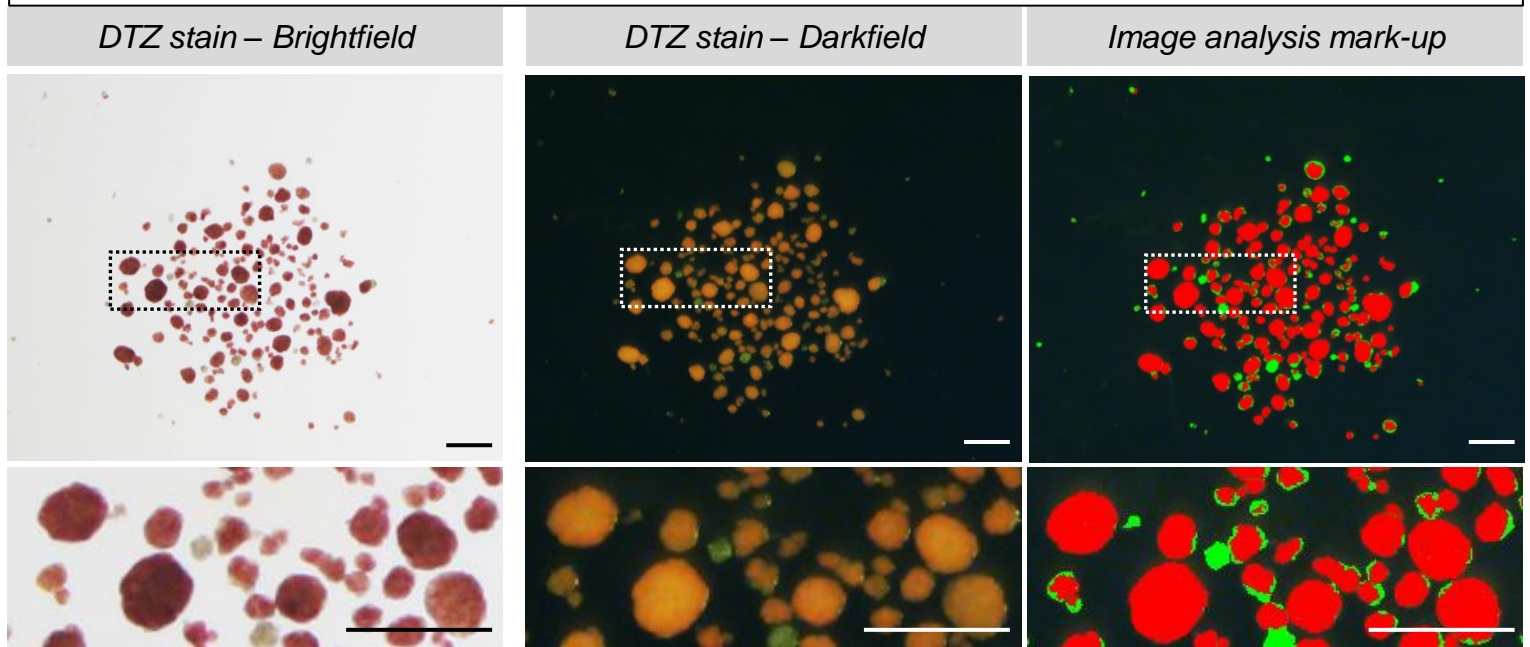


A

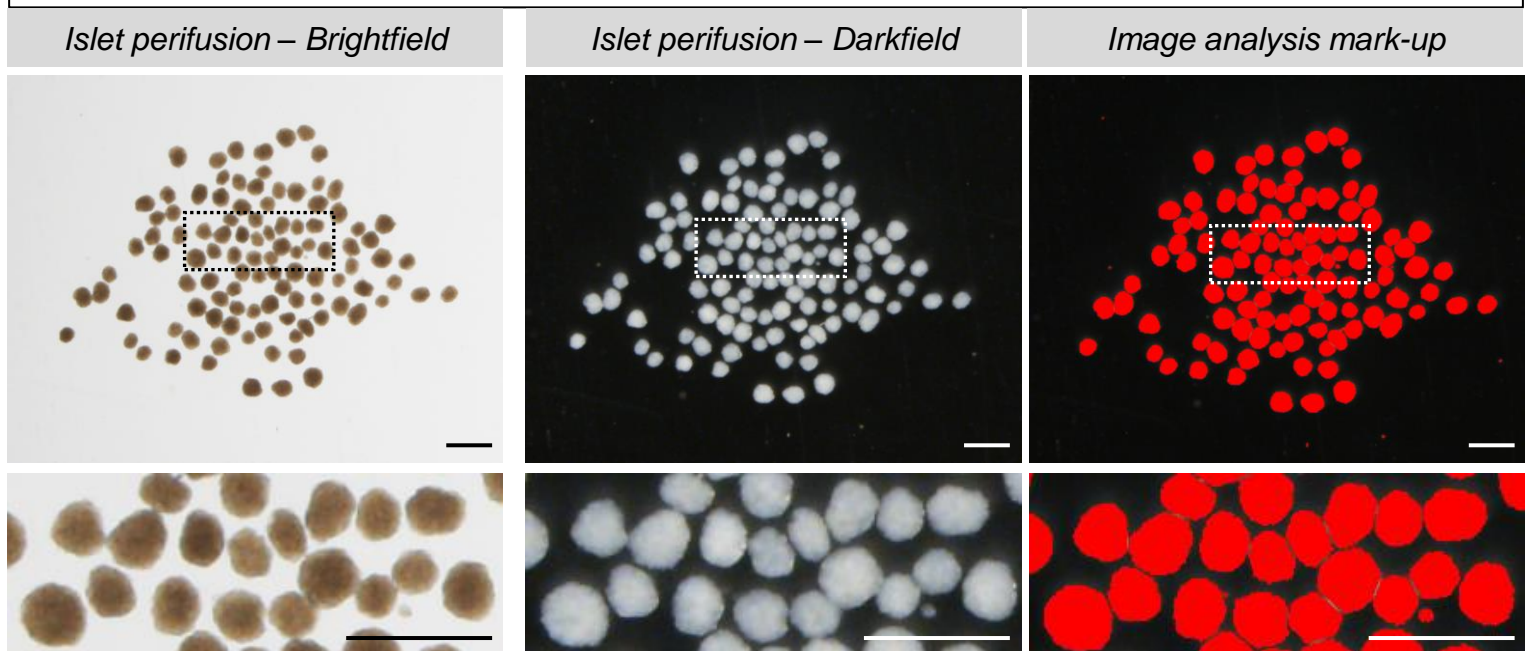
## Imaging of islet preparation for morphology



Calculated IEQ: 94.8; Calculated purity: 85%

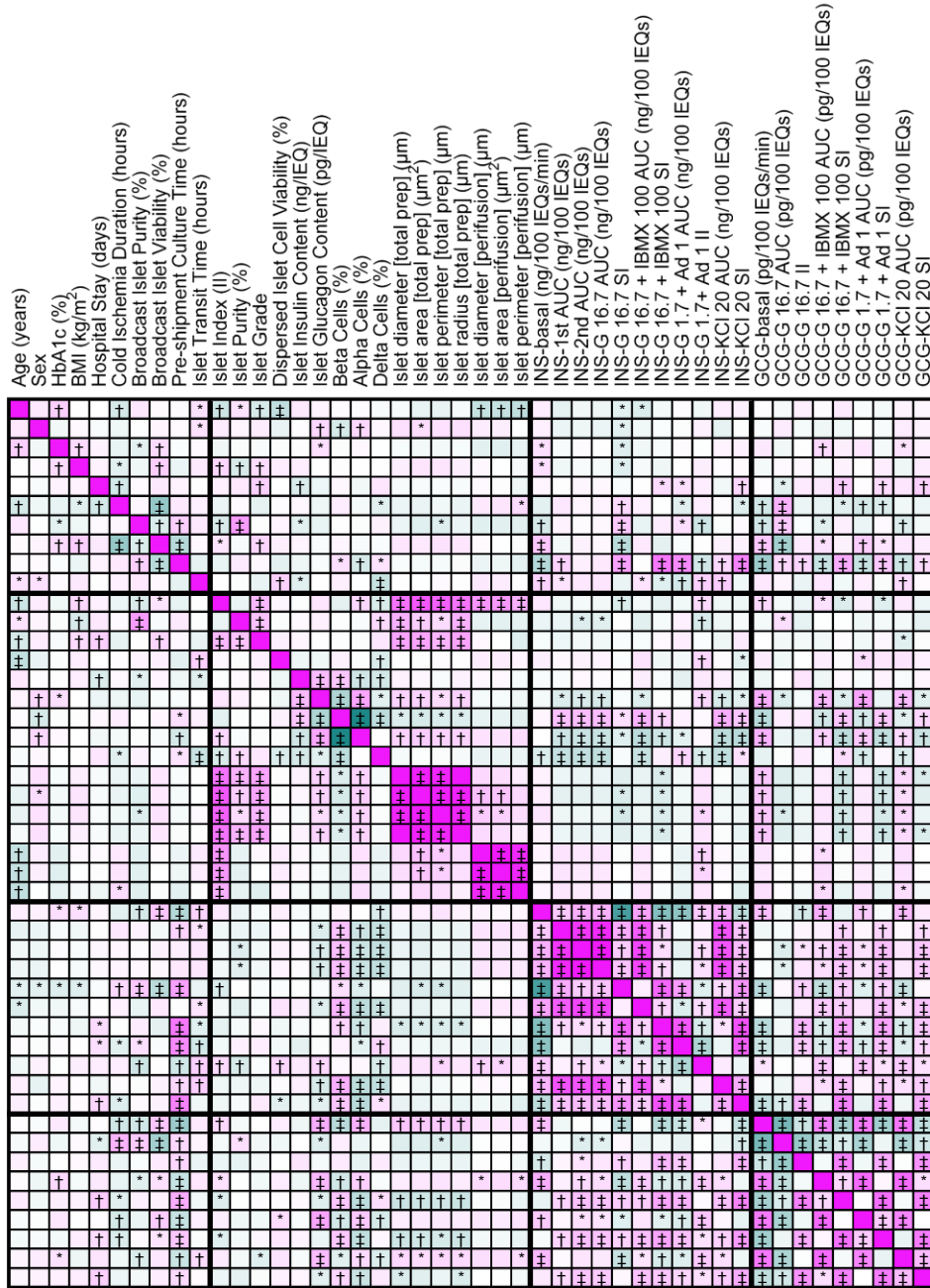
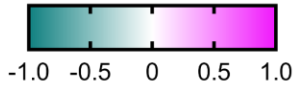
B

## Islet imaging for morphology &amp; functional analysis



Calculated IEQ: 269

Spearman r



Donor traits & islet processing

Islet morphology & composition traits

Insulin secretion traits

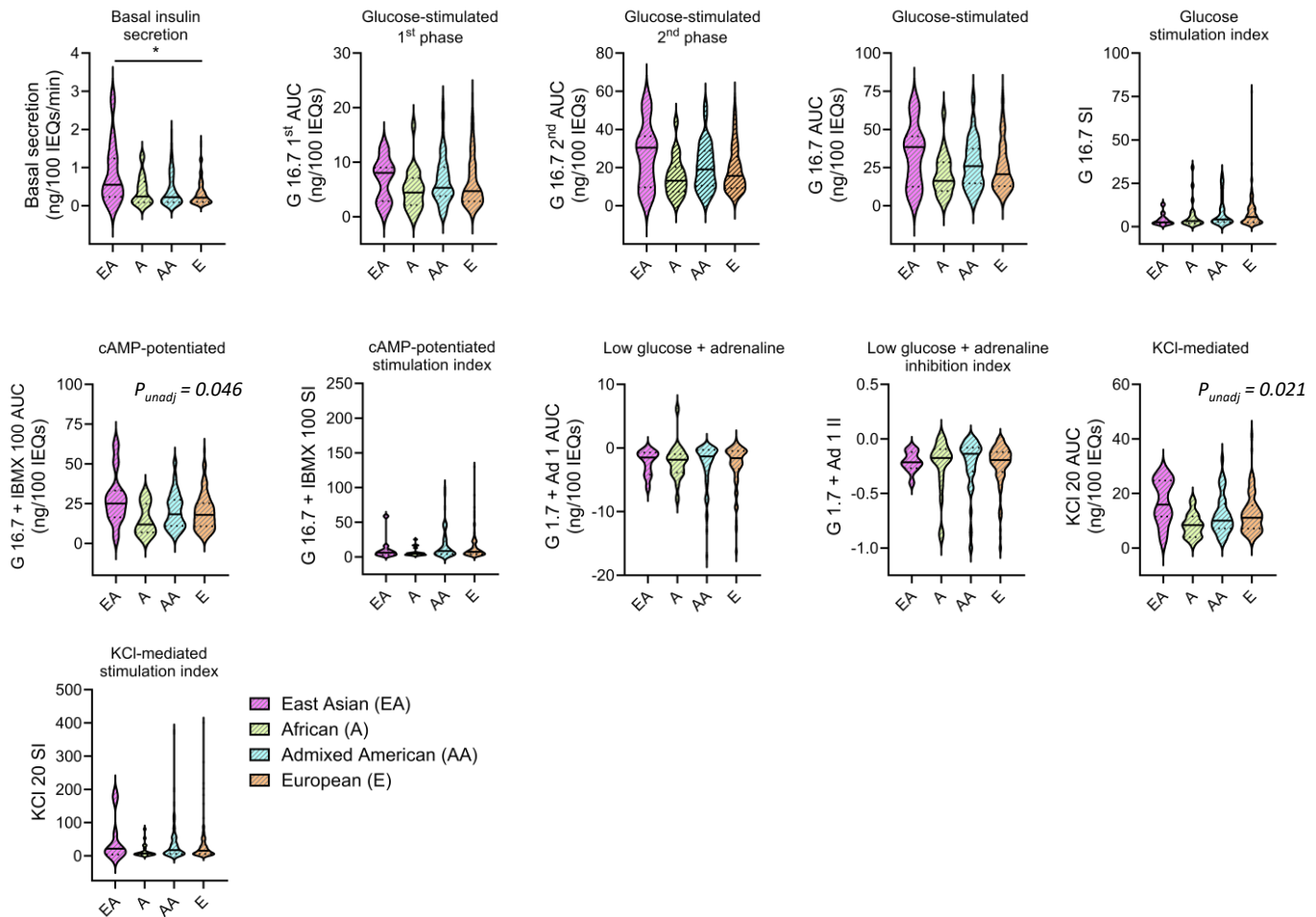
Glucagon secretion traits



$n = 86$  Admixed American,  $n = 21$  African,  $n = 11$  East Asian,  $n = 150$  European

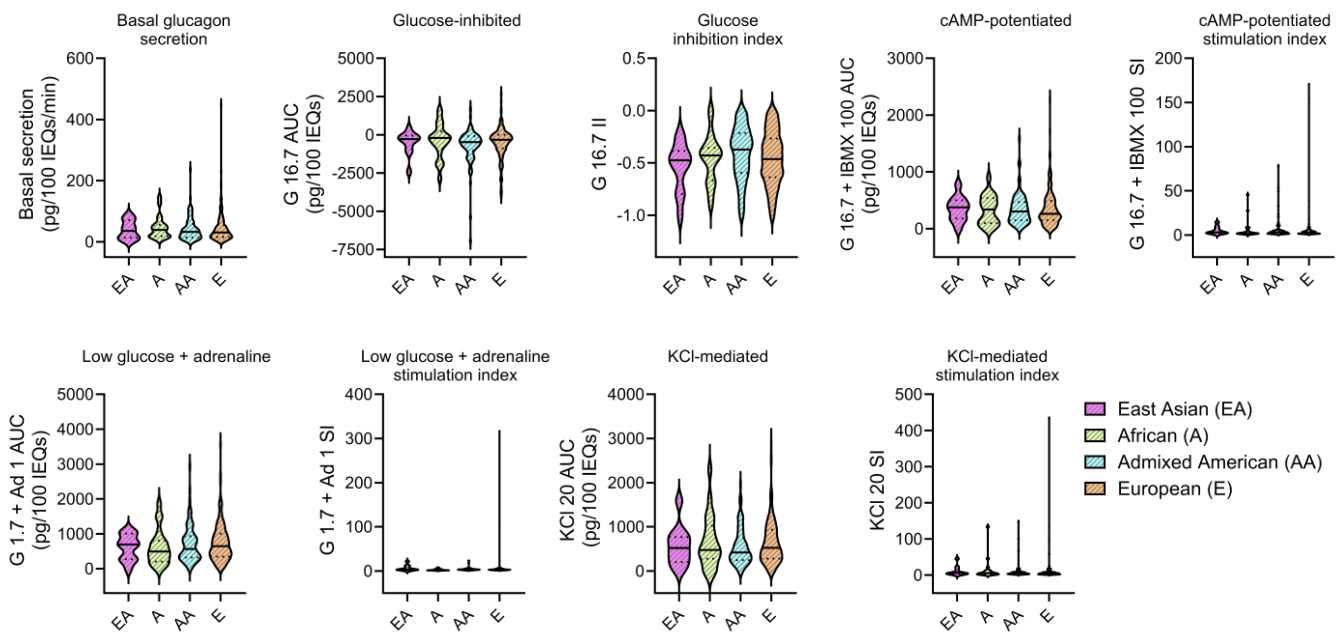
**A**

*Insulin secretion traits*

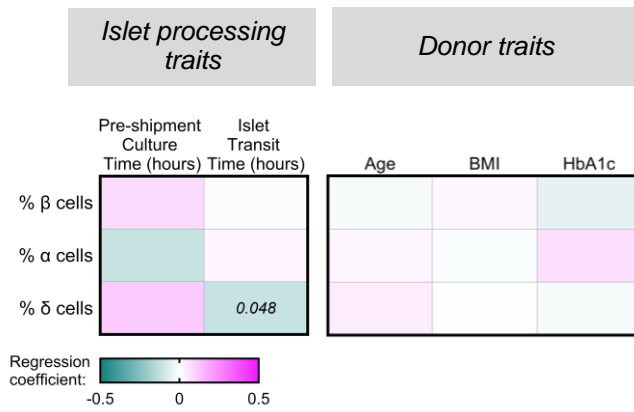


**B**

*Glucagon secretion traits*



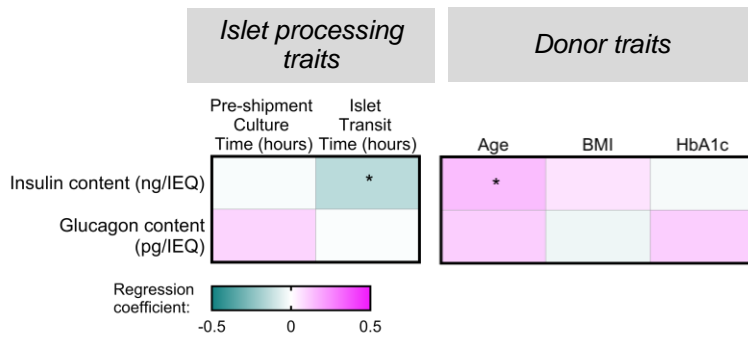
**A**



**B**

Islet composition		% $\beta$ cells	% $\alpha$ cells	% $\delta$ cells
Global adjusted p-value	Sex	0.0065	0.007	n.s.
	Reported race or ethnicity	0.003	0.003	n.s.
	Genetic Ancestry	0.001	0.001	n.s.
	Isolation Center	n.s.	n.s.	n.s.

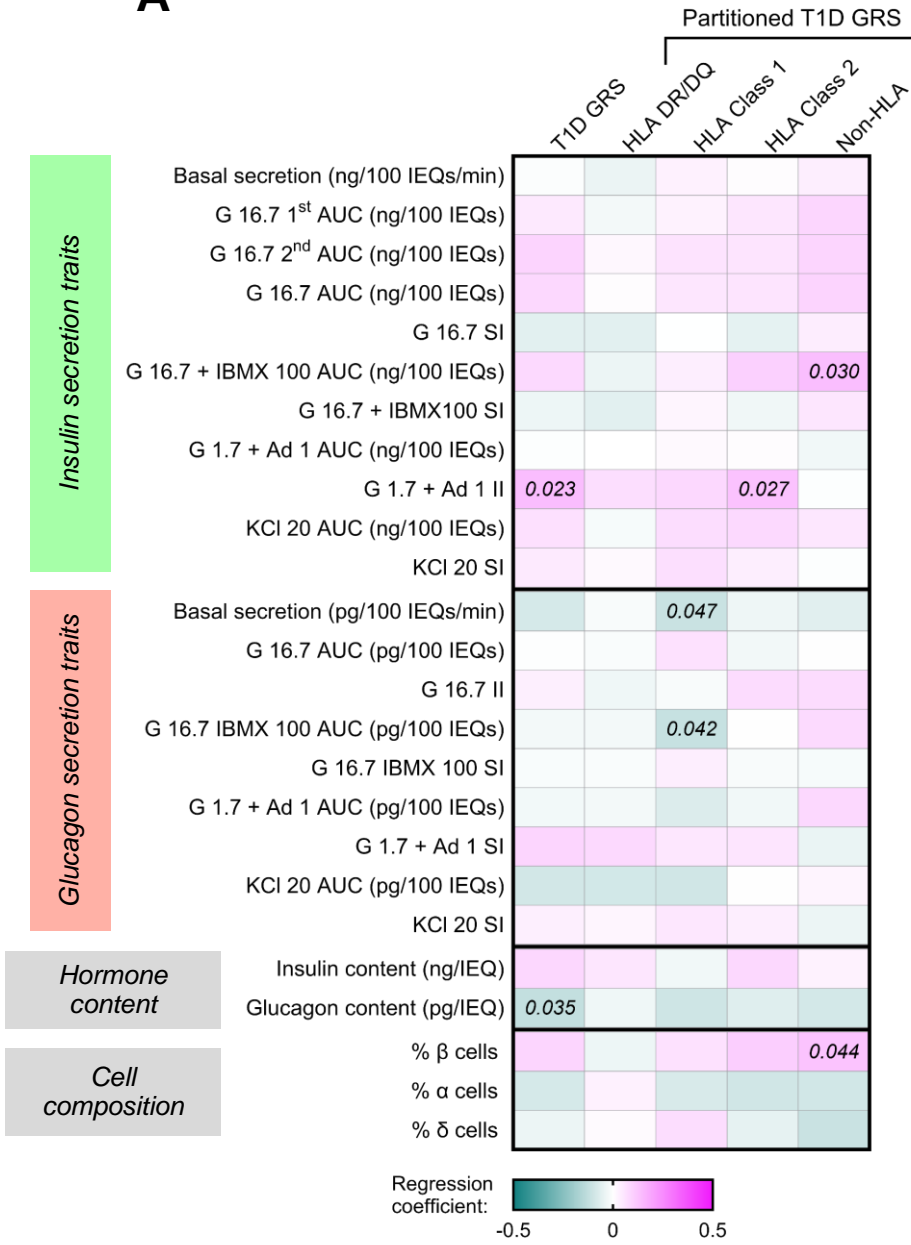
**C**



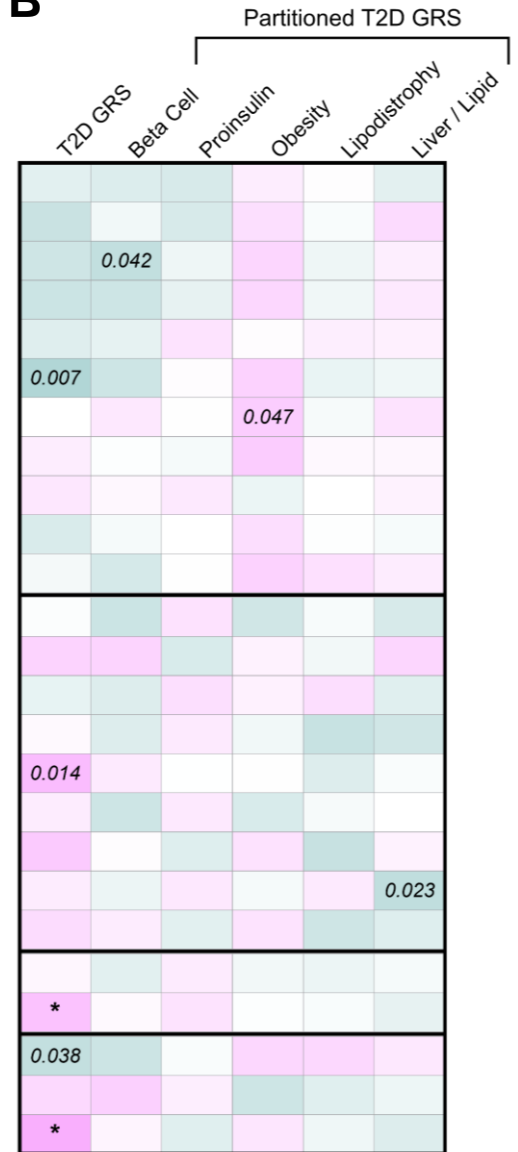
**D**

Hormone content		Insulin content (ng/IEQ)	Glucagon content (pg/IEQ)
Global adjusted p-value	Sex	n.s.	0.015
	Reported race or ethnicity	n.s.	n.s.
	Genetic Ancestry	n.s.	n.s.
	Isolation Center	n.s.	n.s.

**A**



**B**



**Extended Data Table 1, related to Figure 2. Insulin secretion is highly heterogeneous amongst donors.**

Insulin Secretion Trait [Mean ± SD (Range)]	Female (40%)				Male (60%)				Combined
	Asian	Black or African American	Hispanic or Latino/a	White	Asian	Black or African American	Hispanic or Latino/a	White	
Basal secretion (ng/100 IEQs/min)	1.6 ± 0.94 (0.55 – 2.8)	0.42 ± 0.41 (0.04 – 1.3)	0.49 ± 0.43 (0.037 – 1.5)	0.31 ± 0.29 (0.033 – 1.6)	0.38 ± 0.41 (0.053 – 1.2)	0.34 ± 0.44 (0.033 – 1.3)	0.4 ± 0.44 (0.01 – 1.9)	0.36 ± 0.35 (0.02 – 1.7)	0.39 ± 0.41 (0.01 – 2.8)
G 16.7 1st AUC (ng/100 IEQs)	11 ± 2 (9 – 13)	4.5 ± 2.9 (0 – 8.8)	7.7 ± 4.7 (1.9 – 21)	5.2 ± 3.7 (0 – 18)	4.6 ± 2.9 (0.86 – 8.7)	5.3 ± 4.7 (0.16 – 17)	5.9 ± 3.7 (0 – 18)	7.1 ± 4.8 (0 – 22)	6.3 ± 4.3 (0 – 22)
G 16.7 2nd AUC (ng/100 IEQs)	43 ± 11 (31 – 55)	14 ± 8.9 (1 – 30)	21 ± 13 (5.1 – 52)	17 ± 10 (1.4 – 52)	16 ± 10 (3.4 – 32)	18 ± 12 (0.52 – 44)	19 ± 11 (0.69 – 51)	21 ± 13 (1.4 – 57)	19 ± 12 (0.52 – 57)
G 16.7 AUC (ng/100 IEQs)	54 ± 13 (40 – 67)	18 ± 11 (1.1 – 39)	29 ± 17 (9 – 68)	22 ± 14 (3.3 – 70)	20 ± 13 (4.3 – 41)	24 ± 16 (0.68 – 61)	25 ± 15 (0.89 – 69)	28 ± 17 (2 – 75)	26 ± 16 (0.68 – 75)
G 16.7 SI	2.5 ± 0.66 (1.8 – 3.4)	6.3 ± 8.9 (1.5 – 34)	7.6 ± 8 (1.2 – 27)	6.8 ± 6.6 (1.3 – 36)	5.6 ± 4.2 (1.6 – 13)	7 ± 4.8 (1.5 – 15)	9.4 ± 13 (1.7 – 90)	8.5 ± 9.4 (1.4 – 78)	7.9 ± 9.4 (1.2 – 90)
G 16.7 + IBMX 100 AUC (ng/100 IEQs)	37 ± 17 (24 – 62)	15 ± 9.6 (1.6 – 33)	22 ± 12 (6.7 – 52)	18 ± 11 (2.4 – 49)	21 ± 14 (4.5 – 51)	14 ± 10 (0.8 – 31)	19 ± 10 (3.2 – 51)	21 ± 12 (2.3 – 59)	20 ± 11 (0.8 – 62)
G 16.7 + IBMX 100 SI	6.1 ± 3.4 (2.2 – 11)	7 ± 6.4 (2.6 – 25)	20 ± 26 (1.6 – 100)	14 ± 19 (1.3 – 130)	15 ± 19 (2.2 – 59)	4.8 ± 3.5 (1.7 – 13)	19 ± 29 (1.6 – 190)	13 ± 15 (2 – 89)	14 ± 20 (1.3 – 190)
G 1.7 + Ad 1 AUC (ng/100 IEQs)	-2.3 ± 1.7 (-4.4 – -0.88)	-1.9 ± 2.9 (-8 – 6.1)	-3 ± 3.6 (-11 – 0.32)	-2.6 ± 3.3 (-16 – 0.77)	-2 ± 2.1 (-6.1 – -0.44)	-3 ± 3.6 (-11 – 0.03)	-2.5 ± 3.4 (-17 – 1.2)	-2.6 ± 3.1 (-16 – 1.4)	-2.6 ± 3.2 (-17 – 6.1)
G 1.7+Ad 1 II	-0.22 ± 0.071 (-0.29 – -0.12)	-0.26 ± 0.28 (-0.89 – 0)	-0.18 ± 0.23 (-0.89 – 0)	-0.23 ± 0.19 (-0.91 – 0)	-0.21 ± 0.11 (-0.43 – -0.087)	-0.25 ± 0.16 (-0.55 – -0.093)	-0.22 ± 0.21 (-1 – 0)	-0.25 ± 0.23 (-1 – 0)	-0.23 ± 0.21 (-1 – 0)
KCI 20 AUC (ng/100 IEQs)	20 ± 7.2 (12 – 27)	7.8 ± 4.6 (1.4 – 18)	14 ± 8.5 (3 – 33)	10 ± 5.3 (3.9 – 28)	14 ± 8.9 (3.1 – 26)	9 ± 3.5 (1.2 – 13)	11 ± 6.2 (2.2 – 27)	14 ± 7.7 (1.7 – 42)	12 ± 7 (1.2 – 42)
KCI 20 SI	55 ± 76 (3.1 – 168)	14 ± 20 (2 – 81)	54 ± 80 (1.8 – 373)	26 ± 28 (1.9 – 114)	44 ± 63 (2.6 – 188)	29 ± 48 (2.2 – 150)	29 ± 36 (2.7 – 157)	31 ± 57 (2.3 – 401)	31 ± 49 (1.8 – 401)



**Extended Data Table 2, related to Figure 2. Glucagon secretion is highly heterogeneous amongst donors.**

Glucagon Secretion Trait [Mean ± SD (Range)]	Female (38%)				Male (62%)				Combined
	Asian	Black or African American	Hispanic or Latino/a	White	Asian	Black or African American	Hispanic or Latino/a	White	
Basal secretion (pg/100 IEQs/min)	30 ± 24 (4.8 – 54)	44 ± 34 (7.7 – 146)	46 ± 38 (3 – 142)	44 ± 61 (0.1 – 447)	46 ± 29 (15 – 90)	34 ± 39 (2.4 – 127)	45 ± 41 (1.4 – 236)	45 ± 42 (0.5 – 230)	44 ± 45 (0.1 – 447)
G 16.7 AUC (pg/100 IEQs)	-525 ± 446 (-1156 – -155)	-360 ± 1165 (-2855 – 1648)	-704 ± 1285 (-5374 – 1177)	-403 ± 1062 (-4027 – 2676)	-580 ± 851 (-2408 – 424)	-334 ± 685 (-1920 – 427)	-823 ± 1135 (-6927 – 631)	-592 ± 966 (-3783 – 1679)	-583 ± 1053 (-6927 – 2676)
G 16.7 II	-0.41 ± 0.12 (-0.49 – -0.23)	-0.44 ± 0.25 (-0.89 – -0.013)	-0.44 ± 0.31 (-0.99 – -0.034)	-0.48 ± 0.26 (-1 – 0)	-0.5 ± 0.24 (-0.8 – -0.097)	-0.47 ± 0.27 (-1 – 0)	-0.41 ± 0.25 (-1 – 0)	-0.44 ± 0.24 (-1 – 0)	-0.45 ± 0.25 (-1 – 0)
G 16.7 + IBMX 100 AUC (pg/100 IEQs)	280 ± 241 (0 – 555)	320 ± 270 (0 – 900)	365 ± 203 (63 – 775)	344 ± 382 (0 – 2265)	372 ± 206 (112 – 772)	307 ± 198 (0 – 589)	383 ± 297 (0 – 1582)	367 ± 293 (0 – 1329)	359 ± 302 (0 – 2265)
G 16.7 + IBMX 100 SI	3.4 ± 1.1 (2.4 – 4.9)	6.8 ± 12 (1 – 46)	9.2 ± 18 (1.2 – 78)	7.1 ± 21 (1 – 170)	3.8 ± 3.2 (1.3 – 10)	19 ± 47 (1.6 – 144)	5.7 ± 7.8 (1 – 50)	5.2 ± 15 (1 – 155)	6.5 ± 17 (1 – 170)
G 1.7 + Ad 1 AUC (pg/100 IEQs)	549 ± 367 (0 – 769)	661 ± 543 (9 – 1862)	744 ± 455 (51 – 1726)	737 ± 574 (0 – 3557)	600 ± 386 (200 – 1085)	470 ± 340 (114 – 1170)	759 ± 566 (71 – 2924)	766 ± 562 (0 – 3195)	734 ± 543 (0 – 3557)
G 1.7 + Ad 1 SI	5.3 ± 4.9 (2.8 – 13)	2.9 ± 1.8 (1.1 – 7.4)	4.4 ± 4.2 (1.1 – 23)	8.3 ± 38 (1.1 – 316)	3.9 ± 3 (1.2 – 10)	3.5 ± 2.1 (1.3 – 8.2)	4.1 ± 3.2 (1.2 – 19)	4.5 ± 10 (1.1 – 109)	5.1 ± 19 (1.1 – 316)
KCI 20 AUC (pg/100 IEQs)	551 ± 351 (128 – 902)	682 ± 633 (0 – 2297)	754 ± 497 (138 – 1976)	641 ± 478 (0 – 2456)	596 ± 475 (0 – 1590)	459 ± 351 (124 – 1247)	513 ± 384 (0 – 1956)	637 ± 532 (0 – 2890)	618 ± 488 (0 – 2890)
KCI 20 SI	15 ± 20 (4.3 – 46)	16 ± 32 (1.6 – 134)	13 ± 22 (2.1 – 101)	17 ± 55 (1.4 – 434)	5.7 ± 4.6 (1.2 – 16)	6.5 ± 3.5 (1.7 – 13)	8.8 ± 19 (1.6 – 148)	8.3 ± 13 (1 – 100)	11 ± 30 (1 – 434)

**Extended Data Table 3, related to Figure 2. Distribution of insulin secretion traits is similar in N=268 subset.**

Insulin Secretion Trait [Mean ± SD (Range)]	Female (40%)				Male (60%)				Combined
	East Asian	African	Admixed American	European	East Asian	African	Admixed American	European	
Basal secretion (ng/100 IEQs/min)	1.3 ± 0.98 (0.36 – 2.8)	0.42 ± 0.41 (0.04 – 1.3)	0.39 ± 0.38 (0.037 – 1.3)	0.31 ± 0.29 (0.04 – 1.6)	0.47 ± 0.45 (0.053 – 1.2)	0.36 ± 0.34 (0.057 – 0.8)	0.41 ± 0.44 (0.01 – 1.9)	0.34 ± 0.35 (0.02 – 1.7)	0.38 ± 0.41 (0.01 – 2.8)
G 16.7 1st AUC (ng/100 IEQs)	9.8 ± 2.5 (6.6 – 13)	4.5 ± 2.9 (0 – 8.8)	6.8 ± 4.9 (1.6 – 21)	5.3 ± 3.9 (0 – 18)	4.4 ± 3.2 (0.86 – 8.7)	7.2 ± 6.5 (2.1 – 17)	6.6 ± 4.2 (0 – 19)	6.9 ± 4.9 (0 – 22)	6.3 ± 4.4 (0 – 22)
G 16.7 2nd AUC (ng/100 IEQs)	39 ± 14 (21 – 55)	14 ± 8.9 (1 – 30)	19 ± 13 (5.1 – 52)	17 ± 11 (1.4 – 52)	16 ± 12 (3.4 – 32)	22 ± 15 (13 – 44)	21 ± 12 (0.69 – 55)	20 ± 13 (1.8 – 57)	20 ± 12 (0.69 – 57)
G 16.7 AUC (ng/100 IEQs)	48 ± 16 (28 – 67)	18 ± 11 (1.1 – 39)	26 ± 17 (9 – 68)	22 ± 14 (3.3 – 70)	21 ± 15 (4.3 – 41)	29 ± 21 (16 – 61)	28 ± 16 (0.89 – 74)	27 ± 17 (2.2 – 75)	26 ± 16 (0.89 – 75)
G 16.7 SI	2.8 ± 0.87 (1.8 – 4)	6.3 ± 8.9 (1.5 – 34)	8.1 ± 8.2 (1.2 – 27)	6.7 ± 6.7 (1.3 – 36)	5.1 ± 4.5 (1.6 – 13)	7.8 ± 5.6 (1.6 – 15)	8.5 ± 8.3 (1.8 – 31)	8.4 ± 9.4 (1.4 – 78)	7.7 ± 8.2 (1.2 – 78)
G 16.7 + IBMX 100 AUC (ng/100 IEQs)	34 ± 17 (20 – 62)	15 ± 9.6 (1.6 – 33)	20 ± 13 (6.6 – 52)	18 ± 10 (2.4 – 49)	24 ± 16 (4.5 – 51)	17 ± 13 (5.8 – 31)	20 ± 11 (3.2 – 51)	21 ± 12 (2.3 – 59)	20 ± 12 (1.6 – 62)
G 16.7 + IBMX 100 SI	6.6 ± 3.2 (2.2 – 11)	7 ± 6.4 (2.6 – 25)	22 ± 26 (1.6 – 100)	14 ± 20 (1.3 – 130)	15 ± 22 (2.2 – 59)	5.7 ± 5 (1.7 – 13)	16 ± 19 (1.6 – 90)	13 ± 15 (2 – 89)	14 ± 18 (1.3 – 130)
G 1.7 + Ad 1 AUC (ng/100 IEQs)	-1.9 ± 1.7 (-4.4 – -0.46)	-1.9 ± 2.9 (-8 – 6.1)	-2.3 ± 3.4 (-11 – 0.32)	-2.8 ± 3.4 (-16 – 0.77)	-2.5 ± 2.2 (-6.1 – -0.53)	-3.1 ± 1.8 (-4.3 – -0.49)	-2.7 ± 3.4 (-17 – 0.48)	-2.5 ± 3.2 (-16 – 1.4)	-2.6 ± 3.2 (-17 – 6.1)
G 1.7+Ad 1 II	-0.25 ± 0.1 (-0.4 – -0.12)	-0.26 ± 0.28 (-0.89 – 0)	-0.21 ± 0.27 (-0.89 – 0)	-0.22 ± 0.18 (-0.91 – 0)	-0.17 ± 0.073 (-0.27 – -0.087)	-0.2 ± 0.068 (-0.3 – -0.15)	-0.24 ± 0.23 (-1 – 0)	-0.24 ± 0.2 (-1 – 0)	-0.23 ± 0.21 (-1 – 0)
KCI 20 AUC (ng/100 IEQs)	19 ± 6.8 (12 – 27)	7.8 ± 4.6 (1.4 – 18)	13 ± 8.6 (3.5 – 33)	11 ± 5.5 (3.9 – 28)	16 ± 9.7 (3.1 – 26)	10 ± 2.9 (6.8 – 13)	12 ± 6.5 (2.2 – 27)	14 ± 7.9 (1.7 – 42)	12 ± 7.1 (1.4 – 42)
KCI 20 SI	48 ± 68 (3.1 – 168)	14 ± 20 (2 – 81)	59 ± 82 (2.8 – 373)	25 ± 28 (1.9 – 114)	47 ± 73 (2.6 – 188)	17 ± 24 (3.1 – 53)	26 ± 31 (2.5 – 156)	36 ± 62 (2.3 – 401)	32 ± 51 (1.9 – 401)

**Extended Data Table 4, related to Figure 2. Distribution of glucagon secretion traits is similar in N=268 subset.**

Glucagon Secretion Trait [Mean ± SD (Range)]	Female (40%)				Male (60%)				Combined
	East Asian	African	Admixed American	European	East Asian	African	Admixed American	European	
Basal secretion (pg/100 IEQs/min)	24 ± 24 (1.6 – 54)	44 ± 34 (7.7 – 146)	40 ± 37 (3 – 142)	47 ± 63 (0.1 – 447)	52 ± 32 (15 – 90)	54 ± 53 (12 – 127)	43 ± 38 (1.4 – 236)	44 ± 42 (0.5 – 230)	44 ± 46 (0.1 – 447)
G 16.7 AUC (pg/100 IEQs)	-420 ± 452 (-1156 – 0)	-360 ± 1165 (-2855 – 1648)	-677 ± 1251 (-5374 – 1177)	-406 ± 1117 (-4027 – 2676)	-590 ± 993 (-2408 – 424)	-466 ± 1012 (-1920 – 427)	-772 ± 1124 (-6927 – 1679)	-585 ± 948 (-3783 – 1489)	-577 ± 1065 (-6927 – 2676)
G 16.7 II	-0.53 ± 0.28 (-1 – -0.23)	-0.44 ± 0.25 (-0.89 – -0.013)	-0.4 ± 0.31 (-0.99 – -0.033)	-0.49 ± 0.26 (-1 – 0)	-0.55 ± 0.22 (-0.8 – -0.27)	-0.5 ± 0.16 (-0.7 – -0.33)	-0.42 ± 0.24 (-1 – 0)	-0.44 ± 0.25 (-1 – 0)	-0.45 ± 0.25 (-1 – 0)
G 16.7 + IBMX 100 AUC (pg/100 IEQs)	250 ± 219 (0 – 555)	320 ± 270 (0 – 900)	278 ± 164 (63 – 606)	365 ± 398 (0 – 2265)	437 ± 193 (208 – 772)	363 ± 192 (124 – 589)	375 ± 297 (0 – 1582)	347 ± 271 (0 – 1329)	350 ± 299 (0 – 2265)
G 16.7 + IBMX 100 SI	5.6 ± 5 (2.4 – 14)	6.8 ± 12 (1 – 46)	9.4 ± 18 (1.2 – 78)	6.9 ± 22 (1 – 170)	4.2 ± 3.6 (1.3 – 10)	2.8 ± 2.3 (1.6 – 6.3)	5.3 ± 7.7 (1 – 50)	5.5 ± 16 (1 – 155)	6.1 ± 16 (1 – 170)
G 1.7 + Ad 1 AUC (pg/100 IEQs)	496 ± 339 (0 – 769)	661 ± 543 (9 – 1862)	617 ± 433 (0 – 1538)	776 ± 588 (30 – 3557)	712 ± 384 (266 – 1085)	431 ± 236 (155 – 723)	749 ± 557 (71 – 2924)	733 ± 526 (0 – 2693)	722 ± 532 (0 – 3557)
G 1.7 + Ad 1 SI	8.6 ± 8.5 (2.8 – 22)	2.9 ± 1.8 (1.1 – 7.4)	4.3 ± 4.4 (1.1 – 23)	8.4 ± 40 (1.1 – 316)	4.3 ± 3.4 (1.2 – 10)	2.4 ± 1.2 (1.3 – 4.1)	4.1 ± 3.1 (1.2 – 19)	4.6 ± 11 (1.1 – 109)	5.2 ± 20 (1.1 – 316)
KCI 20 AUC (pg/100 IEQs)	481 ± 342 (128 – 902)	682 ± 633 (0 – 2297)	637 ± 466 (0 – 1669)	679 ± 487 (54 – 2456)	636 ± 536 (0 – 1590)	577 ± 459 (223 – 1247)	520 ± 396 (0 – 1956)	622 ± 510 (0 – 2890)	614 ± 480 (0 – 2890)
KCI 20 SI	17 ± 18 (4.3 – 46)	16 ± 32 (1.6 – 134)	14 ± 23 (1.4 – 101)	17 ± 58 (1.6 – 434)	6.1 ± 5.3 (1.2 – 16)	4.6 ± 2.2 (1.7 – 6.5)	8.5 ± 18 (1.6 – 148)	8.7 ± 15 (1 – 100)	12 ± 32 (1 – 434)