 4 Related to Fig. 1

Human PBMCs derived macrophages (left) were treated with HepG2-MPs, A375-MPs or HCC827-MPs at the ratio 1: 20 (macrophages: MPs). 12 h later, *IL-1* β expression was analyzed by real-time PCR. Mouse BMDMs (right) were treated with Hepa1-6-MPs, B16-MPs or Lewis-MPs at the ratio 1: 20 (macrophages: MPs) for 12 h. Then *IL-1* β mRNA levels were analyzed by real-time PCR. Error bars indicate mean \pm SEM; n=3 independent experiments. **P* < 0.05, ***P* < 0.01, ****P* < 0.001, *****P* < 0.0001.



Supplementary Fig. 5 Related to Fig. 1

The sizes of HCC827-MPs and Lewis-MPs were detected by Nanoparticle tracking analysis (NS300, Malvern) (A); MHC class I on the surface of HCC827-MPs and Lewis-MPs were detected by flow cytometry (B); MHC class I, Heat shock protein 70 (HSP 70), β -tubulin, histone H2B and apolipoprotein B(ALB) of MPs were detected by western blotting, cells, apoptotic bodies and serum were as positive or negative controls (C).



Supplementary Fig. 6 Related to Fig. 2

Mouse BMDMs (left) or human PBMCs derived macrophages (right) were transfected with *TLR7*, *TLR8* or *TLR9* siRNA, and then treated with Lewis-MPs or HCC827-MPs respectively. 12 h later, *IL-1* β mRNA levels were analyzed by real-time PCR. Error bars indicate mean ± SEM; n=3 independent experiments. ***P < 0.001, ****P < 0.0001.

| Top enriched NO. | Gene short name | Ensembl ID | Туре |
|------------------|-----------------|----------------------|----------|
| 1 | Vaultre5 | ENSMUSG0000065145.1 | misc RNA |
| 2 | Rpph1 | ENSMUSG0000092837.1 | ribozyme |
| 3 | Rmrp | ENSMUSG0000088088.1 | ribozyme |
| 4 | Gm22513 | ENSMUSG0000096349.1 | snRNA |
| 5 | Gm24265 | ENSMUSG0000096243.1 | snRNA |
| 6 | Gm24407 | ENSMUSG0000094377.1 | snRNA |
| 7 | Gm25939 | ENSMUSG0000093843.1 | snRNA |
| 8 | CT010467.1 | ENSMUSG00000106106.2 | rRNA |
| 9 | Rny1 | ENSMUSG0000065701.1 | misc RNA |
| 10 | Gm26917 | ENSMUSG0000097971.3 | lincRNA |

Supplementary Fig. 7 Related to Fig. 3

Ensembl ID and type of the top 10 enriched non-coding RNAs in L-MPs were shown and available from the database http://asia.ensembl.org.



Supplementary Fig. 8 Related to Fig. 3

The secondary structure of U2 and U4 was shown and available from the database http://asia.ensembl.org



Supplementary Fig. 9 Related to Fig. 4

Mouse BMDMs were treated with Lewis-MPs at the ratio 1: 20 (macrophages: MPs) for 24h in the presence of NAC or not. Cells were collected, *caspase-1* and *IL-1\beta* mRNA levels were analyzed by real-time PCR (A); Cell lysate were pulled down by anti-NLRP3 antibody and then ASC were detected by western blotting (B).



Supplementary Fig. 10 Related to Fig. 6

 5×10^4 Lewis tumor cells were injected into the right thigh muscle of mice. Ten days later, 5×10^6 Lewis-MPs were injected into tumor once two days for three times. On day 15, mice were sacrificed and tumor tissue sections were stained with CD31 antibody and the density were counted by random visual field. Error bars indicate mean \pm SEM. ***P* < 0.01. Scale bar: 100 µm.



Supplementary Fig. 11 Related to Fig. 6

 5×10^4 Lewis tumor cells were injected into the right thigh muscle of mice. Ten days later, 5×10^6 Lewis-MPs were injected into tumor once two days for three times. On day 15, mice were sacrificed, tumor cells were collected and incubated with BrdU for 1h and then cells were stained with FITC labeled anti-BrdU antibody and analyzed by flow cytometry (A); tumor tissue section were analyzed by TUNEL assay and TUNEL positive cells were counted by fluorescence microscope (B). Error bars indicate mean ± SEM. **P* < 0.05, ***P* < 0.01. Scale bar: 100 µm.



Supplementary Fig. 12 Related to Fig. 6

 5×10^4 Lewis tumor cells were injected into the right thigh muscle of mice. Ten days later, 5×10^6 Lewis-MPs were injected into tumor once two days for three times. On day 15, mice were sacrificed, and immune cells proportion in the spleen, lymph node (LN), peripheral blood and tumor were analyzed by flow cytometry. Error bars indicate mean ± SEM. **P* < 0.05, ****P* < 0.001.



Supplementary Fig. 13 Related to Fig. 6

Lewis cells were seeded in 90 pa 3D fibrin gels in the presence of 1ng/ml IL-1 β or not. TRCs were collected on day 5, and then *c-kit* and *nanog* mRNA were detected by real time PCR(A); The tumor colony size was observed and analyzed under microscope (B). Error bars indicate mean ± SEM. ***P* < 0.01, *****P* < 0.0001. Scale bar: 20 µm.



Supplementary Fig. 14 Related to Fig. 7

Humanized mice model was established as described in methods. 9 weeks after CD34⁺ HSCs transplantation, cells from PBMCs, bone marrow, and lymphocytes from spleen, liver and lung were stained with human CD45, CD3, CD19, CD56 or CD14 antibody and analyzed by flow cytometry.



Supplementary Fig. 15 Related to Fig 7

Tumor sections were labeled by immunofluorescence assay to indicate the distribution of human macrophages (CD68 red). Cell nucleus was stained by DAPI (blue). Scale bar for $200 \times$, 100 µm. Scale bar for $400 \times$, 200 µm.

Supplementary Table 1

| Gene name | Sequence | Gene name | Sequence |
|--------------------|---------------------|--------------------|---------------------|
| mouse | | | |
| si-caspase-1-1 | GAAGGCCCATATAGAGAAA | si-NLRP3-1 | GTACTTAAATCGTGAAACA |
| si-caspase-1-2 | CCAAGGTGATCATTATTCA | si-NLRP3-2 | CAGCCAGAGTGGAATGACA |
| si-NLRP1b-1 | GCAAGGAATTCCAACTCTT | si- <i>TLR3</i> -1 | GAATCTTACTCACAACCAA |
| si-NLRP1b-2 | GCTGCCAACTAAAGACTTT | si- <i>TLR3</i> -2 | GTATTGAACCTGCAACATA |
| si-AIM2-1 | GGAACAGGCTGCTACAGAA | si- <i>TLR7</i> -1 | CTAGAGCTCTATCTTTATA |
| si-AIM2-2 | GGTCACCAGTTCCTCAGTT | si- <i>TLR7</i> -2 | CAACAACCGGCTTGATTTA |
| si-mucolipin 2-1 | GCTGTAGCATATACACTCA | si- <i>TLR8</i> -1 | CCAATACTCAAGTGTTTAA |
| si-mucolipin 2-2 | GCAGTTCATTCCCGAGAGA | si- <i>TLR</i> 8-2 | CTACCAAGTTCTCTAAGGA |
| si- <i>TLR9</i> -1 | GCCTCTCCTTGATCTCCAA | | |
| si- <i>TLR9</i> -2 | CCATCTGTCTCTGAAGTAT | | |
| human | | | |
| si- <i>TLR3</i> -1 | GCACGAATTTGACTGAACT | si- <i>TLR7</i> -1 | GGGTATCAGCGTCTAATAT |
| si- <i>TLR3</i> -2 | GTTGAACCTTACCCATAAT | si- <i>TLR7</i> -2 | AATTGCCCTCGTTGTTATA |
| si- <i>TLR</i> 8-1 | GAACGGAAATCCCGGTATA | si- <i>TLR9</i> -1 | GCAGACACTGTGTGCACAT |
| si- <i>TLR</i> 8-2 | CTTCCAAACTTATCGACTA | si- <i>TLR9</i> -2 | CCCACCAGCTAATCCTGTT |

Supplementary Table 2

| Gene name | Forward primer | Reverse primer |
|----------------|-------------------------|------------------------|
| human | | |
| β -actin | CATTGCTGACAGGATGCAGAAGG | TGCTGGAAGGTGGACAGTGAGG |
| IL-10 | TCTCCGAGATGCCTTCAGCAGA | TCAGACAAGGCTTGGCAACCCA |
| VEGF | TTGCCTTGCTGCTCTACCTCCA | GATGGCAGTAGCTGCGCTGATA |
| arginase 1 | TCATCTGGGTGGATGCTCACAC | GAGAATCCTGGCACATCGGGAA |
| IL-1β | TGGACCTTCCAGGATGAGGACA | GTTCATCTCGGAGCCTGTAGTG |
| mouse | | |
| β -actin | CATTGCTGACAGGATGCAGAAGG | TGCTGGAAGGTGGACAGTGAGG |
| IL-1β | TGGACCTTCCAGGATGAGGACA | GTTCATCTCGGAGCCTGTAGTG |
| mucolipin 1 | GTCGGTGTCATTCGCTACCTGA | GAACGATCCAGCCACAGAAGCA |
| mucolipin 2 | TACGTCCTGGTCACTATCAGCG | GAGCAAGATGCTGCACACGTCA |
| TPC1 | CCCTGGAGTTACCTCGTGTTTC | GAATGCCGTGACCGAGAAATCG |
| TPC2 | CATCCACCTGTGTCTCTTCACC | GTGAGGTCAGTGCTTCTGGAAG |
| Nanog | GAACGCCTCATCAATGCCTGCA | GAATCAGGGCTGCCTTGAAGAG |
| c-kit | GAGTTCCATAGACTCCAGCGTC | AATGAGCAGCGGCGTGAACAGA |