SUPPLEMENTARY DATA

Supplementary Table 1. Characteristics of non-diabetic participants of the TUEF population

N=602	all (n=602)		NGT (n=433)		IFG (n=59)		IGT (n=70)		IFG+IGT (n=40)	
	Median/ n (%)	IQR/95 %CI	Median/n (%)	IQR/95% CI	Median /n (%)	IQR/95 %CI	Median /n (%)	IQR/95 %CI	Median /n (%)	IQR/95 %CI
Females			288 (67%)		35 (59%)		51 (73%)		23 (58%)	
Age (years)	38	(30-49)	36.0	(28.0 - 44.5)	44.0	(37.0 - 49.0)	41.5	(31.8 - 54.0)	52.0	(36.0 - 58.0)
BMI (kg/m^2)	26.6	(23.4-31.7)	25.4	(22.9 - 30.7)	27.6	(24.8 - 32.3)	29.5	(24.2 - 33.5)	33.6	(28.7 - 37.5)
Fasting glucose (mmol/l)	5.1	(4.8-5.4)	4.9	(4.7 - 5.2)	5.8	(5.7 - 6.1)	5.1	(5.0 - 5.3)	5.9	(5.8 - 6.2)
Postload (120 min) glucose (mmol/l)	6.1	(5.1-7.3)	5.7	(4.9 - 6.5)	6.3	(5.6 - 7.0)	8.4	(8.1 - 9.2)	8.7	(8.1 - 9.6)
Fasting insulin (pmol/l)	46	(31-77)	41.0	(29.0 - 68.0)	58.0	(40.0 - 80.0)	56.5	(37.5 - 78.5)	85.0	(58.5 - 155.0)
Postload (120 min) insulin (pmol/l)	287	(172-532)	241.0	(151.0 - 433.5)	280.0	(205.0 - 436.0)	557.0	(352.5 - 835.8)	661.0	(466.8 - 1110.5)
Fasting glucagon (pg/ml)	18.1	(14.3-23.0)	17.5	(13.9-22.0)	17.8	(14.3-23.7)	20.5	(15.4-20.5)	22.1	(17.0-23.5)
Glucagon$_{30}$ (pmol/l)	17.5	(13.6-21.8)	16.4	(13.4-17.4)	18.1	(14.2-18.7)	19.6	(15.3-19.5)	23.3	(17.5-23.0)
Glucagon$_{60}$ (pmol/l)	15.2	(12.1-19.7)	14.9	(11.7-15.8)	15.9	(13.2-17.5)	15.1	(12.3-17.1)	19.2	(14.6-17.8)
Glucagon$_{90}$ (pmol/l)	14.7	(11.4-18.7)	14.2	(11.2-15.2)	15.5	(12.6-16.1)	15.0	(11.7-16.3)	17.8	(13.2-16.7)
Glucagon$_{120}$ (pg/ml)	15.0	(11.8-18.7)	14.8	(11.6-18.5)	16.1	(12.3-16.4)	14.6	(11.0-14.7)	16.3	(13.9-17.2)
HbA1c (%, [mmol/mol])	5.2	(5.0-5.5)	5.2 (33)	(4.9 - 5.5) (30-37)	5.3 (34)	(5.1 - 5.7) (32-39)	5.4 (31)	(5.0 - 5.7) (31-39)	5.6 (38)	(5.2 - 6.0) (33-42)

SUPPLEMENTARY DATA

Supplementary Table 2. Characteristics of non-diabetic participants in the Botnia-PPP study

	NGT		IFG		IGT		IFG+IGT	
	n=694		n=596		n=31		n=66	
	Median/n (%)	IQR/95% CI	Median/n (%)	IQR/95% CI	Median/n (%)	IQR/95% CI	Median/n (%)	IQR/95% CI
Females	379 (53.2)		329 (54.7)		21 (67.7)		33 (50.0)	
Age (years)	45.2	35.9-57.1	47.3	38.7-60.9	70.8	56.1-73.6	67.7	51.7-73.3
BMI (kg/m)	25.7	23.0-28.2	26	23.5-29.3	27.8	25.8-29.8	27.8	24.8-31.2
Fasting glucose (mmol/l)	5.2	5.0-5.4	5.9	5.7-6.1	5.3	5.1-5.4	6	5.9-6.3
Postload (120 min) glucose	4.9	4.1-5.8	5.3	4.5-6.3	8.3	8.0-9.2	8.9	8.2-9.4
Fasting insulin (pmol/l)	34.1	23.6-51.4	41.7	28.5-57.7	49.3	24.3-75.8	57.7	36.8-102.9
Postload (120 min) insulin (pmol/l)	146.6	89.7-230.7	155.7	92.4-255.1	328.7	224.5-702	439.2	275.9-839.6
Fasting glucagon (pmol/l)	18.1	14.9-22.4	17.8	14.9-21.5	17.5	16.1-25.8	20.5	16.1-26.8
Postload (120 min) glucagon (pmol/l)	15.2	12.6-18.9	14.9	12.6-18.4	13.5	11.5-18.1	16.1	12.6-20.8

SUPPLEMENTARY DATA

Supplementary Table 3. Characteristics of the participants from the longitudinal TULIP study before and after lifestyle-intervention

N=50	before lifestyle-intervention		after 9-months lifestyle-intervention	
	Median/n (%)	IQR/95%CI	Median/n (%)	IQR/95%CI
Females	35 (59%)			
Age (years)	43	(35.75 - 54)		
BMI (kg/m^2)	28.5	(26.4 - 32.0)	27.9	(25.0 - 31.2)
Fasting glucose (mmol/l)	5.1	(4.8 - 5.5)	5.1	(4.8 - 5.4)
Postload (120 min) glucose (mmol/l)	6.7	(5.8 - 8.0)	6.2	(5.4 - 7.6)
Fasting insulin (pmol/l)	46.5	(31.0 - 73.25)	42.0	(27.8 - 60.8)
Postload (120 min) insulin (pmol/l)	360.5	(206.8 - 559.5)	273	(167.0 - 467.25)
Fasting glucagon (pmol/l)	19	(15.2 - 25.6)	17.5	(14.4 - 20.7)
Postload (120 min) glucagon (pmol/l)	16.2	(12.4 - 20.4)	15.2	(13.4 - 18.1)

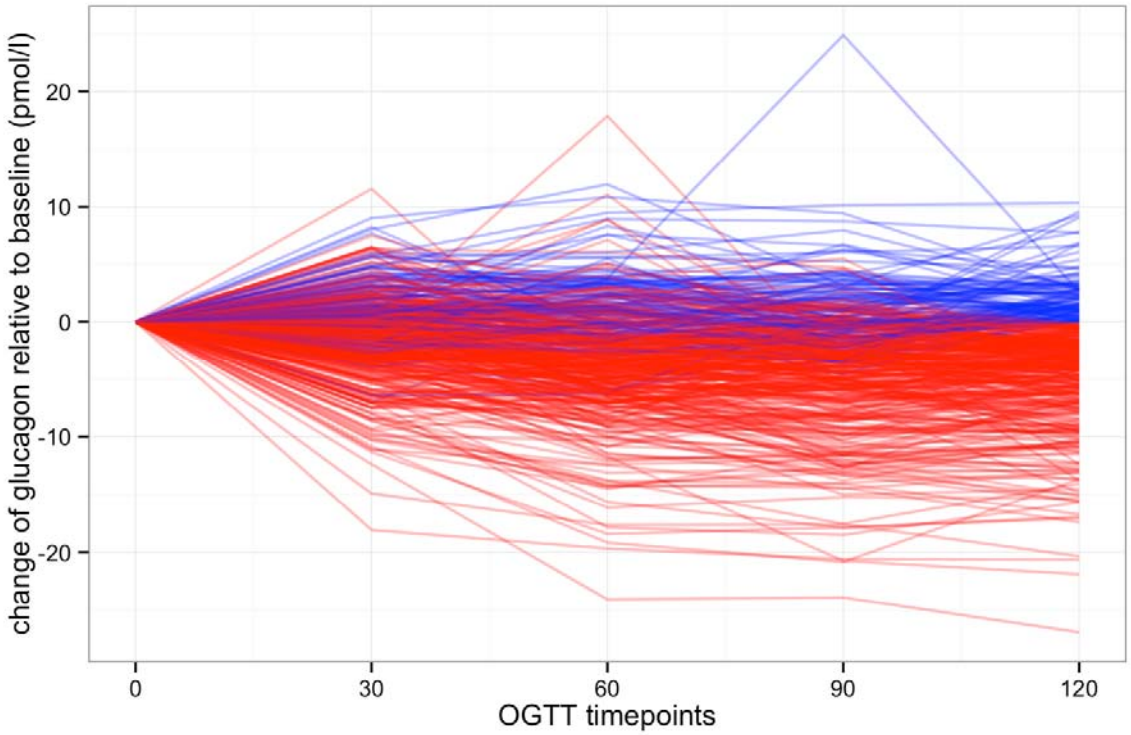
SUPPLEMENTARY DATA

Supplementary Table 4. Mean, minimum, maximum and standard error of glucose (mmol/l), glucagon (pmol/l) and insulin (pmol/l) levels stratified across dynamics of glucagon change during OGTT (suppressed vs. non-suppressed glucagon) in the TUEF cohort. Data are given for time-points 0, 30, 60, 90 and 120 minutes of the OGTT.

mean						
analyte	**glucagon dynamics**	**mean_0**	**mean_30**	**mean_60**	**mean_90**	**mean_120**
glucose	suppressed	5.11	8.43	8.36	7.23	6.44
glucose	non-suppressed	5.08	8.09	7.6	6.12	5.67
glucagon	suppressed	20.43	18.62	16.3	15.46	15.1
glucagon	non-suppressed	14.85	16.46	16.04	15.68	17.62
insulin	suppressed	65.11	507.4	601.21	532.74	450.89
insulin	non-suppressed	42.7	377.18	461.88	327.55	269.87
minimum						
		min_0	**min_30**	**min_60**	**min_90**	**min_120**
glucose	suppressed	3.06	4.67	3.61	3.28	2.89
glucose	non-suppressed	3.28	4.67	2.89	2.99	2.63
glucagon	suppressed	7.16	6.46	1.06	4.3	4.56
glucagon	non-suppressed	3.69	6.23	7.02	5.6	6.7
insulin	suppressed	11	92	36	58	22
insulin	non-suppressed	10	84	51	45	18
maximum						
		max_0	**max_30**	**max_60**	**max_90**	**max_120**
glucose	suppressed	6.88	13.5	18.94	16.83	11.06
glucose	non-suppressed	6.72	13.39	14	12.44	10.33
glucagon	suppressed	45.88	43.05	43.92	38.52	38.47
glucagon	non-suppressed	31.61	27.84	32.51	42.52	59.12
insulin	suppressed	521	2910	3341	2853	2414
insulin	non-suppressed	135	1421	2268	2194	1391
standard error						
		se_0	**se_30**	**se_60**	**se_90**	**se_120**
glucose	suppressed	0.02	0.07	0.11	0.1	0.07
glucose	non-suppressed	0.04	0.14	0.19	0.16	0.12
glucagon	suppressed	0.31	0.3	0.34	0.31	0.24
glucagon	non-suppressed	0.38	0.43	0.48	0.52	0.52
insulin	suppressed	2.28	17.44	19.33	19.8	17.41
insulin	non-suppressed	2	22.91	31.85	24.84	17.38

SUPPLEMENTARY DATA

Supplementary Figure 1. Plot showing individual glucagon courses as change relative to baseline glucagon during OGTT. Participants with suppressed glucagon ($glucagon_{120} < glucagon_0$) are displayed in red, participants with non-suppressed glucagon ($glucagon_{120} >= glucagon_0$) are displayed in blue.



SUPPLEMENTARY DATA

Supplementary Table 5. Fold-change glucagon levels (mean±SD) stratified on NGT and prediabetes for different OGTT time-intervals in the TUEF study.

glucagon-change during OGTT	NGT	Prediabetes (IFG and/or IGT)	p (t-test)
fold-change glucagon 30/0	0.96 (±0.21)	0.99 (±0.21)	0.09
fold-change glucagon 60/0	0.89 (±0.27)	0.89 (±0.27)	0.97
fold-change glucagon 90/0	0.86 (±0.24)	0.85 (±0.32)	0.56
fold-change glucagon 120/0	0.86 (±0.26)	0.80 (±0.25)	**0.01**