

islet insulin production in diabetes model: spatial comparison of mouse strains

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- scientist: Donnie Stapleton, Attie Biochem Lab
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- objective of project:
 - improve methods to distinguish "quality"
 - of insulin production
 - between two strains of mice
 - based on 3-color images of islets in pancreas slices

why do this project?

- Knowledge/Skills needed
 - Basic statistics (t-test, ideally some nonparametrics)
 - R programming (a la biostat training)
- Knowledge/Skills obtained
 - communication skills with scientist (lab biochemist)
 - image analysis basics
 - nonparametric density estimation (mechanics at least)
 - experimental design considerations (nesting, balance, etc.)

project abstract

- insulin is produced in the pancreas
 - specifically the Islets of Langerhans by "beta" cells
 - (there are "alpha" cells as well.)
- scientists in biochemistry have imaged hundreds of islets
 - for two strains of obese mice
 - BTBR.ob mimics type II (mature onset) diabetes mellitus
 - B6.ob appears healthy
- roughly a hundred islets per mouse, 3 mice per strain
 - can visually see differences in production of insulin in beta cells
 - have summary measurements on many islets to compare strains
- opportunity beyond data analysis
 - how to improve measurement process?
 - how to improve experimental design?
- goal: clearly infer differences in "quality" of insulin production
 - between BTBR.ob and B6.ob
- you can meet with the scientist and work with measurement system

of mice and men

- obese strains: BTBR.ob vs. B6.ob
 - obese BTBR mice mimic human diabetes
 - high glucose, low insulin
 - obese B6 mice appear non-diabetic
- congenic substrains A and B
 - mostly BTBR mouse genome
 - A congenic: insert small segment of B6
 - B congenic: essentially BTBR mice

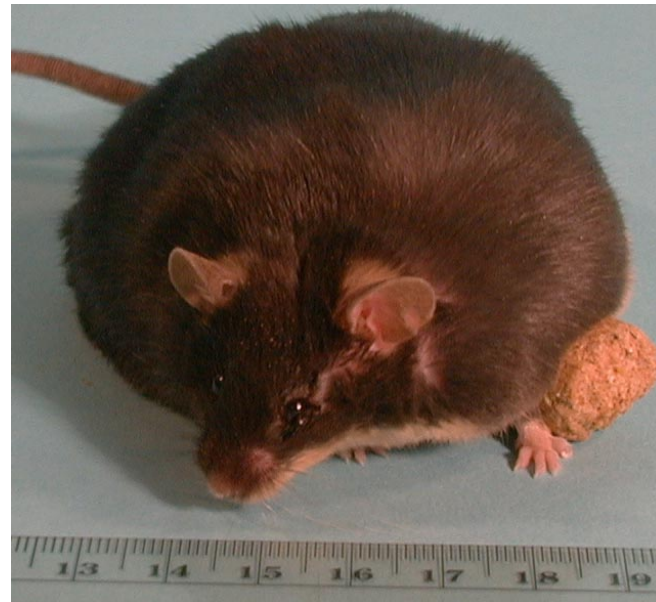
Insulin Resistant Mice



Bill Dove



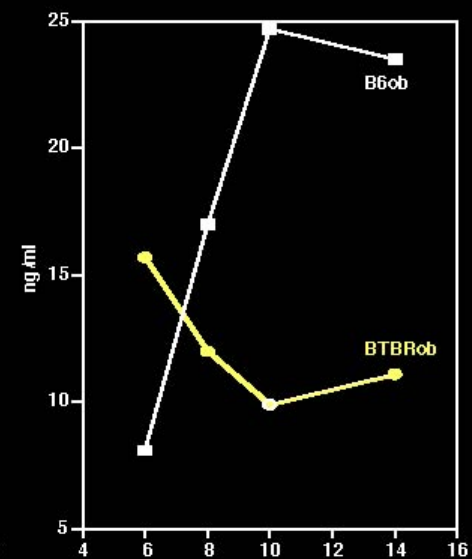
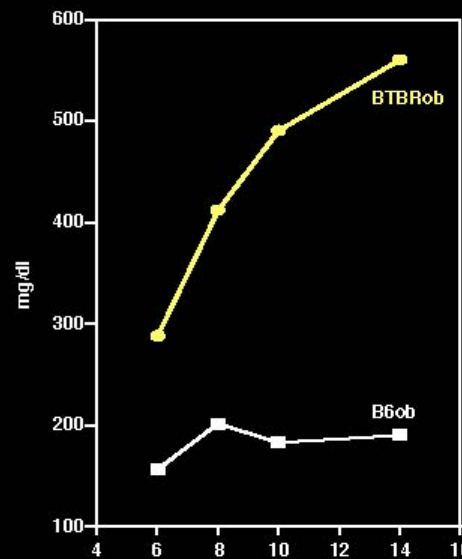
BTBR strain



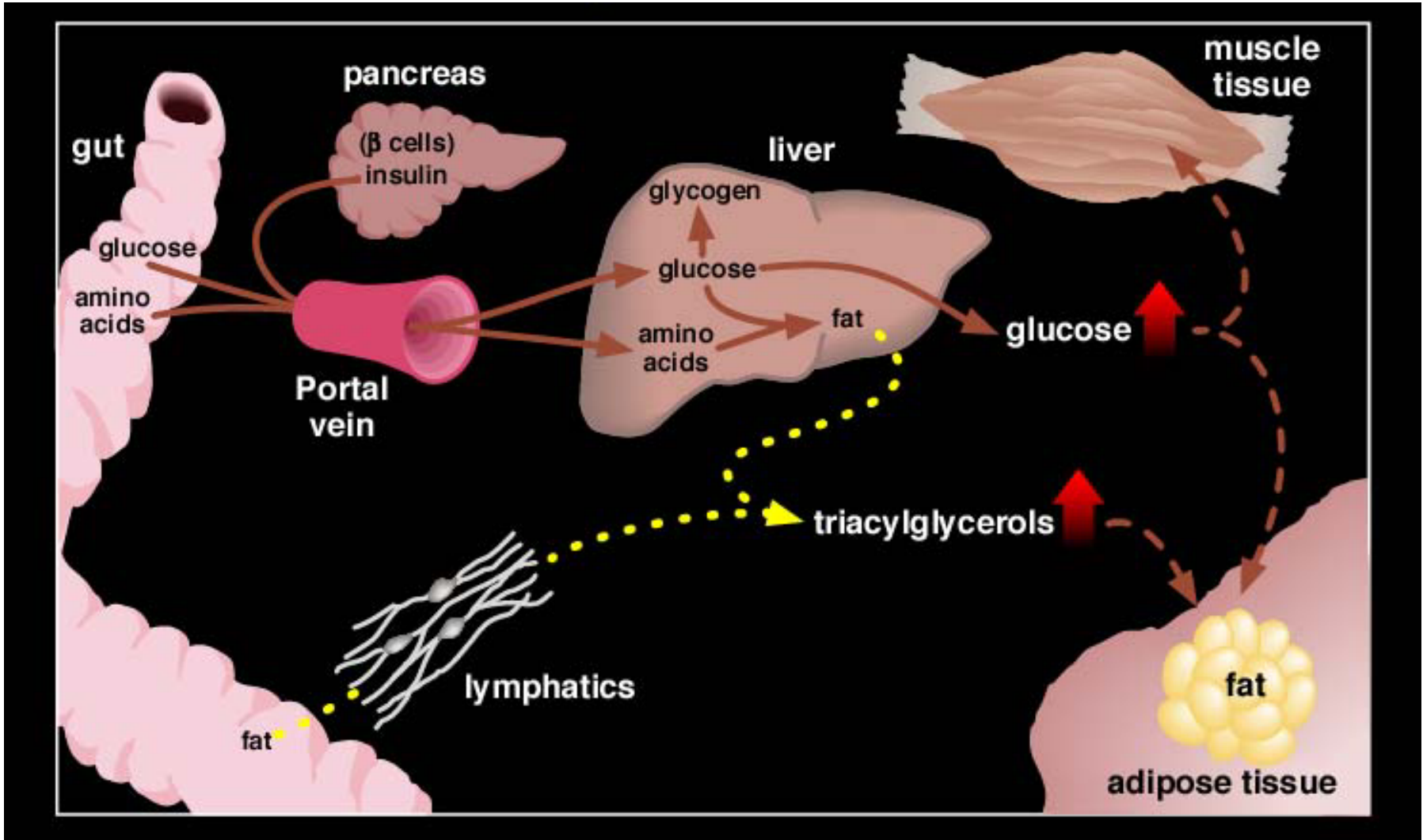
UJW Sumner

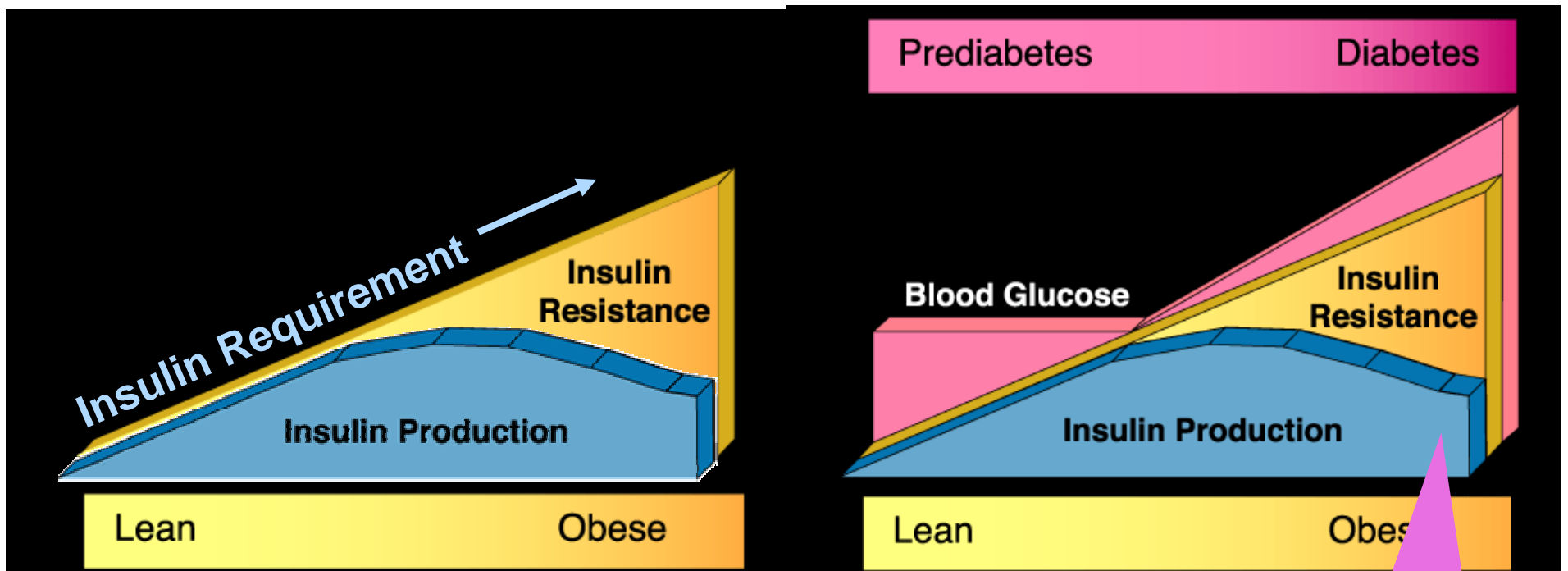
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glucose insulin



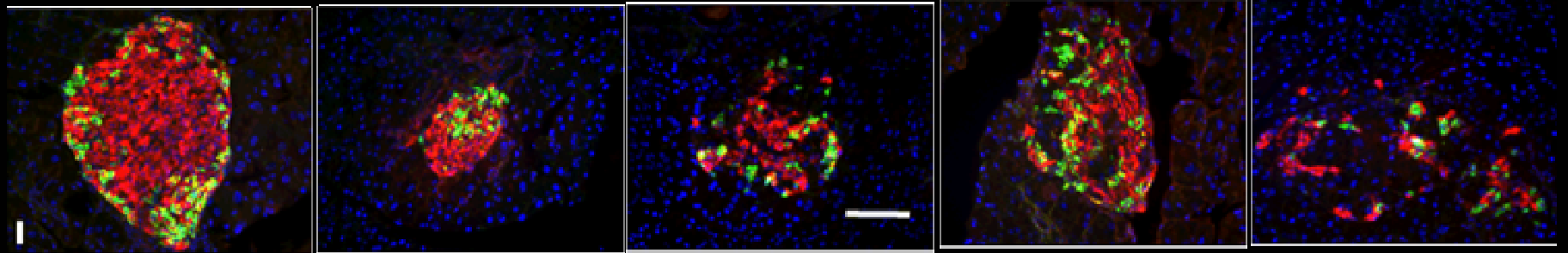
Time (weeks)





decompensation

islet degradation series A vs. B congenics



1
healthy

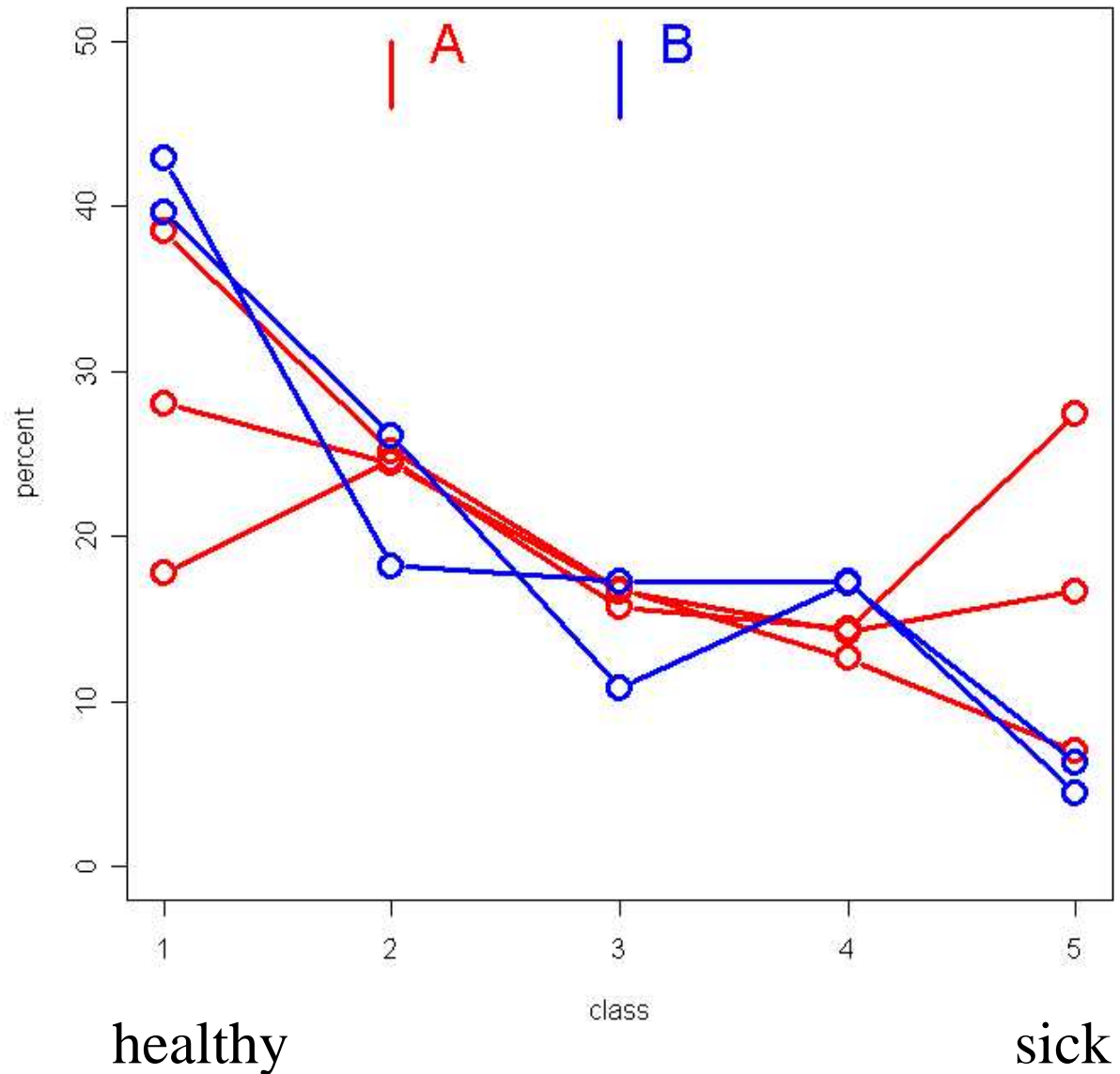
2

3

4

5
sick

comparison
of 3 type A
and 2 type B
congenic
mice



A and B congenic data

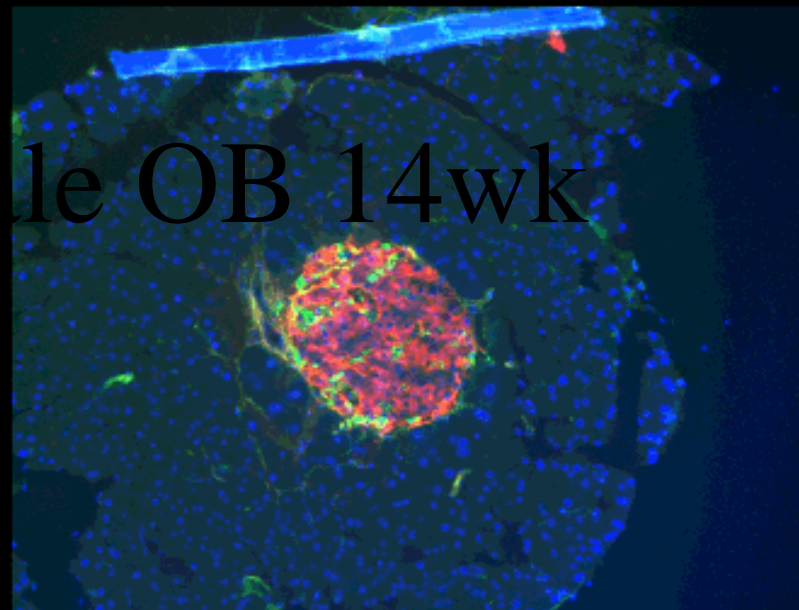
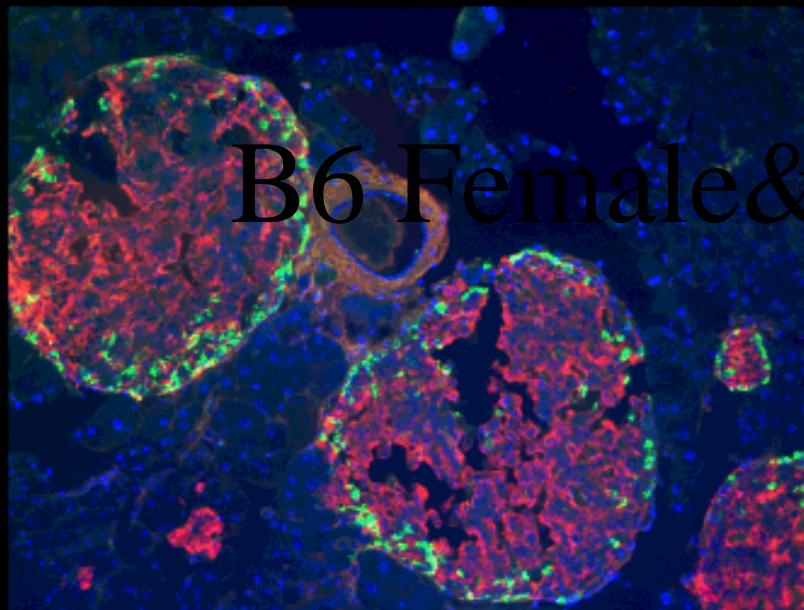
A congenics:

Class.I	Class.II	Class.III	Class.IV	Class.V	Total.Islets	
A33-18	26	36	23	21	40	146
A34-22	55	36	24	18	10	143
A39-15	69	60	41	35	41	246

B congenics:

Class.I	Class.II	Class.III	Class.IV	Class.V	Total.Islets	
A34-19	87	37	35	35	9	203
A48-4	44	29	12	19	7	111

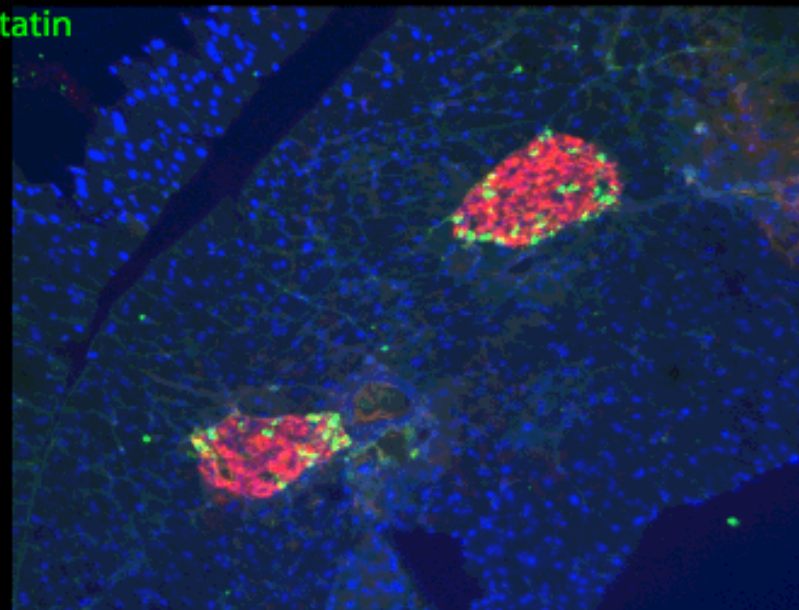
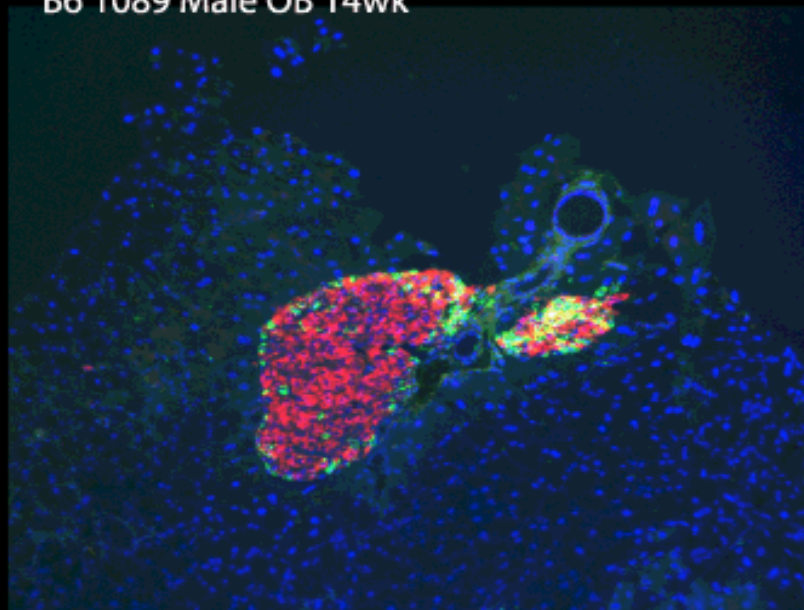
B6 1086 Female OB 14wk



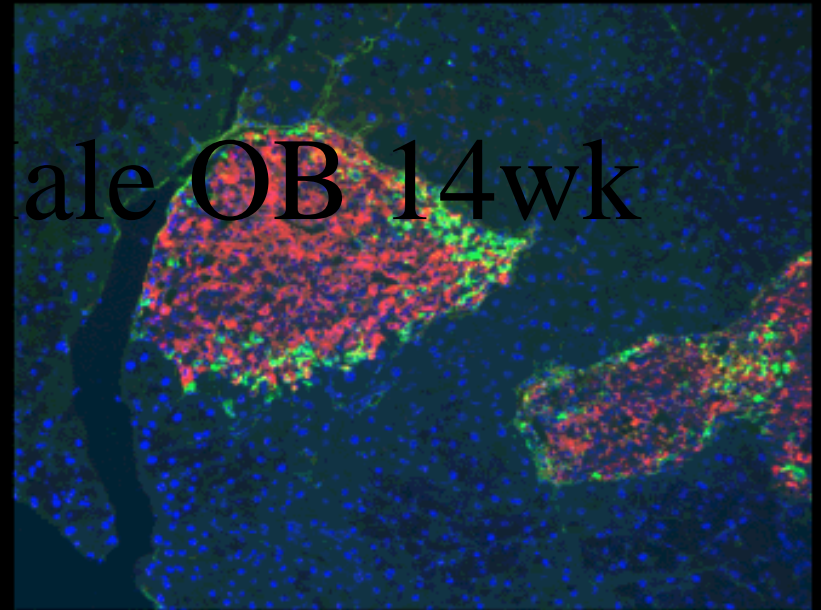
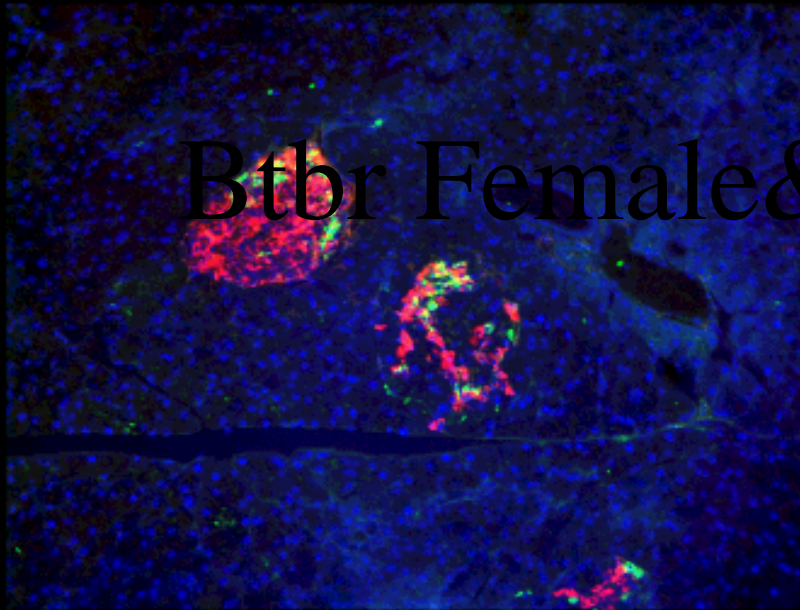
B6 Female & Male OB 14wk

Insulin
Glucagon
Somatostatin
Dapi

B6 1089 Male OB 14wk

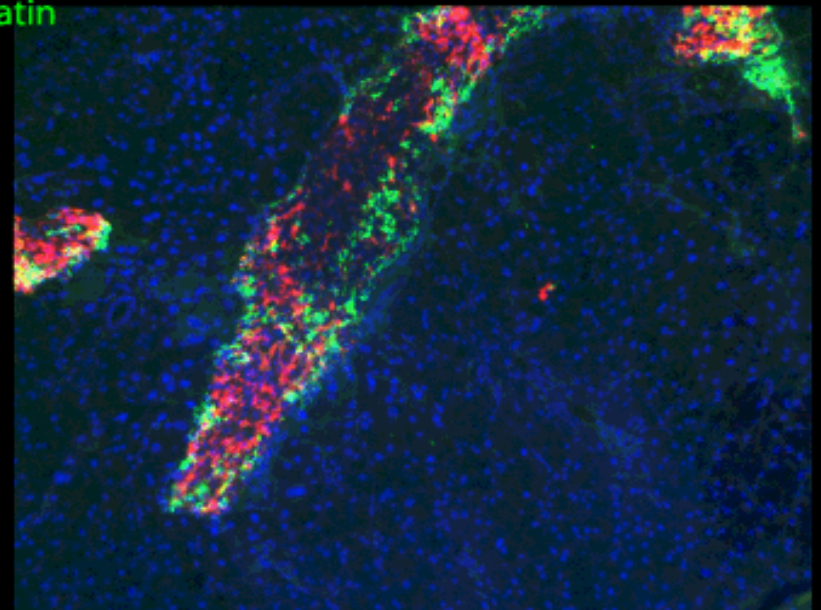
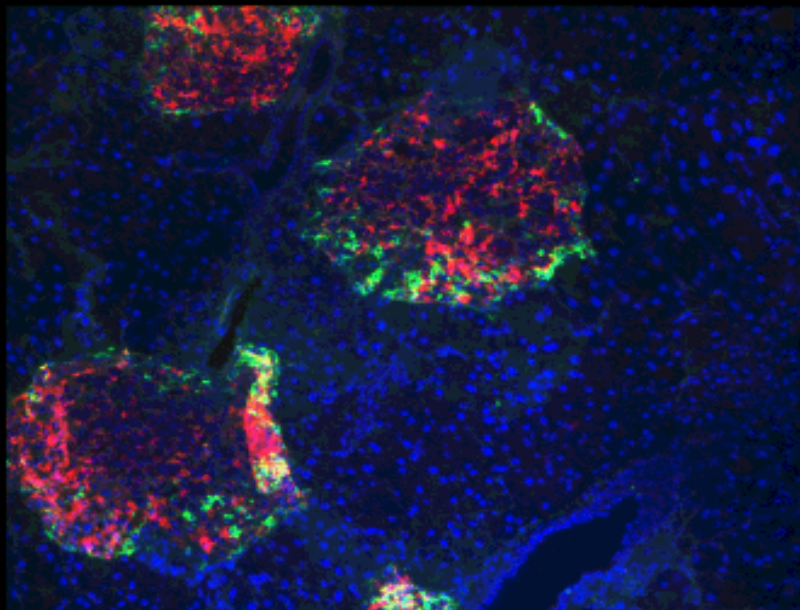


Btbr-1416 Female OB 14wk



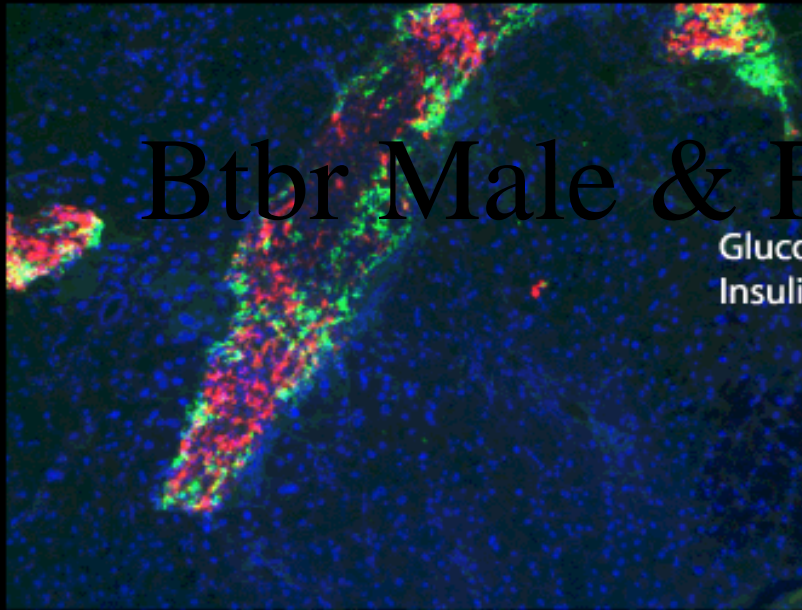
Btbr Female & Male OB 14wk

Btbr-1420 Male OB 14wk



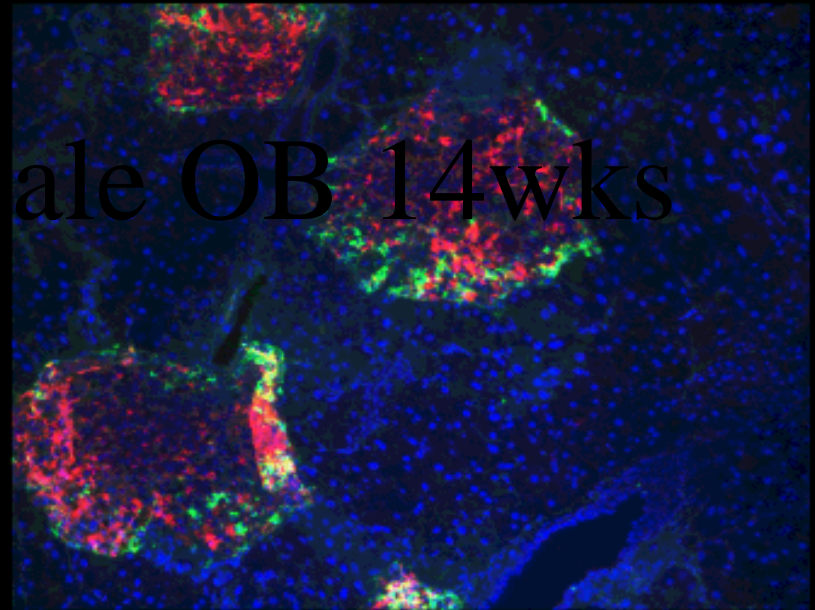
Insulin
Glucagon
Somatostatin
Dapi

Btbr 1420 Male

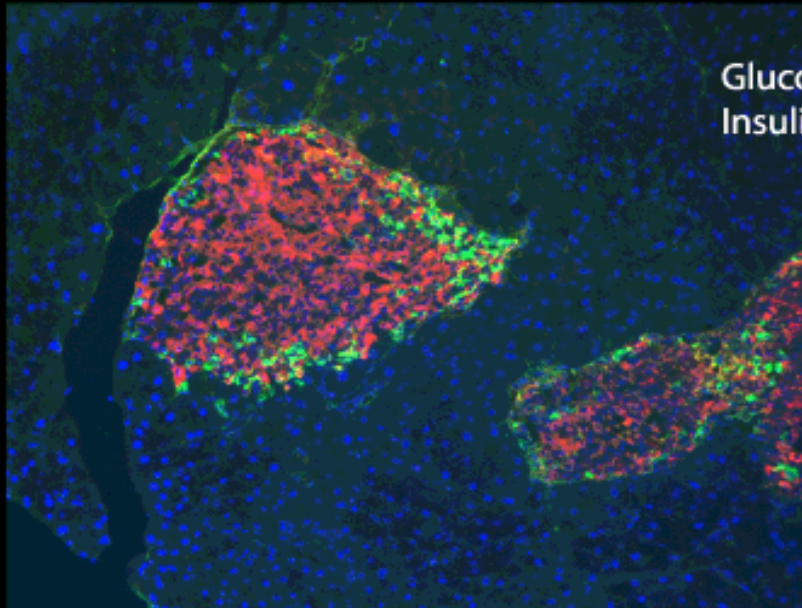


Btbr Male & Female OB 14wks

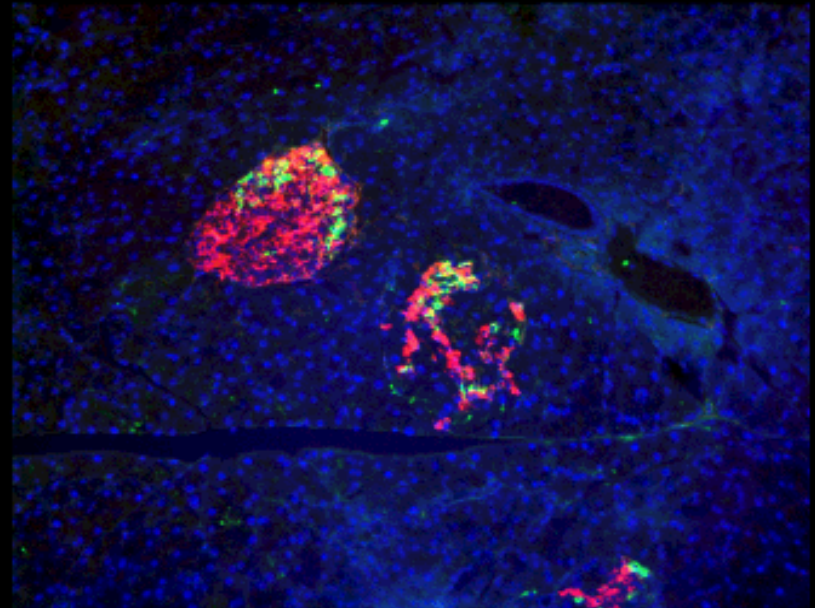
Glucose= 575
Insulin= 15.75



Btbr 1416 Female



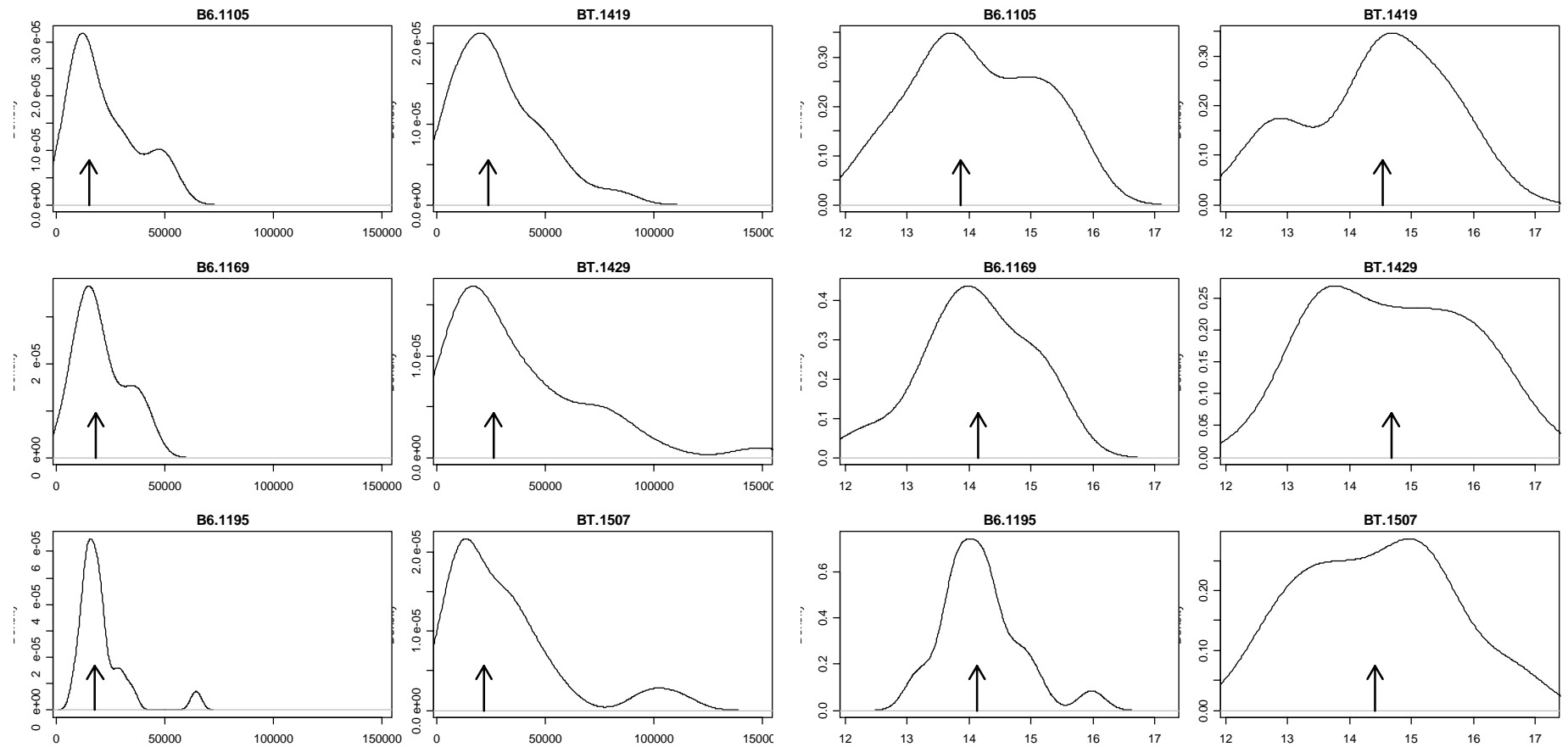
Glucose=321
Insulin=47.4



total percent area for islets

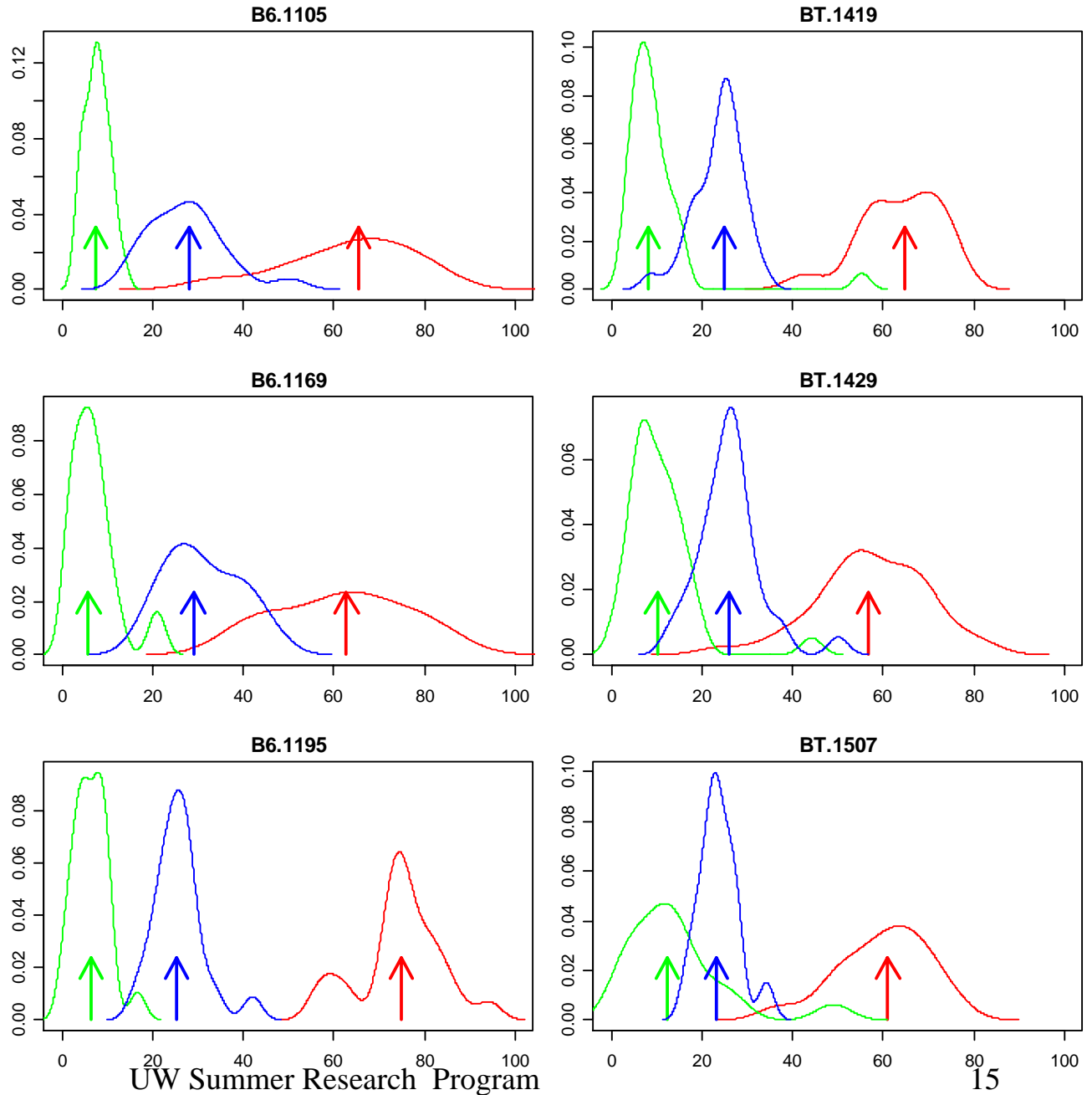
raw totals

log2 totals

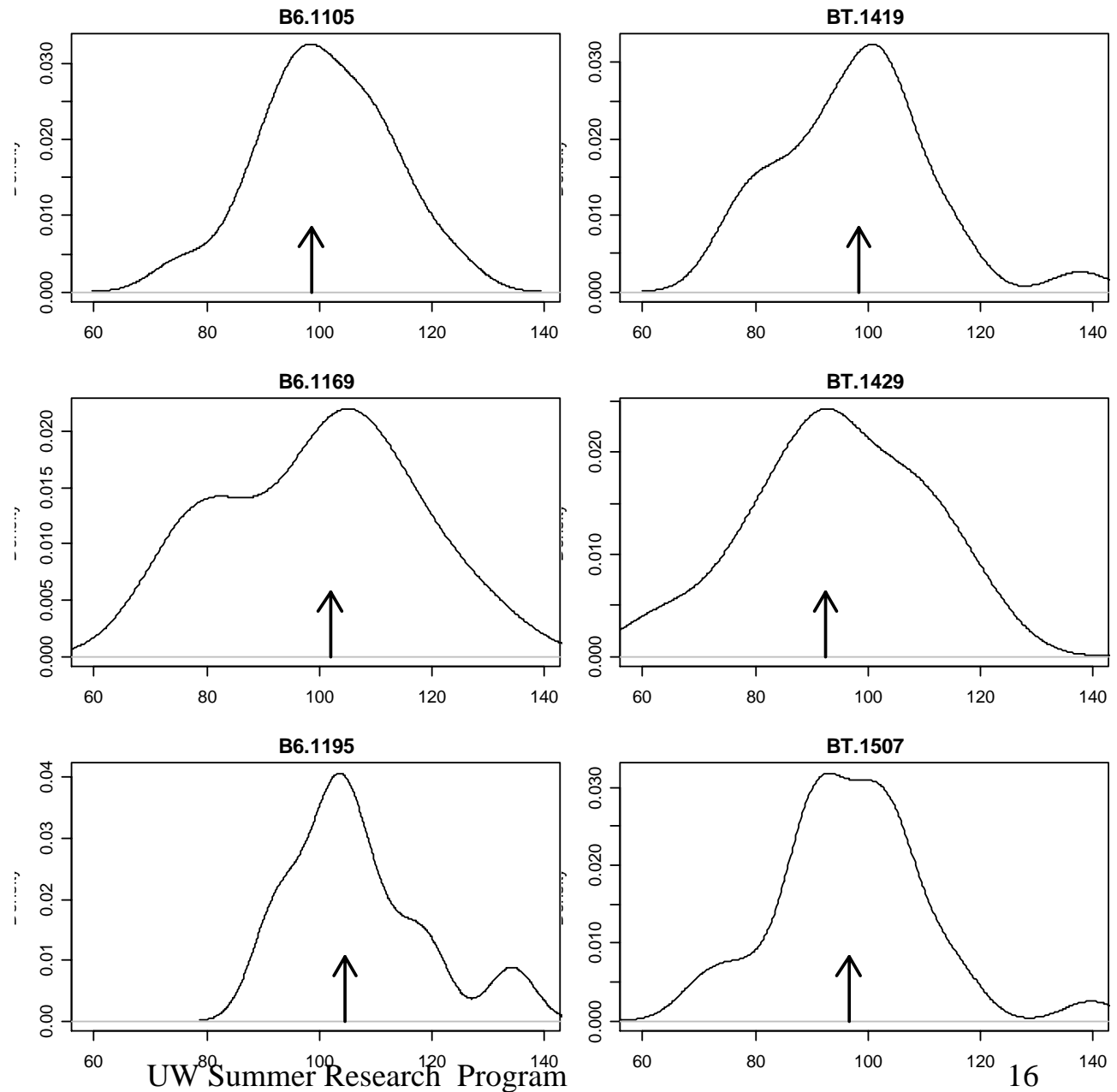


percent
glu/som,
dapi,
insulin
by mouse

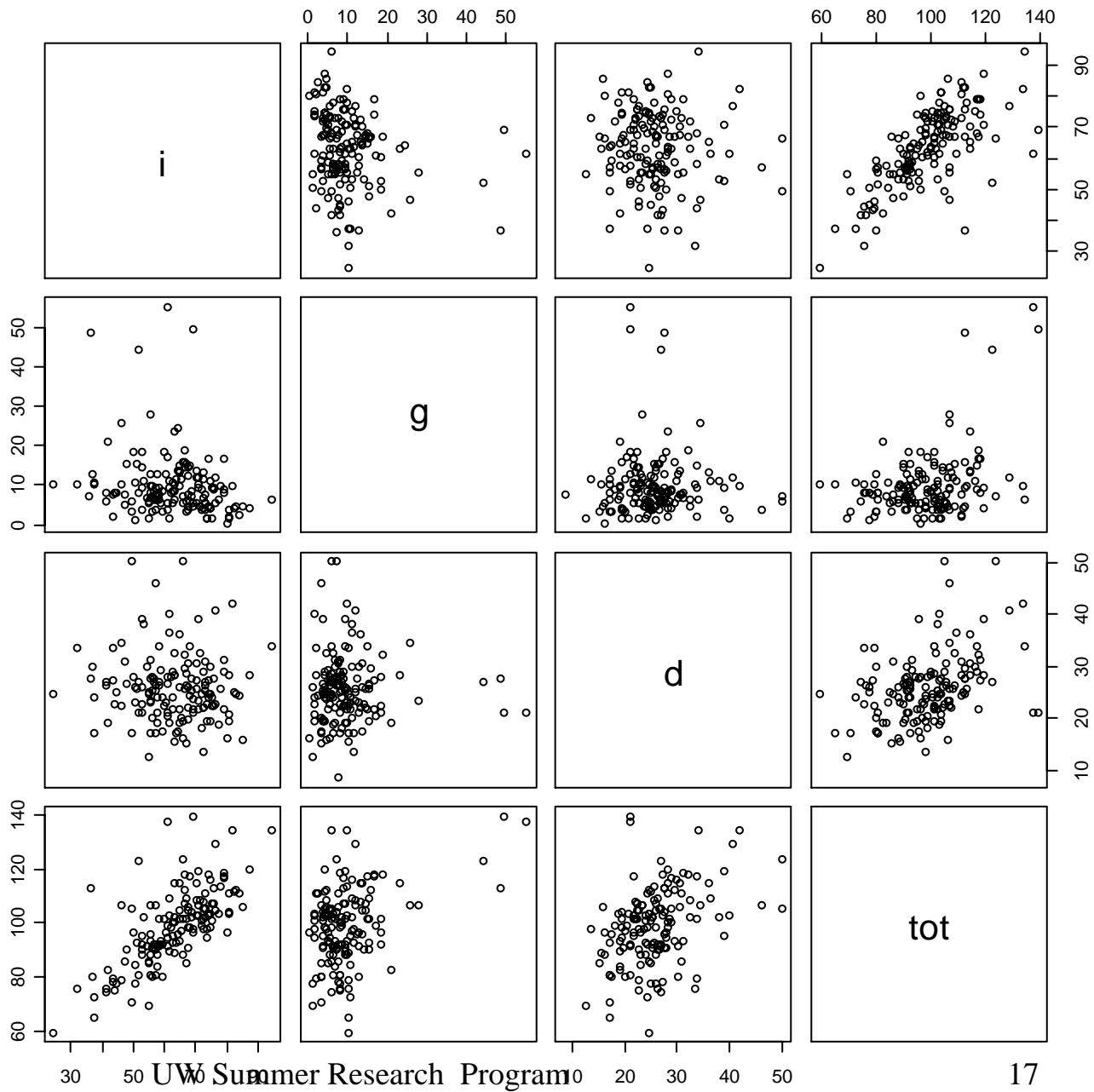
(smooth
histogram +
median)



sum of
insulin,
glu/som,
dapi
percents

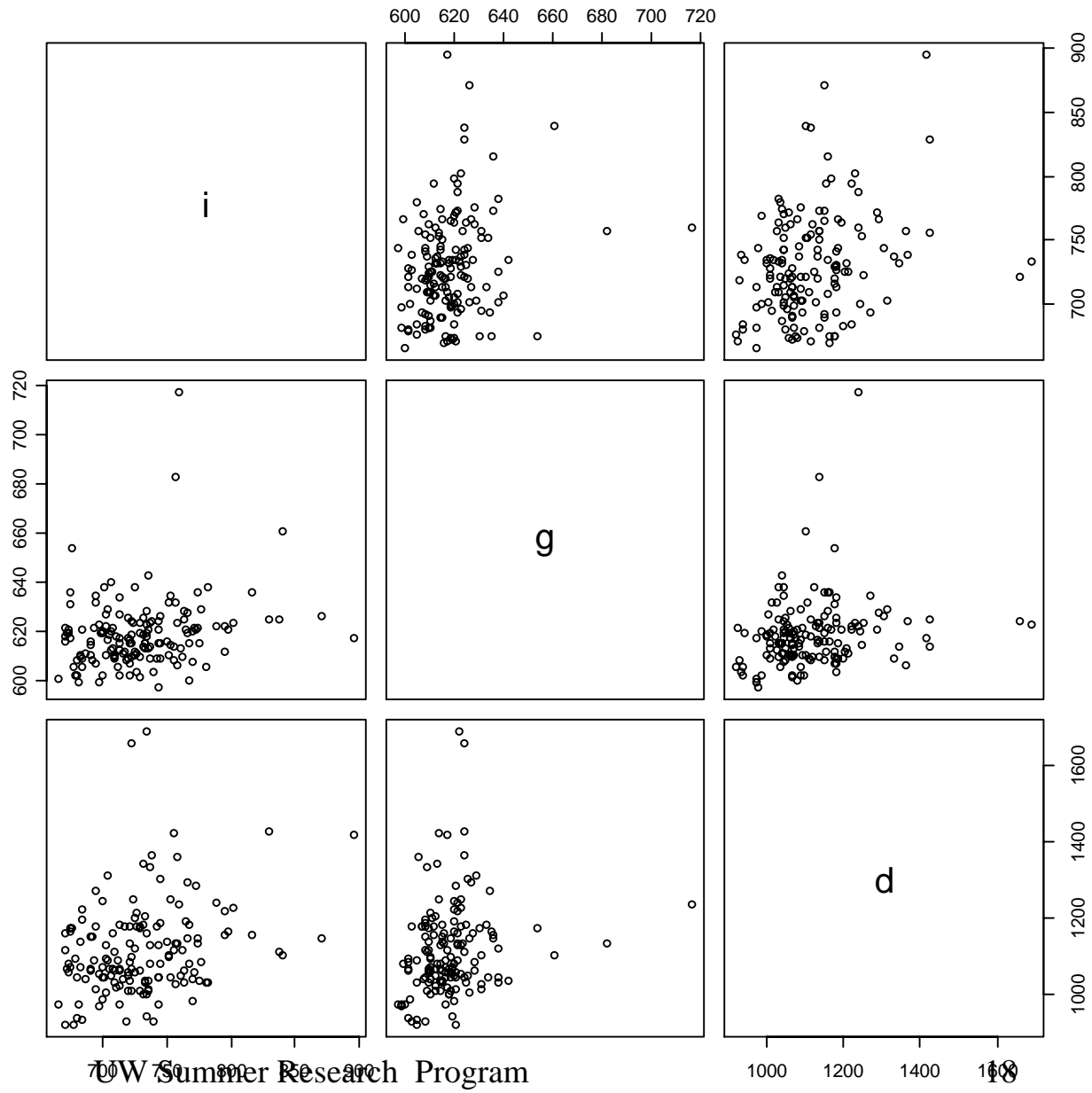


percent pairs (correlation) plot

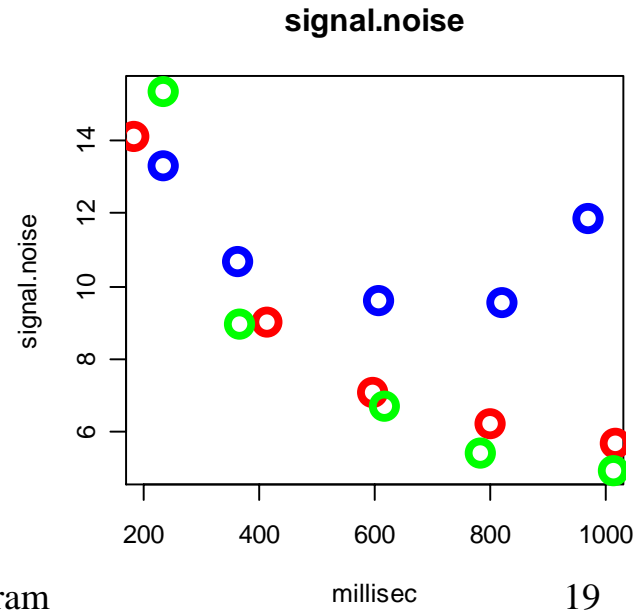
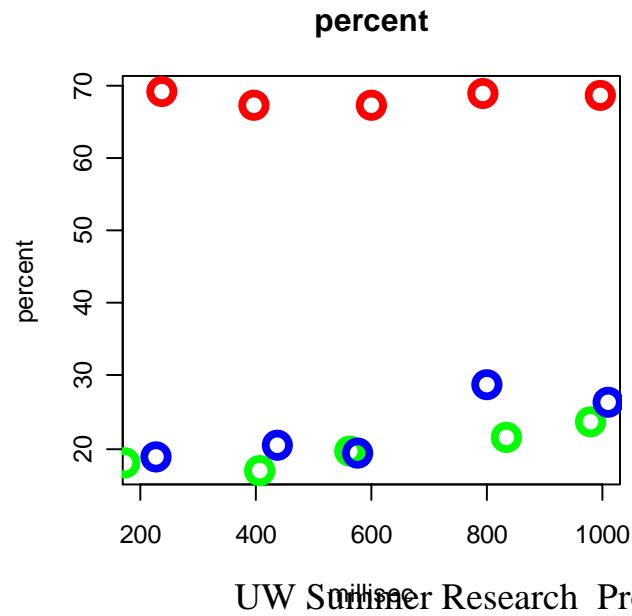
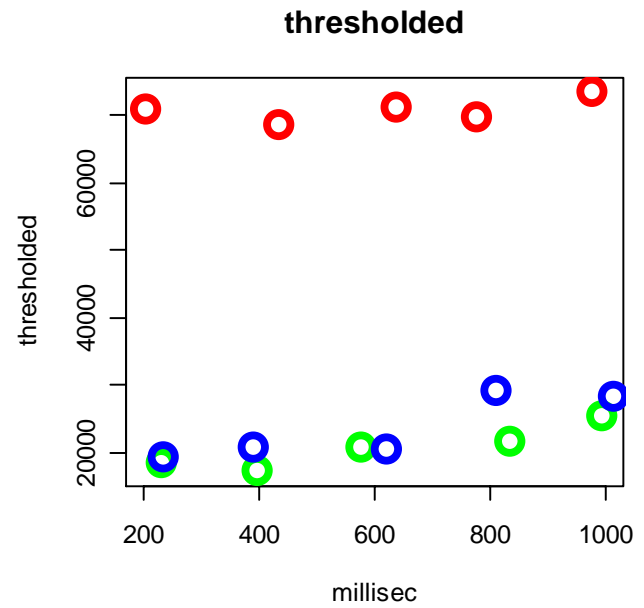
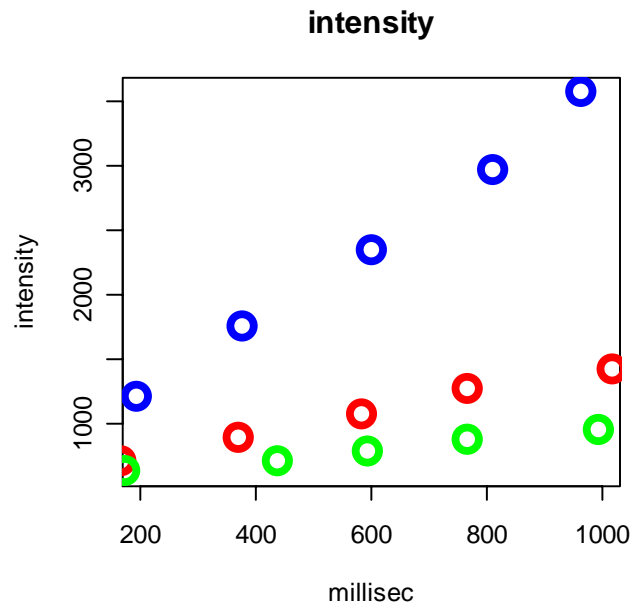


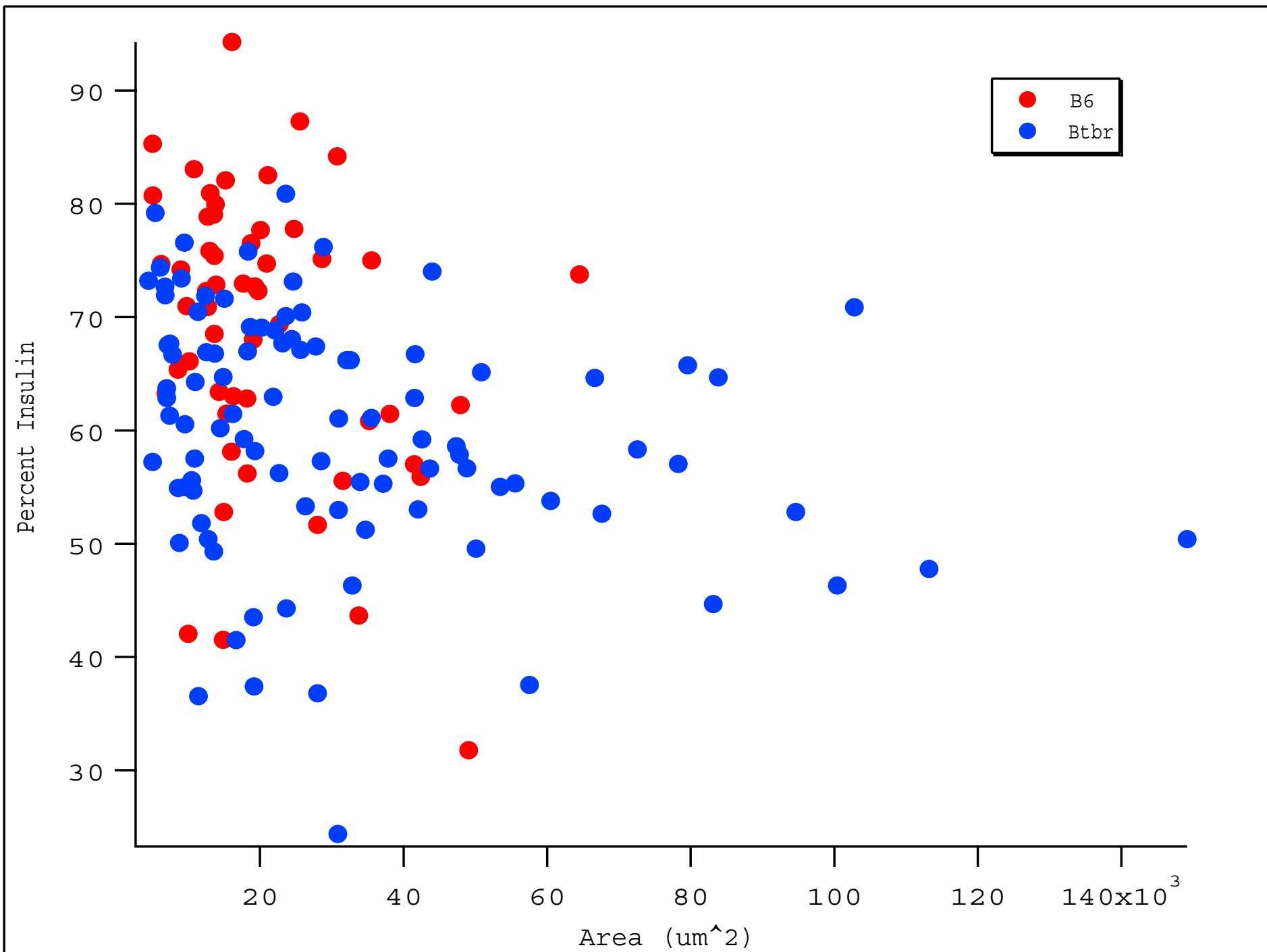
intensity pairs (correlation) plot

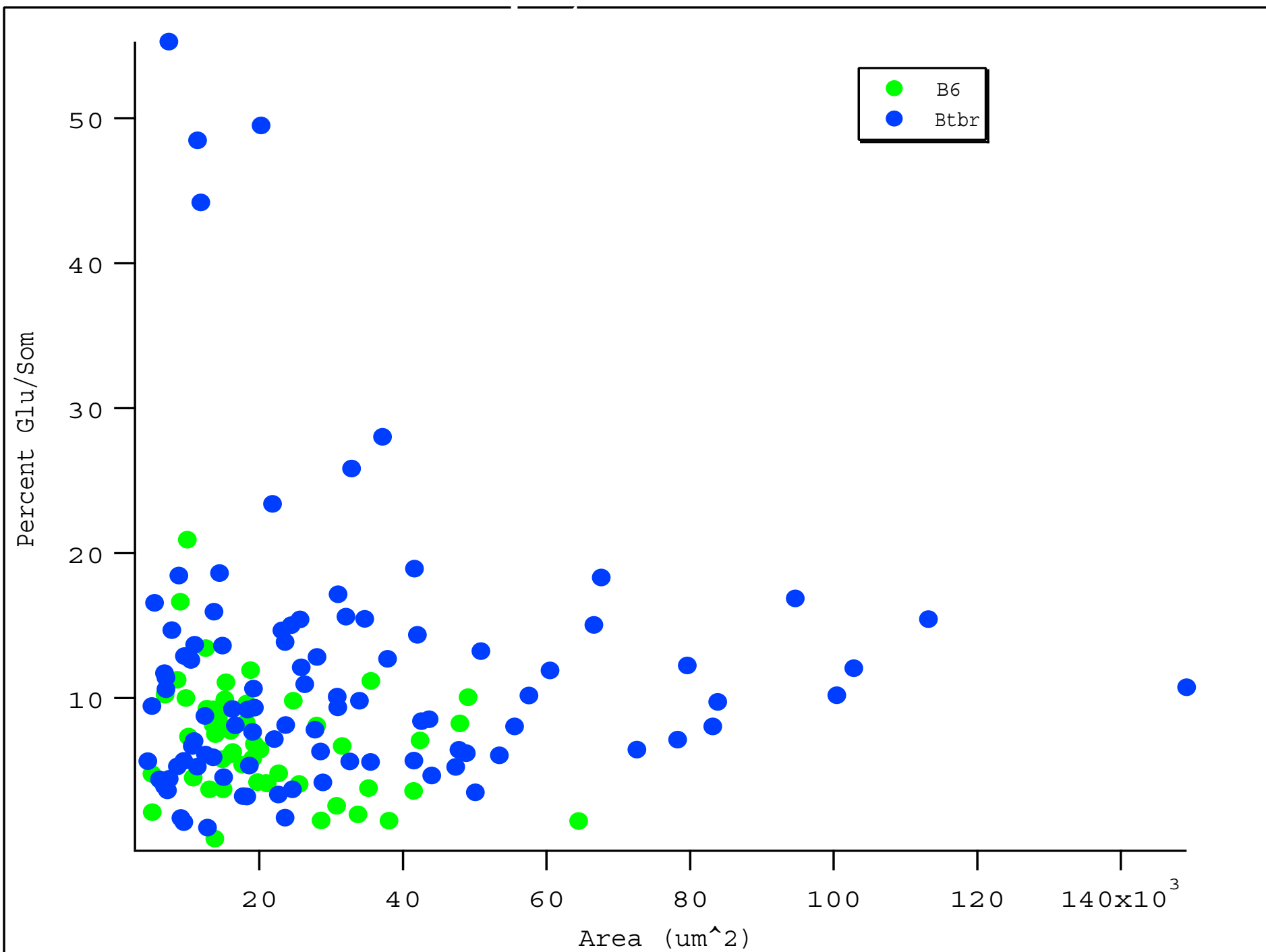
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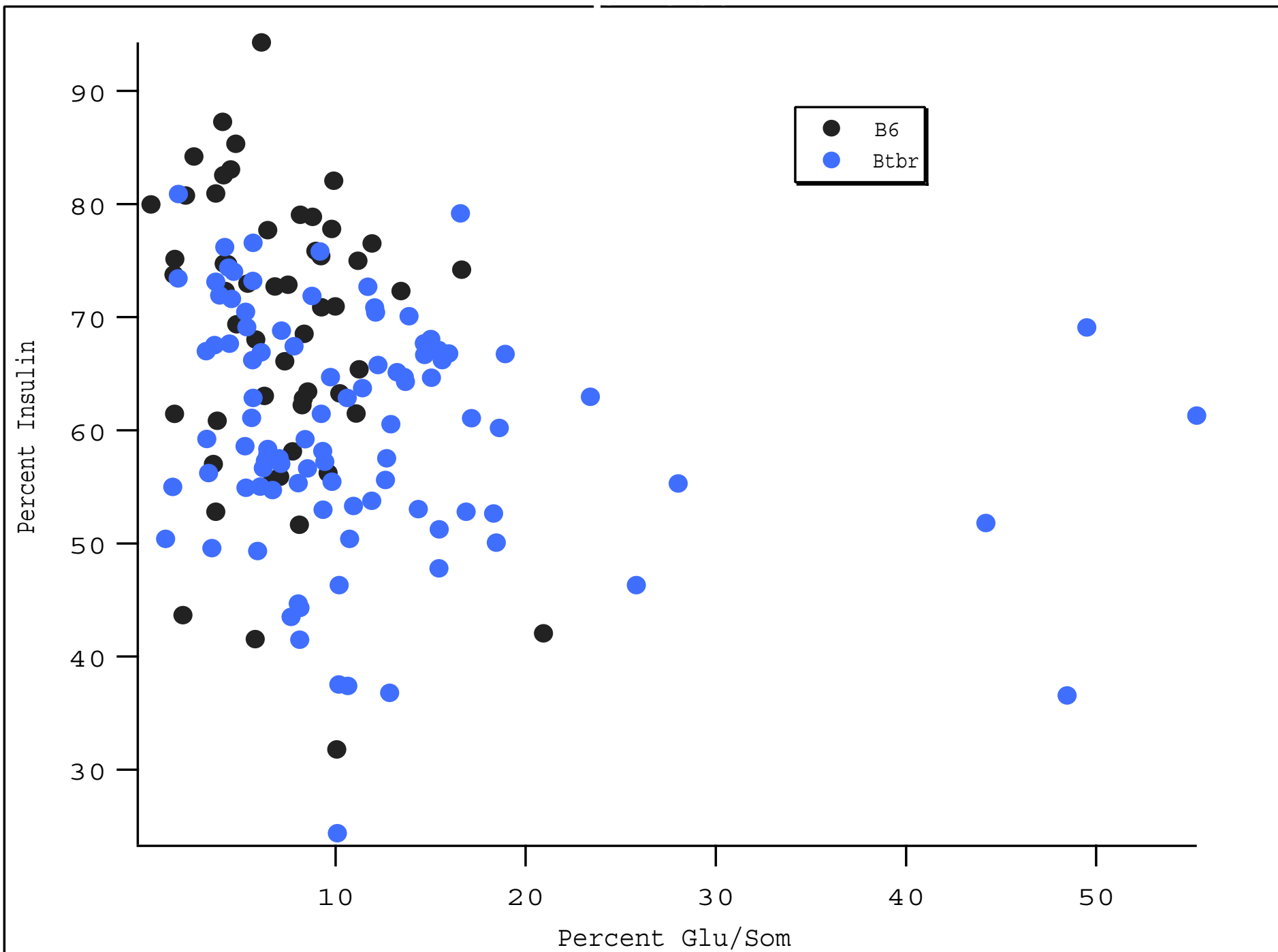


calibration study

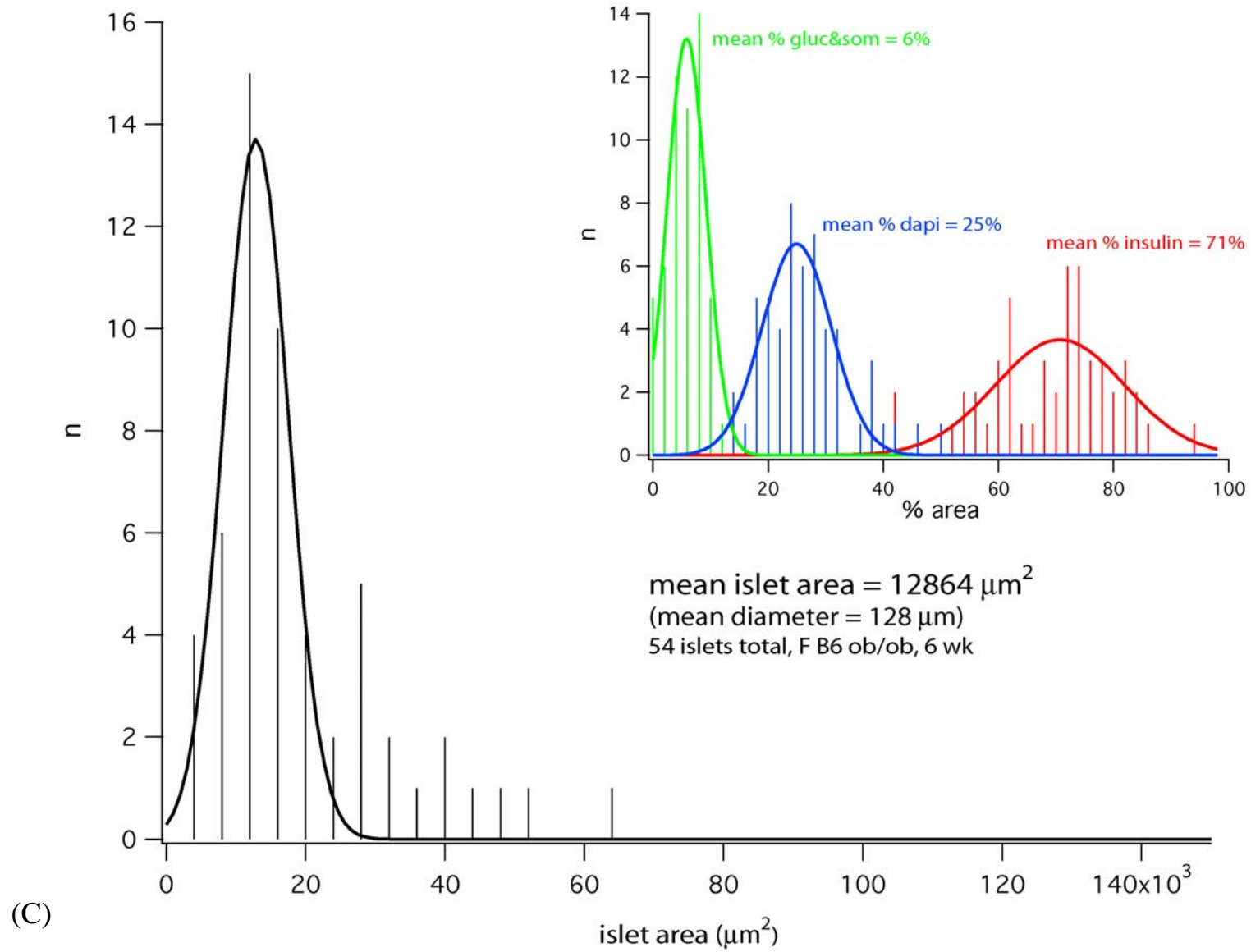




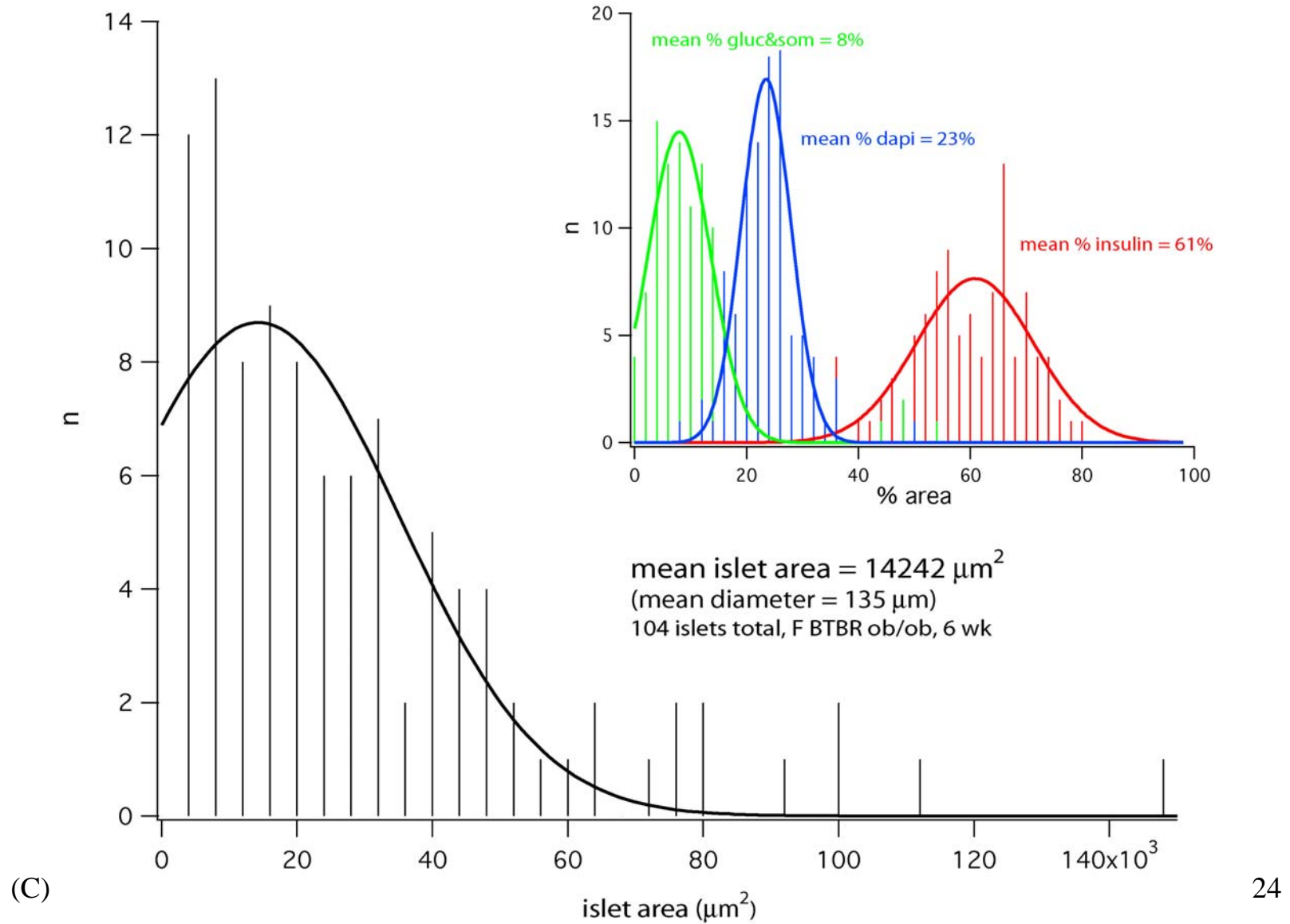




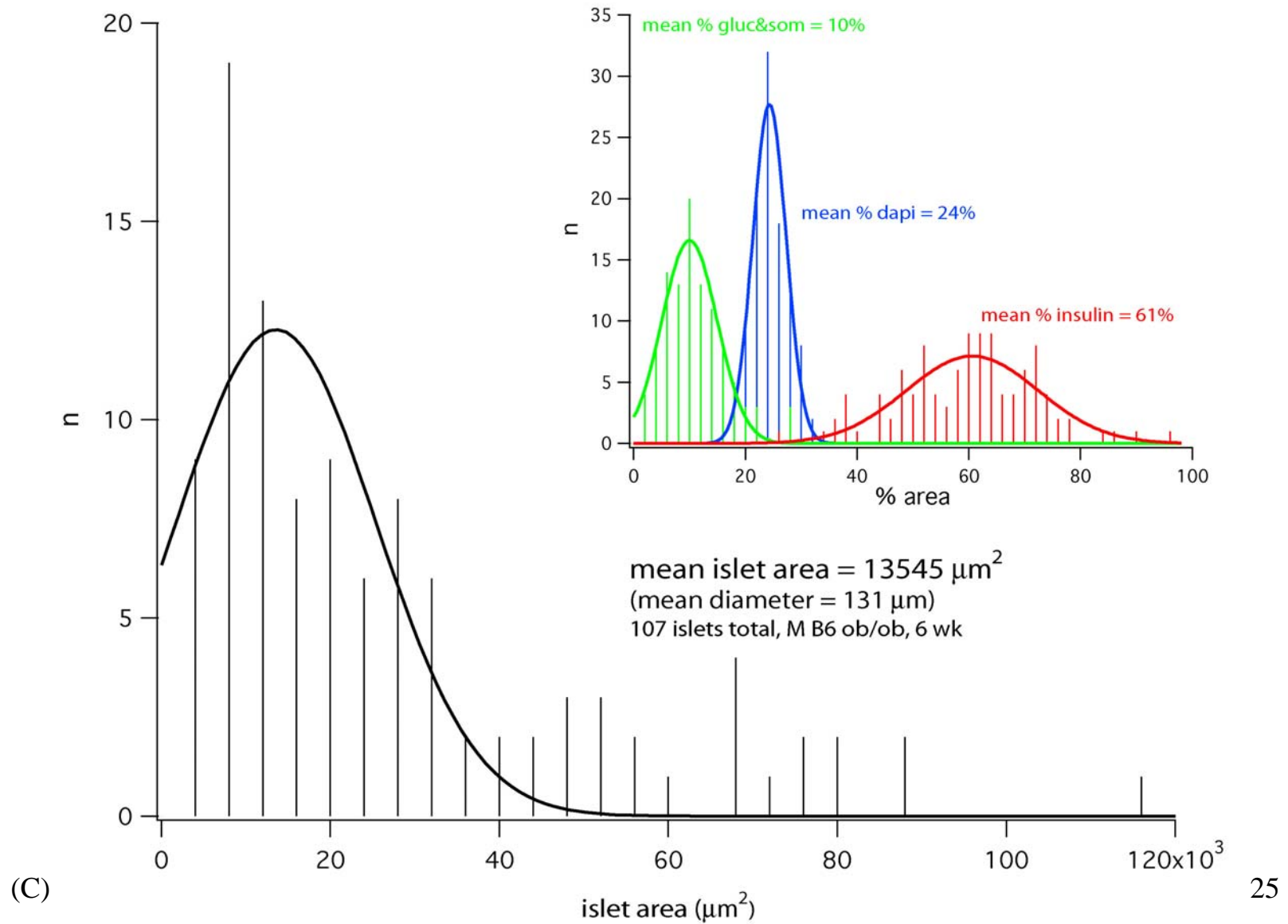
Female ob/ob B6



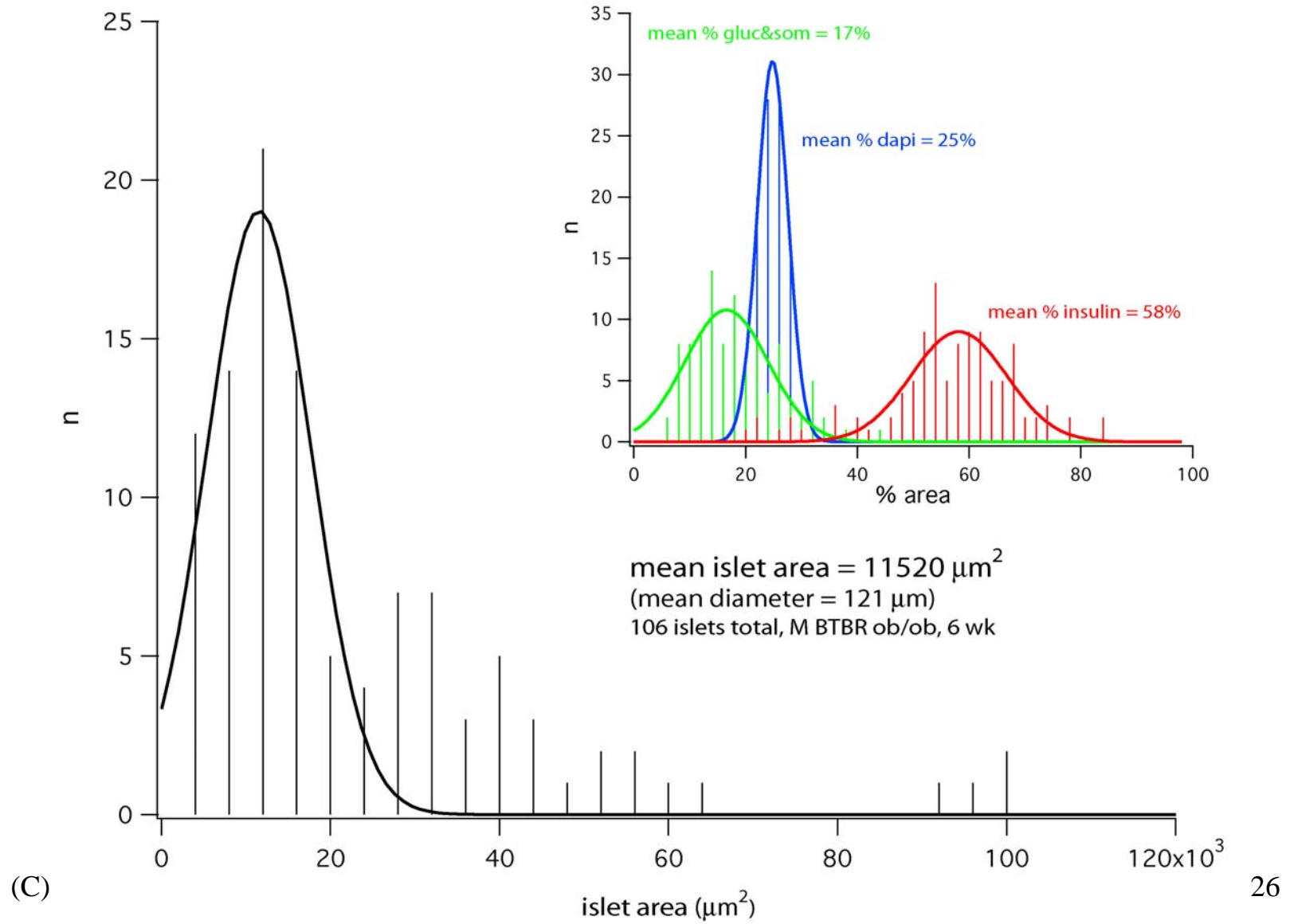
Female ob/ob BTBR



Male ob/ob B6



Male ob/ob BTBR



Summary table for ob/ob B6 and Btbr islets

All animals ob/ob and 6 wk of age.

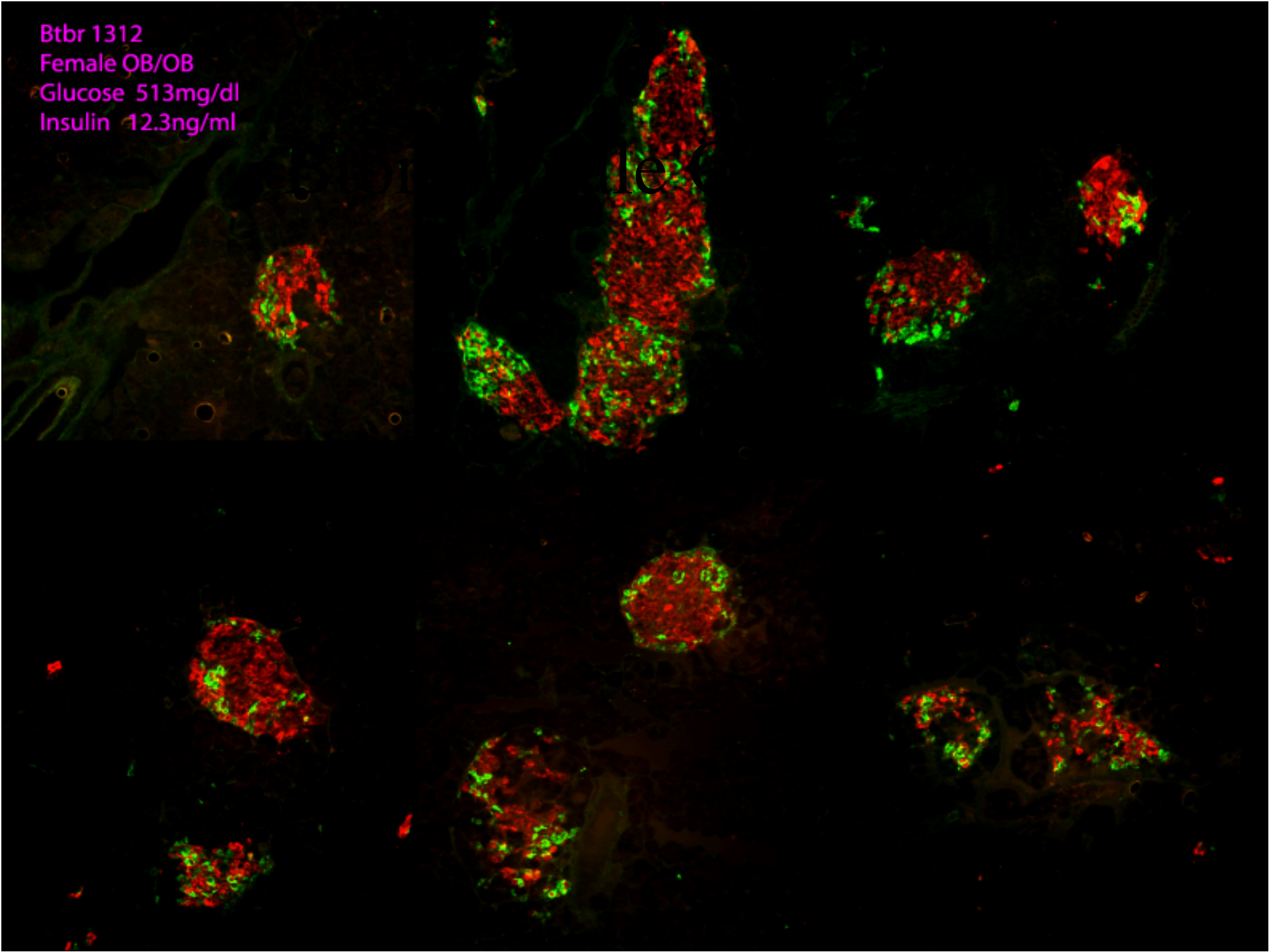
#'s show mean of gaussian fit for all islets analyzed.

Strain	# islets	Islet area (μm^2)	Islet diameter (μm)	% Gluc&Som	% DAPI	% Insulin	Total %
B6 F	54	12864	128	6	25	71	102
Btbr F	104	14242	135	8	23	61	92
B6 M	107	13545	131	10	24	61	95
Btbr M	106	11520	121	17	25	58	100

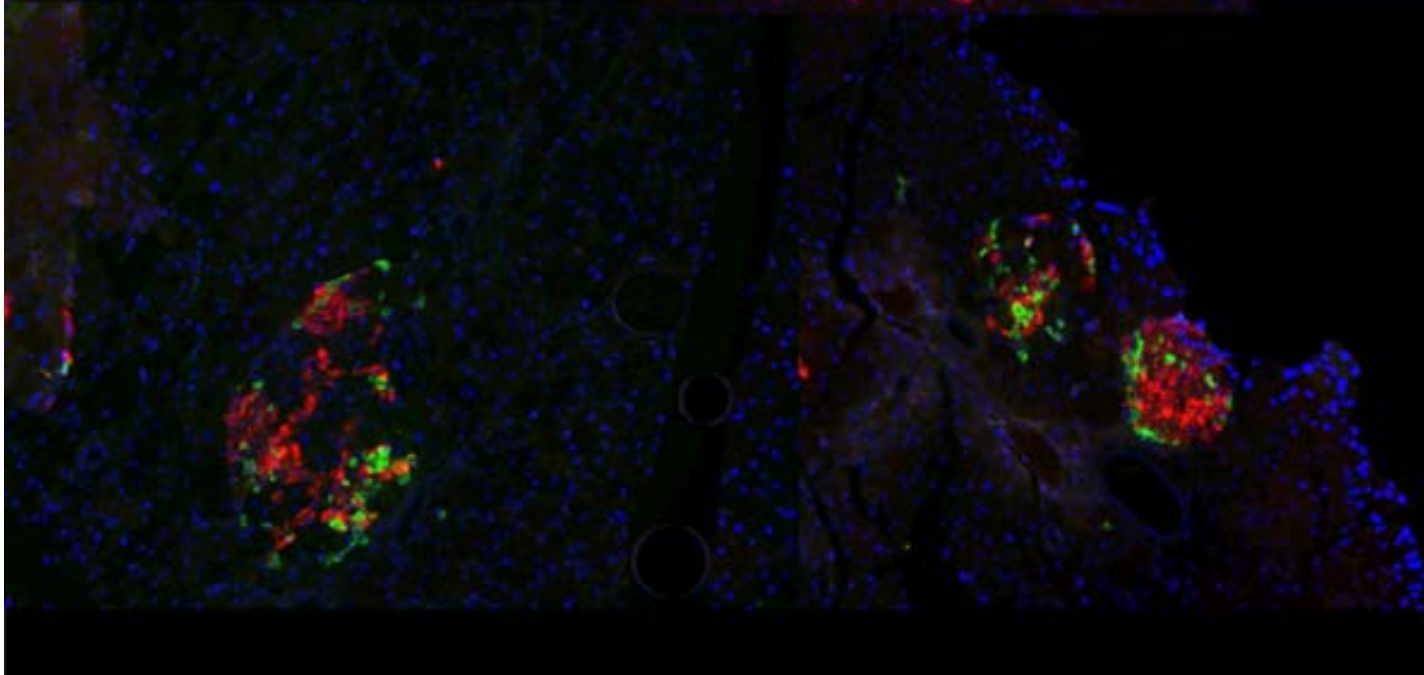
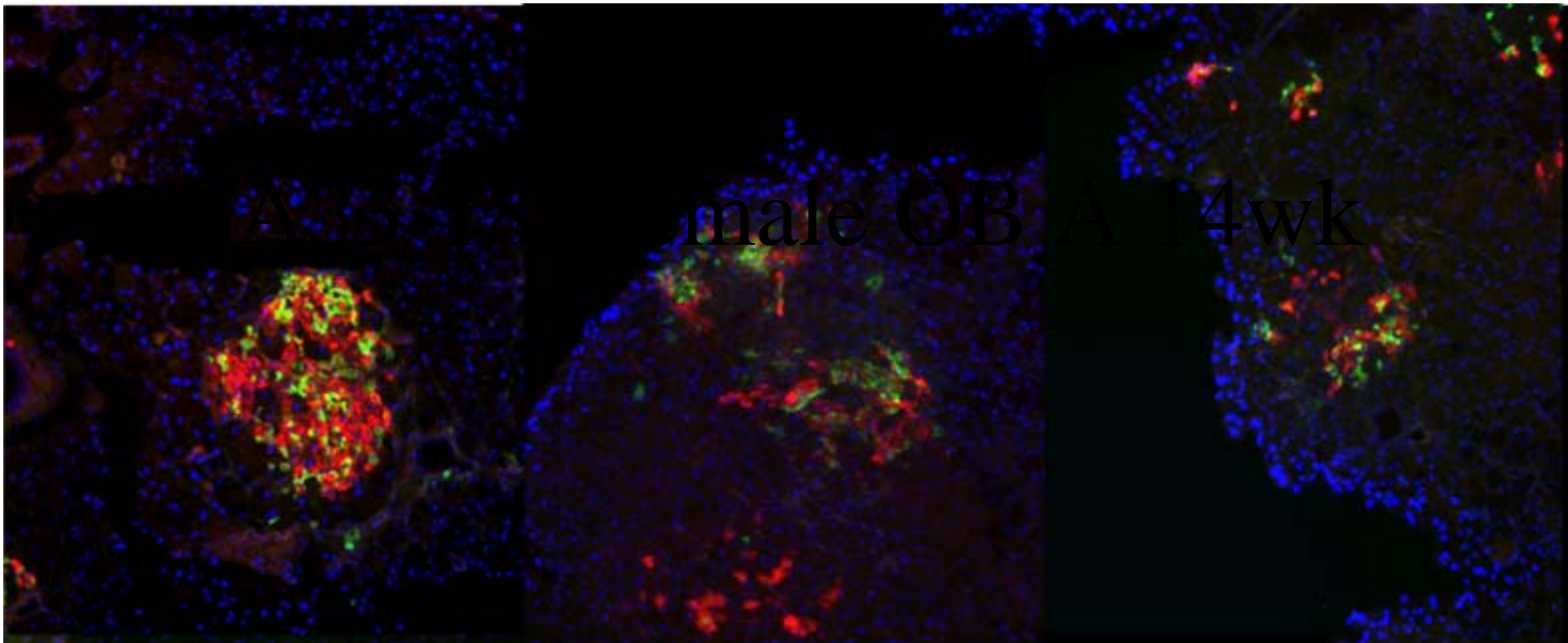
14 week Congenic Females

- Is there a difference between A & B congenics?
- Is there a difference between Btbr and the B congenic strain?
- How does the glucose and insulin values effect our comparisons?

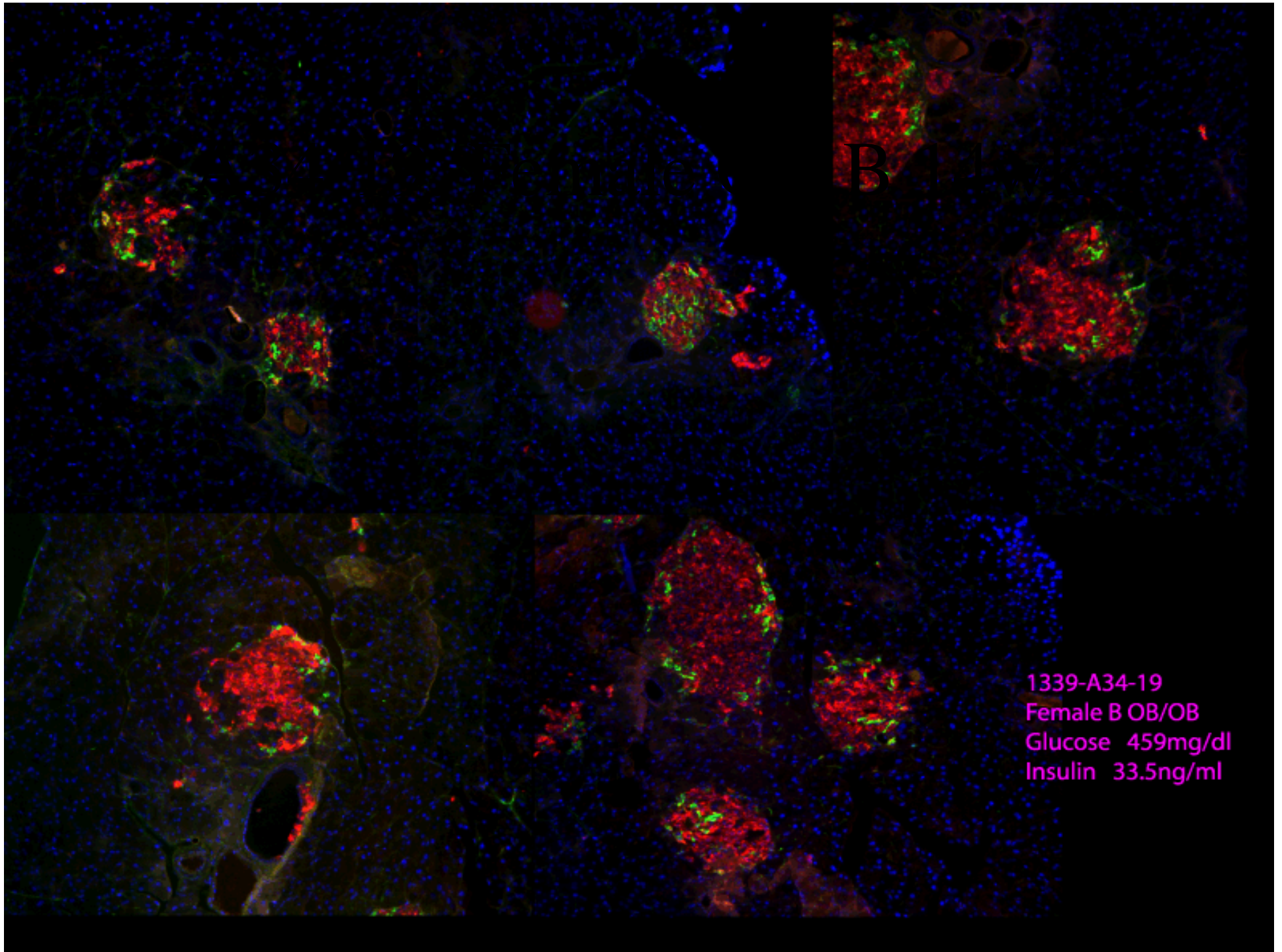
Btbr 1312
Female OB/OB
Glucose 513mg/dl
Insulin 12.3ng/ml



A33-18 male OB A 14wk

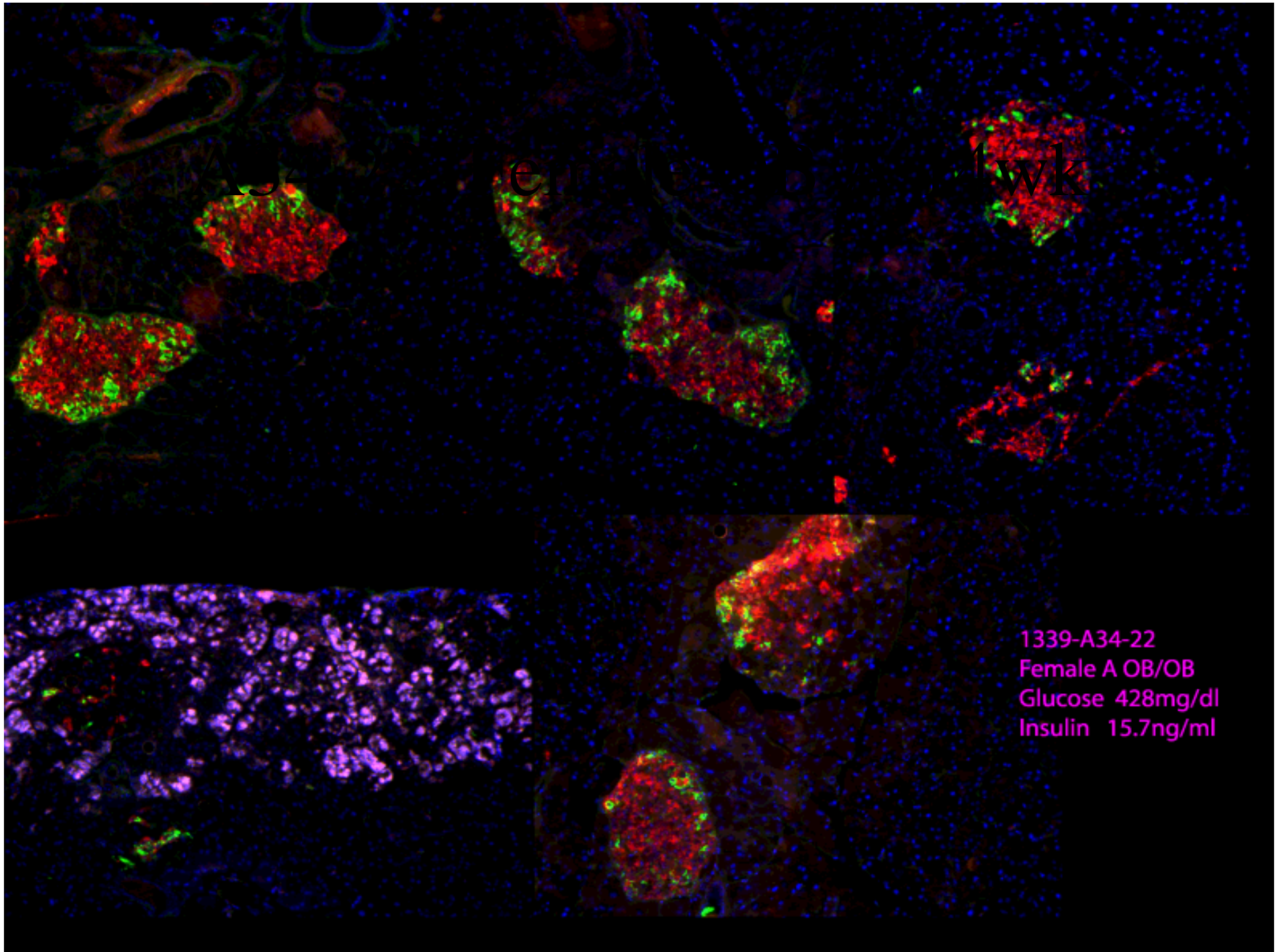


1339-A33-18
Female A OB/OB
Glucose 467mg/dl
Insulin 8.6ng/ml



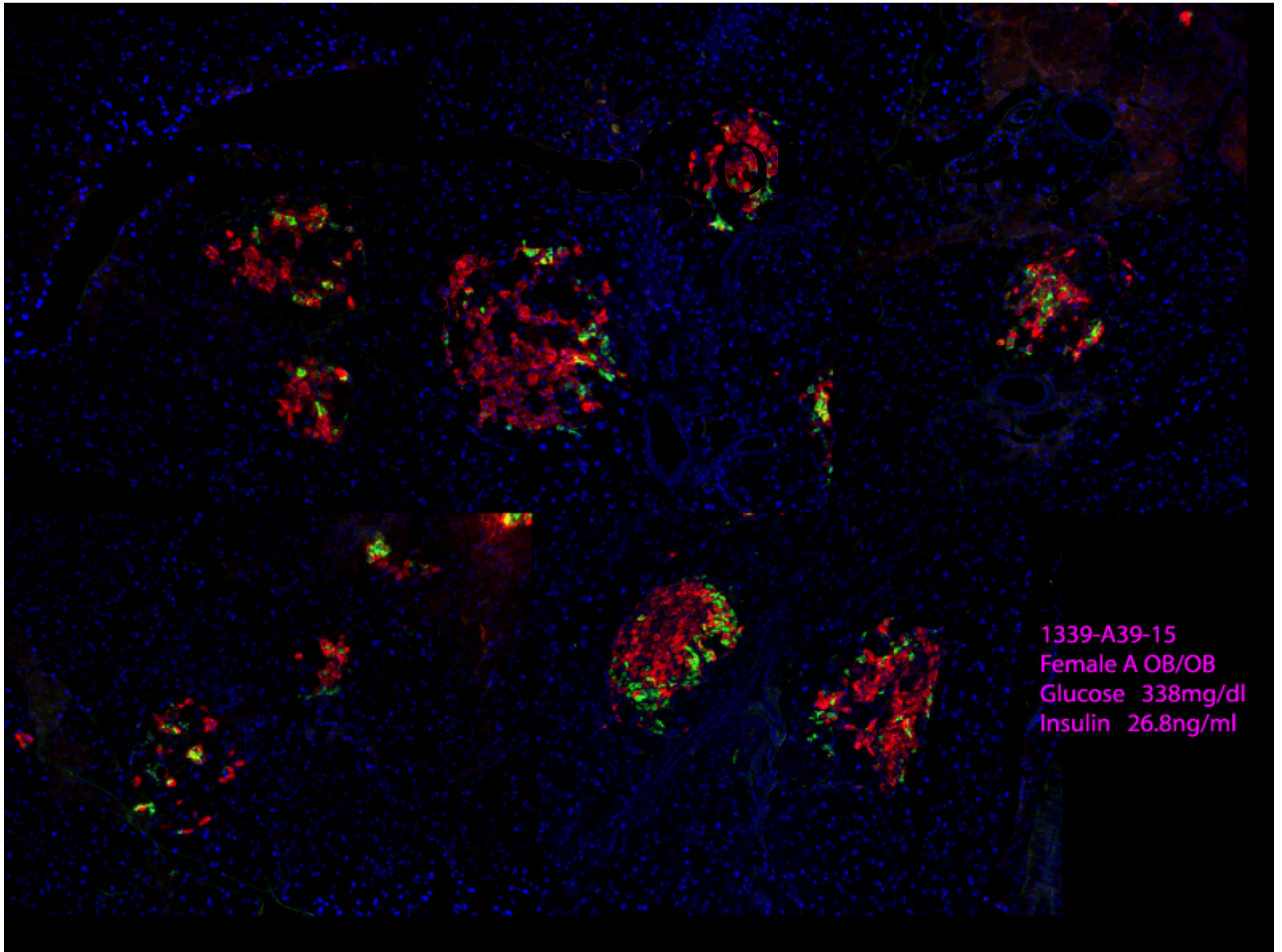
B

1339-A34-19
Female B OB/OB
Glucose 459mg/dl
Insulin 33.5ng/ml



1339-A34-22

Female A OB/OB
Glucose 428mg/dl
Insulin 15.7ng/ml



1339-A39-15
Female A OB/OB
Glucose 338mg/dl
Insulin 26.8ng/ml

A48-4 male OB 14y

1339-A48-4
Female B OB/OB
Glucose 265mg/dl
Insulin 11.0ng/ml

