Supplementary method

Animals.

For BMS309403 treatment, female 4-week old NOD mice were treated with FABP4 pharmacological inhibitor BMS309403 (40 mg kg\(^{-1}\)d\(^{-1}\)) or vehicle (PBS) by oral gavage for 8 weeks. For depletion of macrophages, 2-week old FABP4\(^{+/+}\)NOD and FABP4\(^{-/-}\)NOD mice received Gdcl3 (1mg kg\(^{-1}\), every 3 days, i.v., Sigma–Aldrich) for 6 weeks. To monitor the effect of FABP4 deficiency on development of T1D, a large number of mice (n=18-20) were used in each group and monitored the diabetes incidence till 30 weeks. To investigate the changes in immune cells and insulitis caused by FABP4 deficiency, independent sets of experiment were designed, and 5-6 mice in each group were sacrificed in each group at different time point, and the experiments were repeated at least twice independently.

Flow cytometry analysis.
For analysis of macrophages, DCs, neutrophils and NK cells were stained with rat anti-mouse F4/80-FITC (1:100, clone BM8, Biolegend), rat anti-mouse CD11b-BV421 (1:100, clone M1/70, BD Biosciences), hamster anti-mouse CD11c-PE (1:100, clone HL3, BD Biosciences), and rat anti-mouse CD206-Alexa Fluor® 647 (1:100, clone C068C2, Biolegend), rat anti-mouse Ly-6G-FITC (1:100, clone 1A8, Biolegend), rat anti-mouse CD123-PE (1:100, clone 5B11, Biolegend), rat anti-mouse CD335-APC (1:100, clone 29A1.4, Biolegend) or their isotype controls (Biolegend) respectively on ice for 30 min in dark. For analysis of T lymphocytes, cells were stained with rat anti-mouse CD3-APC (1:100, clone 17A2, Biolegend), rat anti-mouse CD4-FITC (1:100, clone GK1.5, Biolegend), rat anti-mouse CD8a-PE (1:100, clone 53-6.7, BD Biosciences), rat anti-mouse CD8a-Alexa Fluor® 594 (1:100, clone GK1.5, Biolegend), rat anti-mouse CD8a-Alexa Fluor® 647 (1:100, clone 53-6.7, Biolegend) on ice for 30 min in dark. For analysis of Treg cells, cells were first stained with Rat mAb against mouse CD4-FITC (1:100, clone GK1.5, Biolegend) and then incubated
in the FoxP3 Fixation/Permeabilization working solution (eBioscience, San Diego, USA), followed by staining with Rat mAb against mouse Foxp3 (1:80, clone R16715, BD Biosciences) for 1 hour. For staining of intracellular cytokines including IFN-γ, IL-4, IL-17, granzyme B, perforin, cells were cultured in RPMI 1640 medium supplemented with 10% FBS and stimulated with phorbol 12-myristate 13-acetate (PMA, 50 ng ml⁻¹, Sigma) and ionomycin (1 μg ml⁻¹, Sigma) for 5 hours in the presence of GolgiStopTM protein transport inhibitor (BD Biosciences, New Jersey, USA). Afterwards, cells were collected and stained with rat anti-mouse CD8a-Alexa Fluor® 594 (1:100, Biolegend) or rat anti-mouse CD4-FITC (1:100, clone GK1.5, Biolegend) and fixed in 2% (w/v) paraformaldehyde or 25 min on ice. After washing with PBS containing 0.2% saponin twice, cells were subsequently stained with rat anti-mouse IFN-γ-Alex Fluor 647 (1:50, clone XMG1.2, BD Biosciences), rat anti-mouse IL-4-PE (1:50, clone 11B11, BD Biosciences), rat anti-mouse IL-17A-PE (1:50, clone TC11-18H10, BD Biosciences), mouse anti-human/mouse granzyme B-PE (1:50, clone QA16A02, Biolegend), rat anti-mouse perforin-PE (1:50, clone S16009B,
Biolegend) or their isotype controls (Biolegend) respectively in the presence of 0.2% saponin for 1 hour on ice in dark.

**Histological and immunohistochemistry analysis.**

Paraffin-embedded pancreas tissue was prepared at the thickness of approximately 5 μm. Deparaffinized and dehydrated sections were stained with haematoxylin and eosin (Sigma-Aldrich) as previously described. For the immunofluorescent staining, sections were incubated with a primary antibody against insulin (1 mg ml⁻¹, mouse monoclonal; Antibody and Immunoassay Services, University of Hong Kong, cleaved Caspase 3 (5 mg ml⁻¹, rabbit polyclonal; 9664, Cell Signaling, Beverly, MA, USA), F4/80 (5 mg ml⁻¹, rat polyclonal; Abcam, UK), FABP4 (2.5 mg ml⁻¹, goat polyclonal; AF1443, R&D Systems), Alexa Fluor 488-Ly6G (1:50, clone 1A8, 127626, Bio-legend), CD123 (1:50, clone 5B11, Bio-legend), CD335 (1:50, clone 29 1.4, Bio-legend), followed by incubation with Alexa Fluor 488 or 594-labeled or HRP-conjugated secondary antibodies as specified in each figure legend. The sections were
visualized under a fluorescence microscope (QImaging, Olympus IX71, USA) after counterstaining with DAPI.

Adoptive transfer of T cell.

CD4$^+$ or CD8$^+$ T lymphocytes from 6-week-old FABP4$^{+/+}$NOD or FABP4$^{-/-}$NOD mice were enriched from pooled spleen by depletion of non-T cells with magnetic beads (CD4$^+$ T Cell Isolation Kit, Miltenyi Biotech; CD8$^+$ T Cell Isolation Kit, Miltenyi Biotech). CD4$^+$ or CD8$^+$T lymphocytes were purified by FACS sorting. Isolated T cells were labeled with 5 μM CFSE (Molecular Probes) at a density of 50 × 10$^6$ cells/ml in Hanks’ balanced salt solution (HBSS; Invitrogen, Carlsbad, CA) at room temperature for 5 min. Afterwards, cells were washed three times in HBSS and adjusted to approximately 5 × 10$^6$ T cells per 0.2 ml PBS. Labeled CD4$^+$ or CD8$^+$T cells were i.p injected into 6-week-old FABP4$^{-/-}$NOD mice. Pancreatic lymph node cells were isolated from one batch of mice 6 days after adoptive transfer, flow cytometry to confirm the success of
the T cell transfer. Diabetes incidence in FABP4−/−NOD mice was monitored till 16 weeks after adoptive transfer of diabetogenic T cells.