## **Supplementary Information Titles**

Please list each supplementary item and its title or caption, in the order shown below.

Note that we do NOT copy edit or otherwise change supplementary information, and minor (nonfactual) errors in these documents cannot be corrected after publication. Please submit document(s) exactly as you want them to appear, with all text, images, legends and references in the desired order, and check carefully for errors.

## Journal: Nature Medicine

| Article Title: | LTB4 causes macrophage-mediated inflammation and directly induces |
|----------------|-------------------------------------------------------------------|
|                | insulin resistance in obesity                                     |
| Corresponding  | Jerrold M. Olefsky                                                |
| Author:        |                                                                   |
|                |                                                                   |

| Supplementary<br>Item & Number<br>(add rows as necessary) | Title or Caption                                                                                                                                                                            |
|-----------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Supplementary Figure 1                                    | GTT in WT and Ltb4r1 KO mice fed chow.                                                                                                                                                      |
| Supplementary Figure 2                                    | GTT of HFD female ovariectomized (OVX) mice treated with vehicle or Ltb4r1 inhibitor.                                                                                                       |
| Supplementary Figure 3                                    | Effect of Ltb4r1 inhibitor treatment on viability of RAW cells.                                                                                                                             |
| Supplementary Figure 4                                    | Fluorescence minus one (FMO) for the FACS analysis. Epididymal fat pads were dissected and separated into adipocyte and SVC populations.                                                    |
| Supplementary Figure 5                                    | Effect of Ltb4r1 inhibitor treatment (2 weeks) in adipose tissue.                                                                                                                           |
| Supplementary Figure 6                                    | Effect of pertussis toxin (PT) pretreatment on p-Akt in (a) L6 myocytes and (b) hepatocytes                                                                                                 |
| Supplementary Figure 7                                    | Effect of Jnk inhibitor treatment on glucose uptake and p-Akt in L6 cells                                                                                                                   |
| Supplementary Figure 8                                    | <ul><li>(a) Effect of Ltb4r1 inhibitor on LTB4 induced hepatic glucose production in primary hepatocytes. (b) Effect of LTB4 on glucose uptake in 3T3L1 differentiated adipocyte.</li></ul> |



**Supplementary Fig.1** GTT in WT and Ltb4r1 KO mice fed chow. Data were analyzed by two-way ANOVA followed by Bonferroni post tests. Values are expressed as mean  $\pm$  s.e.m. n=8.



**Supplementary Fig. 2** GTT of HFD female ovariectomized (OVX) mice treated with vehicle or Ltb4r1 inhibitor. Data were analyzed by two-way ANOVA followed by Bonferroni post tests. Values are expressed as mean  $\pm$  s.e.m. n=10. \* P<0.05, \*\* P<0.01 for vehicle versus treatment.



**Supplementary Fig. 3** Effect of Ltb4r1 inhibitor treatment on viability of RAW cells. Data were analyzed by two-way ANOVA followed by Bonferroni post tests. Values are expressed as mean ± s.e.m. n=6.



**Supplementary Fig. 4** Fluorescence minus one (FMO) for the FACS analysis. Epididymal fat pads were dissected and separated into adipocyte and SVC populations. Stromal vascular cells (SVCs) were stained with antibody with F4/80-APC, CD11b-FITC, CD11c-PE or PI. (**a**) SVCs were stained with CD11b-FITC, CD11c-PE, and PI. (**b**) SVCs were stained with F4/80-APC, CD11b-FITC and PI. (**c**) SVCs were stained with F4/80-APC, CD11c-PE and PI.

## Supplementary Fig.5 Li



**Supplementary Fig. 5** Effect of Ltb4r1 inhibitor treatment (2 weeks) in adipose tissue. (**a**) Epi-WAT mass. (**b**) HE staining of Epi-WAT. (**c**) Effect of LTB4 on insulin induced Glut4 translocation to the plasma membrane in L6 cells. Data were analyzed by two-way ANOVA followed by Bonferroni post tests. Values are **empars** stedies on. n=6 in a-b. Western blot data are represented of more than 3 independent experiments.

Supplementary Fig.6 Li

## **a** L6 myocytes



**Supplementary Fig. 6** Effect of pertussis toxin (PT) pretreatment on p-Akt in (a) L6 myocytes and (b) hepatocytes. Western blot data are represented of more than 3 independent experiments.

Supplementary Fig.7 Li



**Supplementary Fig. 7** Effect of Jnk inhibitor treatment on glucose uptake and p-Akt in L6 cells. Data were analyzed by two-way ANOVA followed by Bonferroni post tests. Values are expressed as mean ± s.e.m. n=6. Western blot data are represented of more than 3 independent experiments.

а

b







**Supplementary Fig. 8** (a) Effect of Ltb4r1 inhibitor on LTB4 induced hepatic glucose production in primary hepatocytes. (b). Effect of LTB4 on glucose uptake in 3T3L1 differentiated adipocyte. Data were analyzed by two-way ANOVA followed by Bonferroni post tests. Values are expressed as mean ± s.e.m. n=6. \*\* P<0.01.