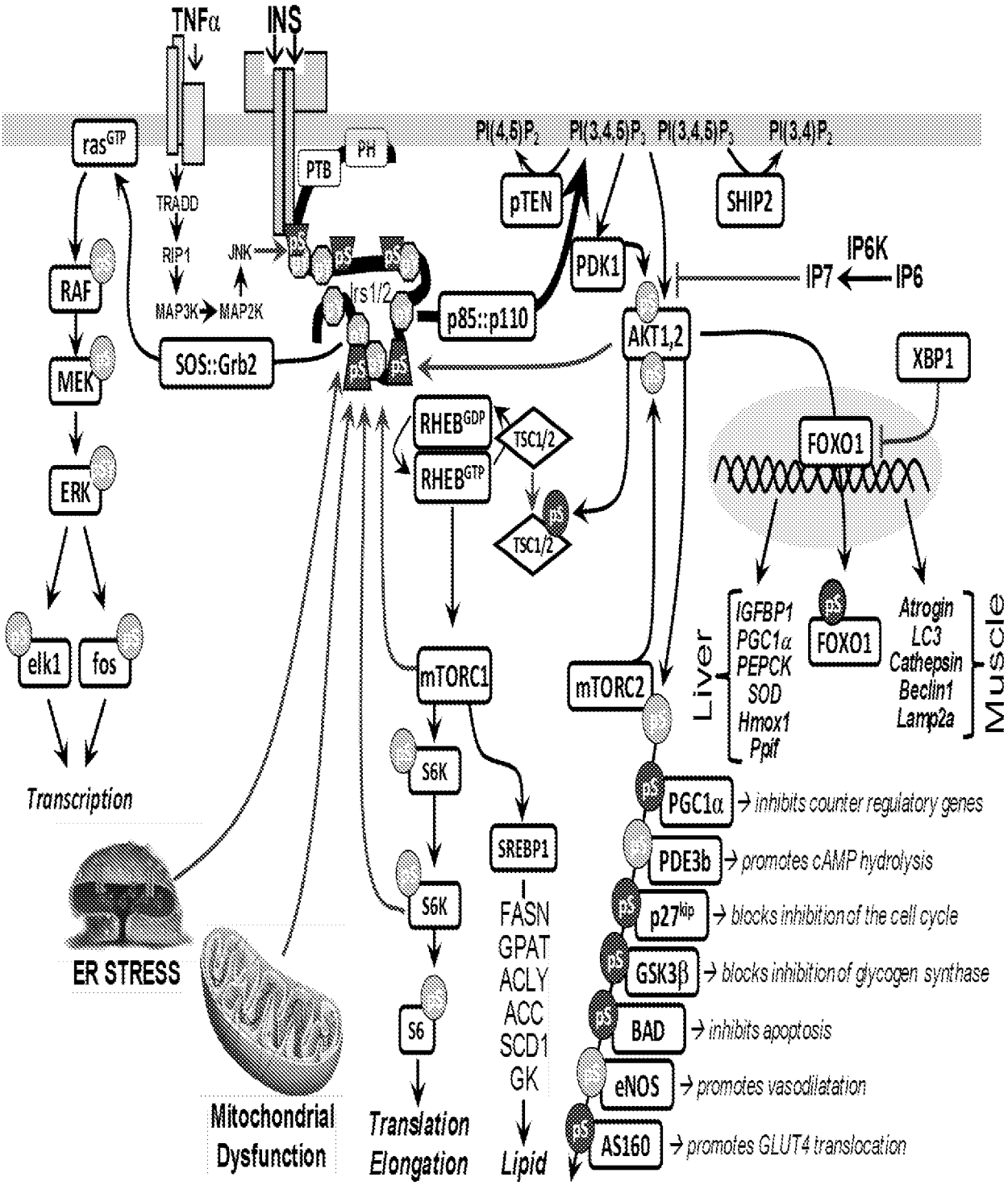

TNFα
INS
ras^GTP
PTB
PH
PI(4,5)P2
PI(3,4,5)P3
PI(3,4)P2
pTEN
SHIP2
TRADD
RIP1
JNK
MAP3K
MAP2K
RAF
MEK
ERK
elk1
fos
Transcription
SOS::Grb2
Irs1/2
p85::p110
PDK1
IP6K
IP7
IP6
AKT1,2
XBP1
FOXO1
RHEB^GDP
RHEB^GTP
TSC1/2
mTORC1
mTORC2
S6K
S6
SREBP1
FASN
GPAT
ACLY
ACC
SCD1
GK
Lipid
Translation
Elongation
ER STRESS
Mitochondrial
Dysfunction
Liver
IGFBP1
PGC1α
PEPCK
SOD
Hmox1
Ppif
Muscle
Atrogin
LC3
Cathepsin
Beclin1
Lamp2a
PGC1α → inhibits counter regulatory genes
PDE3b → promotes cAMP hydrolysis
p27^kip → blocks inhibition of the cell cycle
GSK3β → blocks inhibition of glycogen synthase
BAD → inhibits apoptosis
eNOS → promotes vasodilatation
AS160 → promotes GLUT4 translocation

Fig. 1A

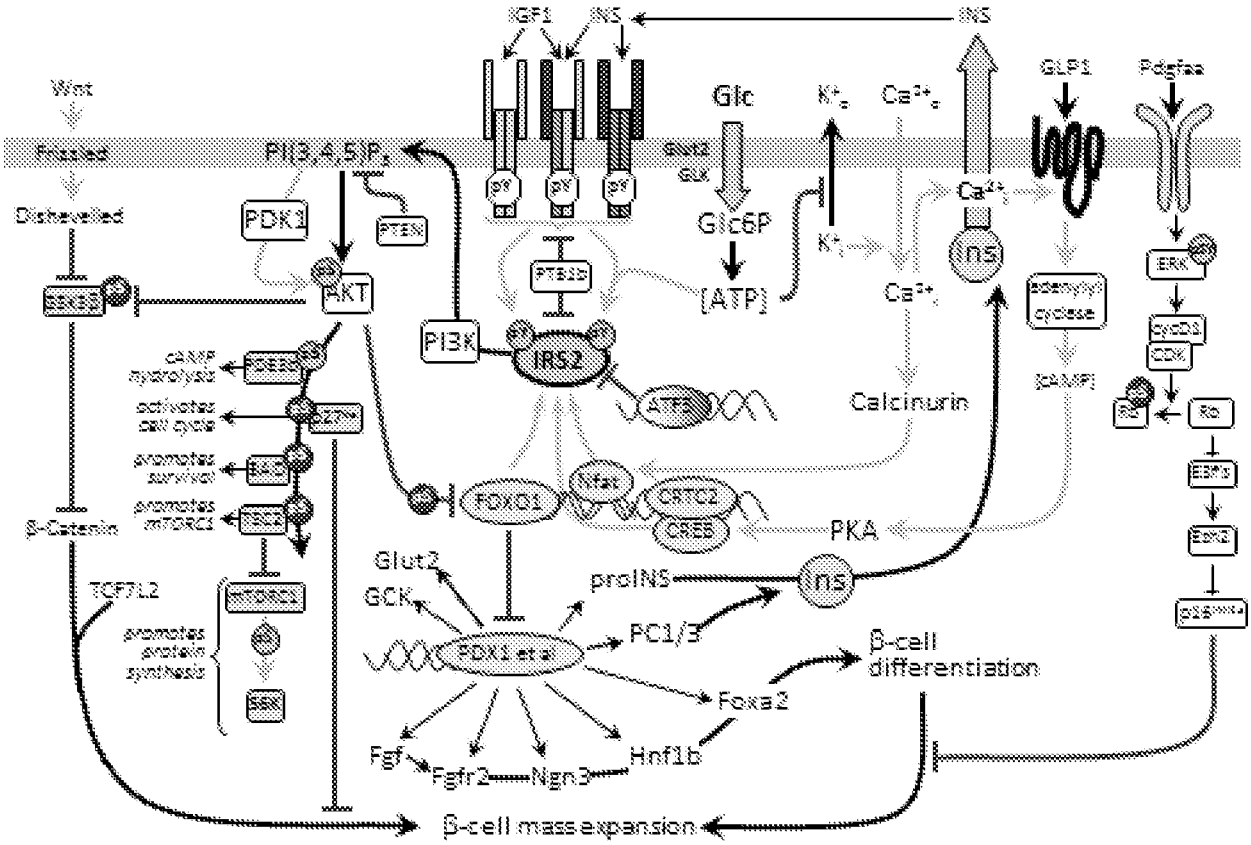
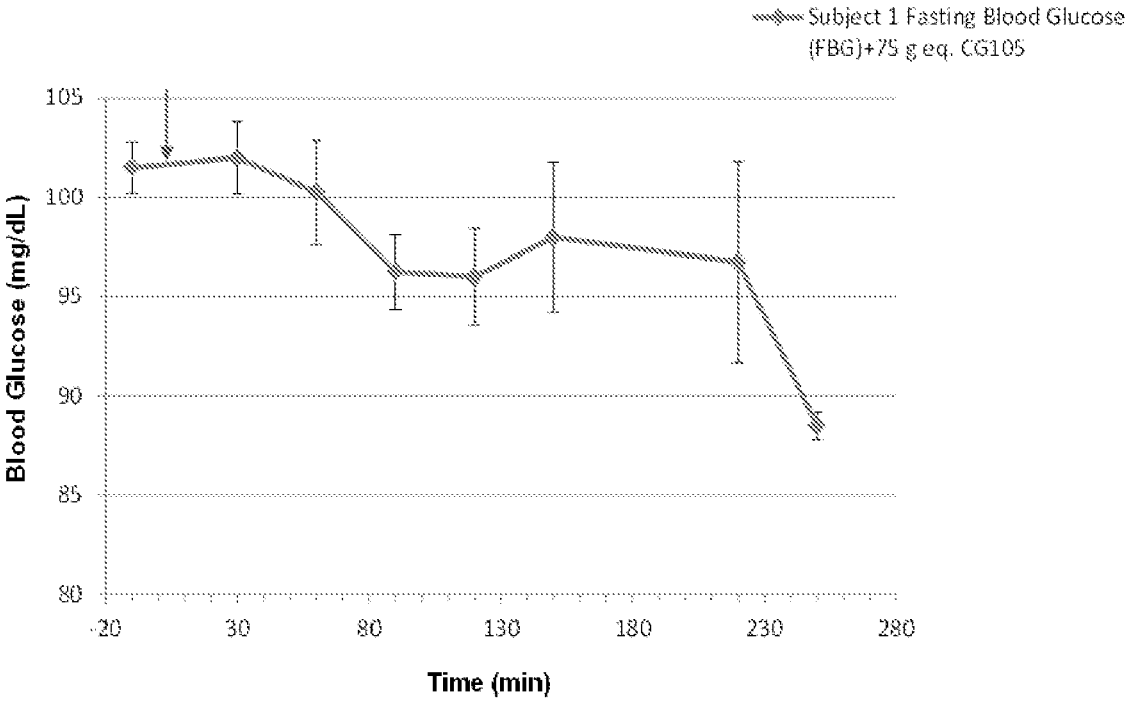

IGF1
INS
INS
Wnt
Glc
GLP1
Pdgfbb
Frizzled
PI(3,4,5)P3
Glut2
GLK
Dishevelled
PDK1
PTEN
Glc6P
Ca2+c
Ca2+i
ins
GSK3β
AKT
PTEN
[ATP]
K+c
K+i
ERK
cAMP hydrolysis
PI3K
IRS2
Adenylyl cyclase
cyclin D1
activates cell cycle
CDK
[cAMP]
ATF6
Calcinurin
promotes survival
Rb
promotes mTORC1
FOXO1
Nfat
CRTC2
β-Catenin
CREB
PKA
E2F1
Glut2
GCK
proINS
ins
TCF7L2
mTORC1
PC1/3
β-cell differentiation
promotes protein synthesis
PDX1 et al
Foxa2
Fgf
Fgfr2
Ngn3
Hnf1b
β-cell mass expansion

Fig. 1B

A.


Subject 1 Fasting Blood Glucose (FBG)+75 g eq. CG105
Blood Glucose (mg/dL)
105
100
95
90
85
80
-20
30
80
130
180
230
280
Time (min)

B.

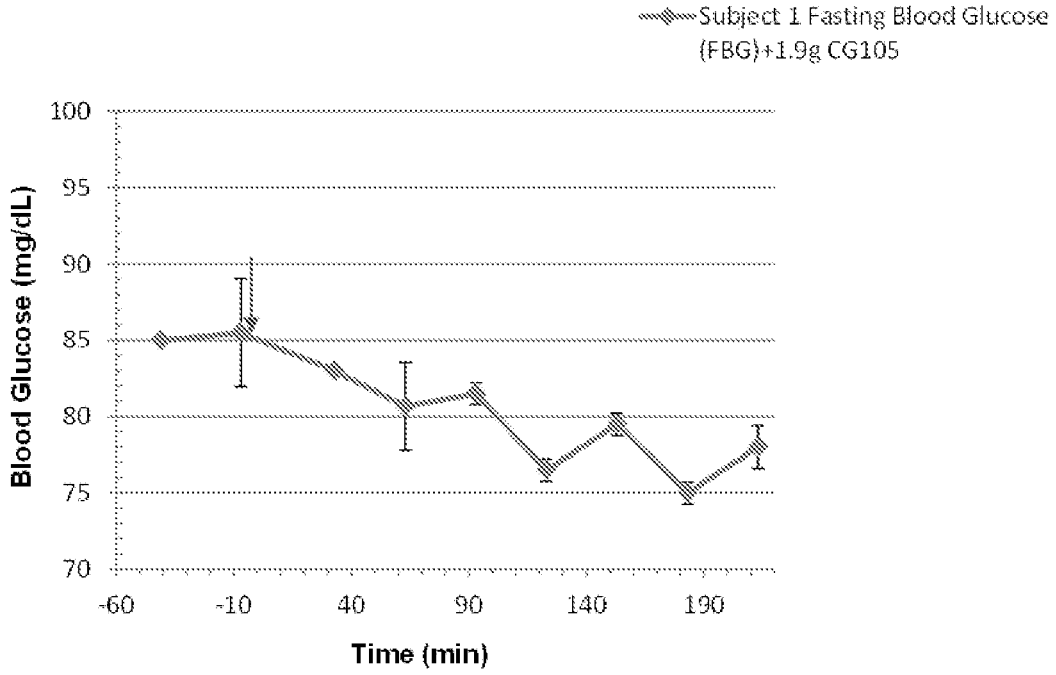

Subject 1 Fasting Blood Glucose (FBG)+1.9g CG105
Blood Glucose (mg/dL)
100
95
90
85
80
75
70
-60
-10
40
90
140
190
Time (min)

Fig. 2

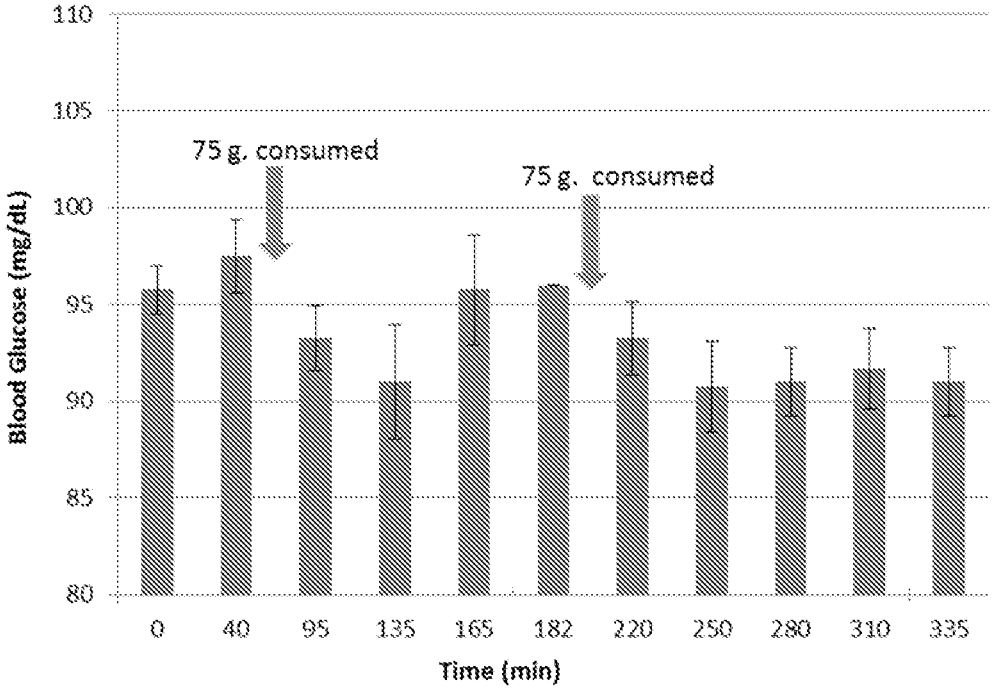
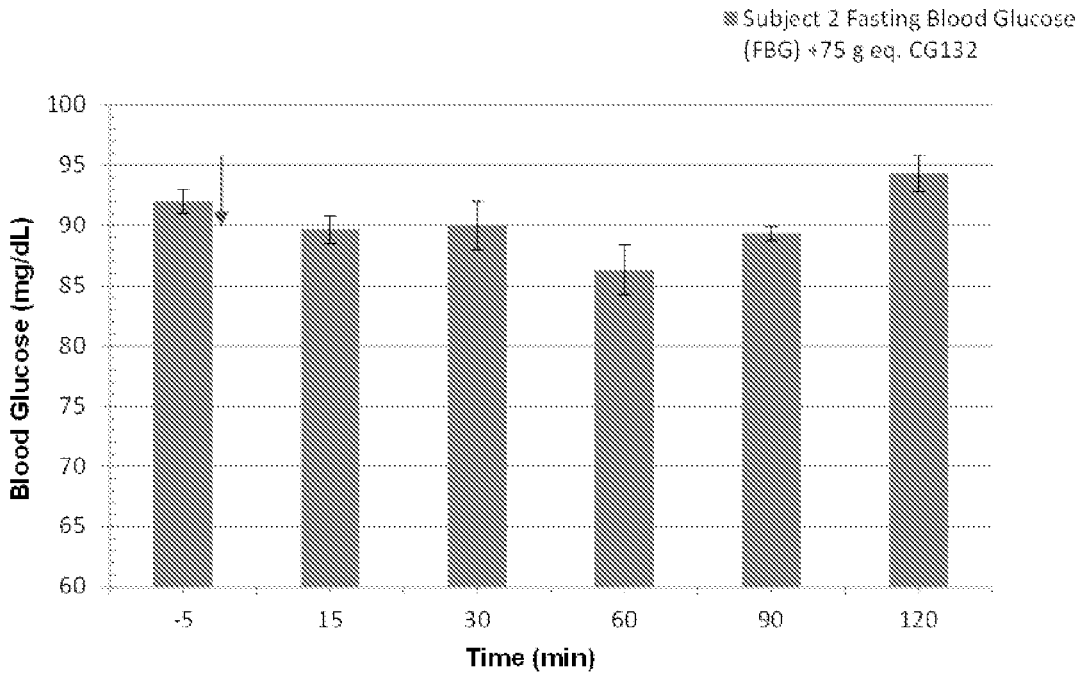

110
105
100
95
90
85
80
Blood Glucose (mg/dL)
75 g. consumed
75 g. consumed
0
40
95
135
165
182
220
250
280
310
335
Time (min)

Fig. 3

A.


Subject 2 Fasting Blood Glucose (FBG) +75 g eq. CG132
Blood Glucose (mg/dL)
100
95
90
85
80
75
70
65
60
-5
15
30
60
90
120
Time (min)

B.

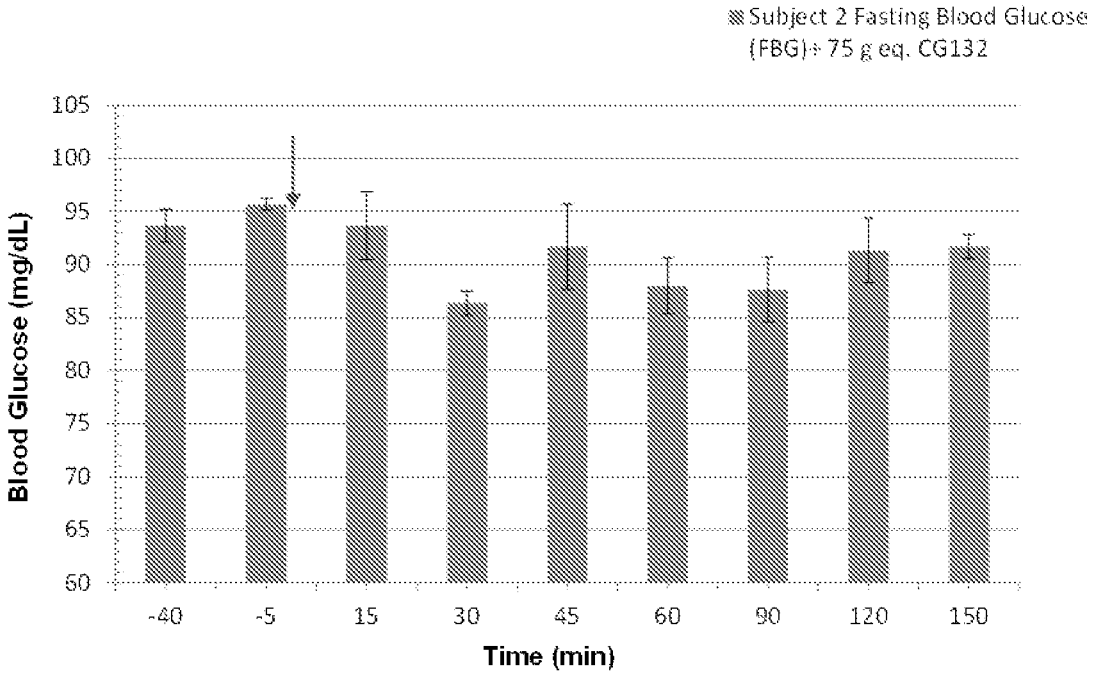

Subject 2 Fasting Blood Glucose (FBG)+ 75 g eq. CG132
Blood Glucose (mg/dL)
105
100
95
90
85
80
75
70
65
60
-40
-5
15
30
45
60
90
120
150
Time (min)

Fig. 4

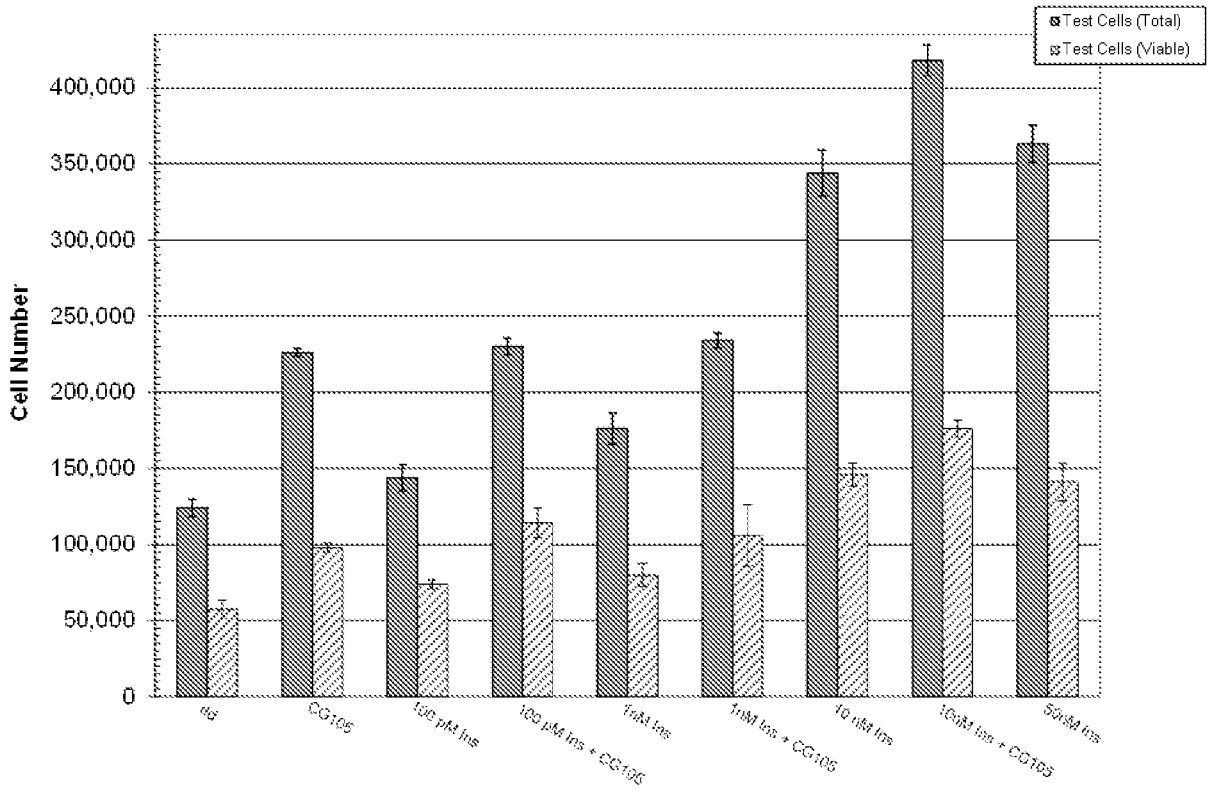

Test Cells (Total)
Test Cells (Viable)
Cell Number
400,000
350,000
300,000
250,000
200,000
150,000
100,000
50,000
0
dd
CG105
100 pM Ins
100 pM Ins + CG105
1nM Ins
1nM Ins + CG105
10 nM Ins
10nM Ins + CG105
50nM Ins

Fig. 5