SUPPLEMENTARY MATERIAL

Supplementary Figure S1. Purification of conglutin proteins β1, β2, β3, β4, and β6. (A) Five purified β-conglutin proteins were stained with Coomassie, with a high level of purity (> 95%). (B) Immunoblotting shows the same five purified β-conglutin proteins identified by the anti- β-conglutin antibody. **MW**, molecular weight standard (kDa).

Supplementary Figure S2. Insulin resistance cell model. (A) Increasing concentrations of insulin from $3x10^{-5}$ to $3x10^{-9}$ nmol/L showed that C cell culture did uptake the lower level of glucose at $3x10^{-7}$ nmol/L, taking this concentration as the level of insulin where cells acquired the resistance state. (B) C cells were cultured for one, two and three days, testing the glucose uptake of cultures including $3x10^{-7}$ nmol/L (white bars), in comparison to control C cells (black bars). In these assays were showed that insulin resistance state is preserved for 48 hours.

p*<0.05 IR-C *vs* C.

Supplementary Table S1. Cell viability (%) and dose effects of each purified NLL β-conglutin proteins (β1, β3 β6, β2, and β4) on insulin resistance cell model.

Cytotoxicity of β1, β3, β6, β2, and β4 assayed on IR—C pancreatic cells. Cells were treated with 5µg and 10µg of individual β-conglutin isoforms or a mix including all β-conglutins for 24h. Data represent cell viability (%) corresponding to three independent experiments (mean ± SEM). Control sample was assayed only with insulin.

Samples	**5µg**	**10µg**
Control	100	100
β1	114.0 ± 8.6	82.0 ± 3.6
β2	114.0 ± 3.8	88.0 ± 1.8
β3	106.0 ± 5.8	96.9 ± 3.1
β4	102.0 ± 2.9	89.7 ± 0.5
β6	101.0 ± 1.9	88.9 ± 3.2
β-conglutin mix	99.0 ± 4.7	90.0 ± 1.5

Supplementary Table S2. Characteristics of the study groups. Values represent the median (25th percentile, 75th percentile). To detect differences between groups, we used analysis of variance; statistical significant P-values ($p< 0.01$); bmi, body mass index; HbA1c, glycosylated hemoglobin 1c; BPM, beats per minute; T2D, type 2 diabetes.

Patient characteristics	**Control group**	**T2D**	***P*-value**
Male	14	14	–
Age	50 (40, 53)	48 (45, 58)	0.007
Fasting glycaemia (mg/dL)	83 (80, 91)	165 (132, 198)	<0.001
Blood pressure (mmHg)	12/7 (11/7, 12/7)	15/8 (14/8, 15/7)	<0.001
BMI (kg/m^2)	24.8 (23.0, 26.6)	33.3 (27.5, 46.7)	<0.001
Heart rate (bpm)	64 (65, 76)	84 (96, 80)	<0.001
HbA1c (%)	5.5 (5.4, 5.7)	6.7 (6.0, 7.4)	<0.001

Supplementary Table S3. Effect of NLL conglutin proteins β1, β3 β6, β2, and β4 on inflammation diabetes-related genes in isolated PBMC from type 2 diabetic patients' blood.

Numbers represent fold-change obtained from qPCR array data analysis of inflammation diabetes-related genes. Treatments with β1, β3, β6, β2, and β4, resulted in a significant up- or down-regulation of these genes compared to control patients. Data represent three independent experiments. Values presenting statistical significant (P<0.05) differences with T2DM are depicted in bold.

Gene name	Gene acronym	Up-/Down-regulation*	T2D	β1	β3	β6	β2	β4
Metabolic enzymes								
Glucagon-like peptide 1 receptor	GLP-1R	β2, β4↑	1.00	1	1.68	1.20	**23.68**	**22.93**
Glycogen synthase kinase 3 beta	GSK3B	β1, β3, β6↓	24.76	**3.88**	**2.93**	**2.44**	22.96	25.95
Protein kinase, AMP-activated, α1 catalytic subunit	AMPKα1/PRKAα1	β2↑	27.97	26.95	24.99	22.70	**36.07**	22.05
Protein kinase, AMP-activated, γ2 non-catalytic subunit	AMPKγ2/PRKγ2	β1↑	25.876	**34.70**	26.75	24.90	29.55	25.81
Protein tyrosine phosphatase, non-receptor type 1	PTPN1	β1, β3, β6↓	30.09	**3.72**	**6.13**	**2.97**	34.18	24.99
Cytokines and growth factors								
Interferon, gamma	IFNγ	β1, β3, β6↓	2.36	**–3.73**	**–2.55**	**–3.44**	3.77	6.97
Tumor necrosis factor	TNFα	β1, β3, β6↓	34.39	**5.94**	**2.4**	**2.71**	32.81	22.97
Insulin	INS	β1, β3, β6↑	–6.98	**17.03**	**26.96**	**26.96**	–2.47	–1.73
Cell Signalling								
V-akt murine thymoma viral oncogene homolog 2	AKT2/PKBβ	β1, β3, β6↑	1.40	**20.93**	**25.97**	**21.49**	2.70	2.00
RAB4A, member RAS oncogene family	RAB4A	β1, β3, β6↓	31.09	**8.96**	**3.91**	**2.96**	36.94	23.50

* indicate particular β-conglutin isoforms that up- or down-regulated the mRNA expression level of each gene in comparison with the control (T2D).