**Supplementary Data**

## S1. LC-HRMS Instrumentation and Analytical Conditions

**Instrumentation.**
LC-HRMS analyses were conducted using a Thermo Scientific™ Vanquish™ UHPLC Binary Pump system coupled with an Orbitrap high-resolution mass spectrometer (Thermo Fisher Scientific Inc., Waltham, MA, USA).

**Chromatographic Conditions.**
Analyses were performed on a Thermo Scientific Accucore Phenyl-Hexyl column (100 mm × 2.1 mm ID, 2.6 µm particle size), maintained at 40 °C. The mobile phases consisted of:

- **A:** MS-grade water with 0.1% formic acid
- **B:** MS-grade methanol with 0.1% formic acid

A gradient program was employed at a flow rate of 0.3 mL/min as follows:

- 0–16 min: B increased to 90%
- 16–20 min: B maintained at 90%
- 20–25 min: returned to 5%
  The injection volume was 3 µL.

**Mass Spectrometry Conditions.**
Mass spectrometric detection was carried out in **positive electrospray ionization (ESI+) mode** with the following settings:

- Capillary voltage: **3.30 kV**
- Capillary temperature: **320 °C**
- Scan range: **m/z 66.7–1000**

Data acquisition was performed using **full-MS data-dependent MS2 (ddMS2)** mode.

**Data Processing and Compound Annotation.**
Raw data were processed using Thermo Scientific™ Compound Discoverer™ 3.3 software, including feature alignment, peak detection, and baseline correction. Fragmentation patterns were evaluated using the HighChem Fragmentation Library and matched against reference databases:

- **ChemSpider** (www.chemspider.com)
- **mzCloud** (www.mzcloud.org)

Additional data handling and visualization were carried out using Xcalibur™ 4.7 software.

**S2. HbA1C Procedure**

A total of 2 µL of erythrocyte lysates was used for the HbA1c analysis. A calibration curve was created using HbA1c concentrations of 200, 100, 50, 25, 12.5, 6.26, and 3.125 ng/mL. Erythrocyte lysates were diluted 1:10,000. After washing the wells, 100 µL of various standard concentrations was dispensed into each well. Subsequently, 100 µL of diluent was introduced into the blank well, while 100 µL of the erythrocyte lysate specimen was applied to the wells coated with the HbA1c monoclonal antibody, followed by incubation at 37 °C for 2 hours. The plate underwent three successive washes. Subsequently, each well received 100 µL of the biotin-labeled antibody conjugate and was incubated at 37 °C for one hour. Following this, the wells were washed three times before adding 100 µL of streptavidin-horseradish peroxidase (HRP), then incubated at 37 °C for 30 minutes. After another series of three washes, 90 µL of the 3,3',5,5'-tetramethylbenzidine (TMB) substrate was introduced into each well. The plate was gently agitated to ensure uniform mixing and incubated in the dark at 37 °C for 15 minutes to allow color development. Finally, absorbance readings were taken at 450 nm using a microplate spectrophotometer (Multiskan FC, Thermo Fisher, China). HbA1c concentration was calculated from the calibration curve.

**S3. Histological Preparation and H&E Staining Protocol (15,16)**

**Fixation and Tissue Processing.**
Pancreatic tissues were rinsed in 0.9% NaCl and fixed in 10% neutral buffered formalin at room temperature for 48 hours. Fixed tissues were cut into 0.5–1 cm slices, placed into labeled cassettes, and processed through a graded ethanol series (70%, 90%, and 100%), followed by clearing in toluene. Paraffin infiltration was performed in two stages (2 h and 3 h), and tissues were embedded into paraffin blocks.

**Sectioning and Slide Preparation.**
Paraffin blocks were sectioned at 5–6 µm thickness using a rotary microtome. Sections were floated on a 40 °C water bath and mounted on gelatin-coated glass slides (5 g gelatin in 100 mL distilled water). Slides were air-dried on a warming plate for approximately 1 hour prior to staining.

**Hematoxylin–Eosin Staining.**
Deparaffinization was performed with xylene (2 × 2 min), followed by rehydration through graded ethanol (100% and 95%, each 1 min × 2 repeats). Slides were stained with Mayer's hematoxylin for 15 min and rinsed under running tap water for 20 min. Counterstaining with eosin was performed for 2 min. Slides were dehydrated through 95% and 100% ethanol (2 × 2 min each) and cleared in xylene (3 × 2 min). Finally, slides were mounted with coverslips.

**Histological Analysis.**
Only sections containing at least 10 islets of Langerhans were selected. The diameters of islets were measured, averaged, and statistically analyzed. Microscopic evaluation was performed using a bright-field light microscope at 400× magnification.

**S4. Immunohistochemistry (IHC) Procedure**

**Washing and Blocking.**
Residual substances were removed by washing tissue sections with phosphate-buffered saline (PBS; pH 7.4) for 3 minutes. The slides were then treated with the Dako REAL EnVision Detection System and incubated for 30 minutes at room temperature.

**DAB Development.**
Following incubation, the slides were washed with PBS containing Tween 20. Chromogenic development was performed by applying 3,3’-diaminobenzidine (DAB) substrate buffer (Dako) for 2–5 minutes, after which the sections were rinsed under running tap water for 10 minutes.

**Counterstaining and Dehydration.**
Sections were counterstained with hematoxylin for 1–2 minutes, rinsed again for 5 minutes, and then dehydrated sequentially in 70%, 80%, 96%, and absolute ethanol (5 minutes each).

**Clearing and Mounting.**
Tissue sections were cleared in xylene (three changes, 5 minutes each). Finally, slides were mounted using a permanent mounting medium and covered with glass coverslips.