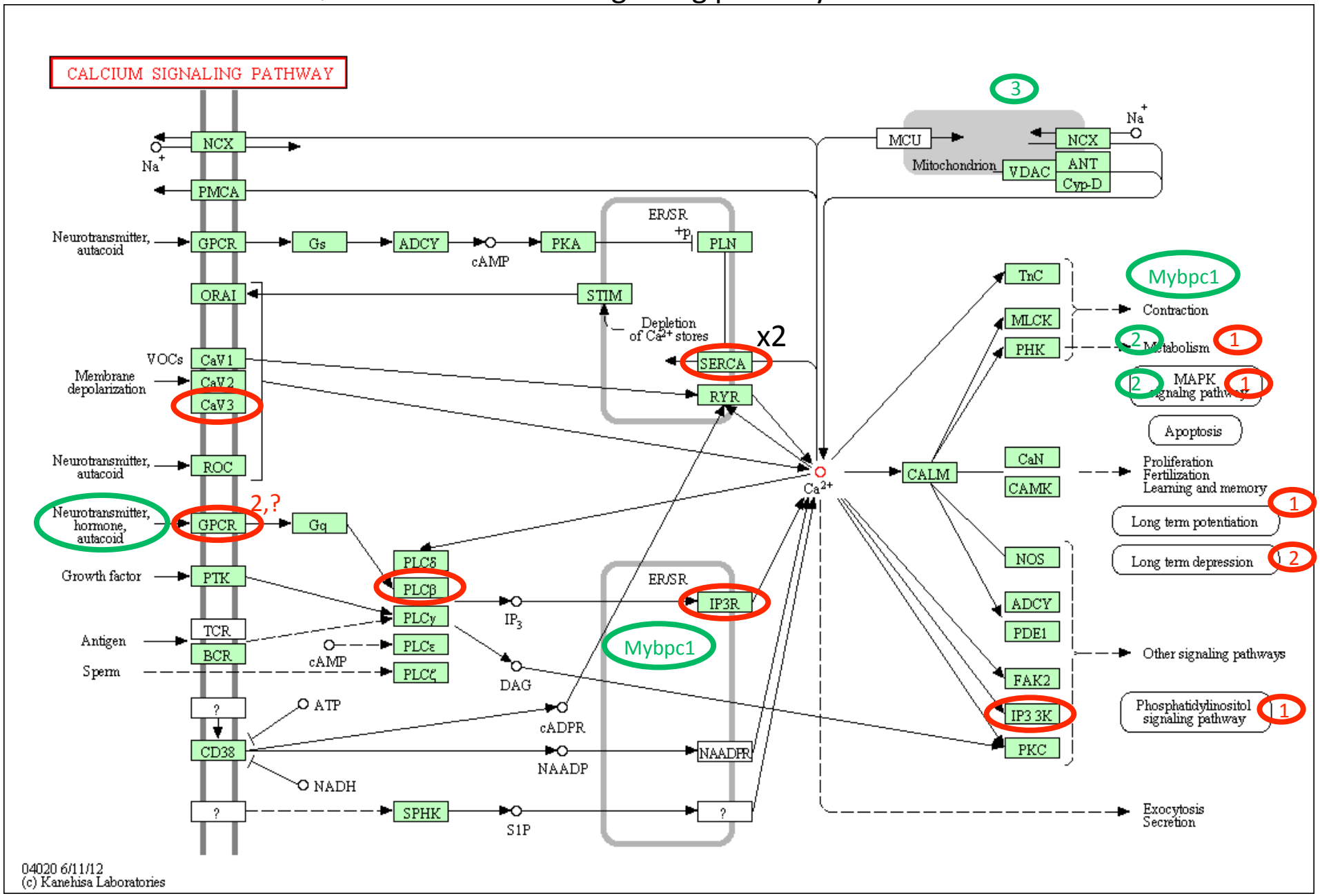
Comparison of RNA expression patterns in some well known pathways (Q127 vs WT)

Key: A significant difference in expression is represented by a circle. Red signifies lower expression relative to WT, green signifies higher expression. Open circles represent 4 week-old comparisons, filled circles represent 8 week-old comparisons.

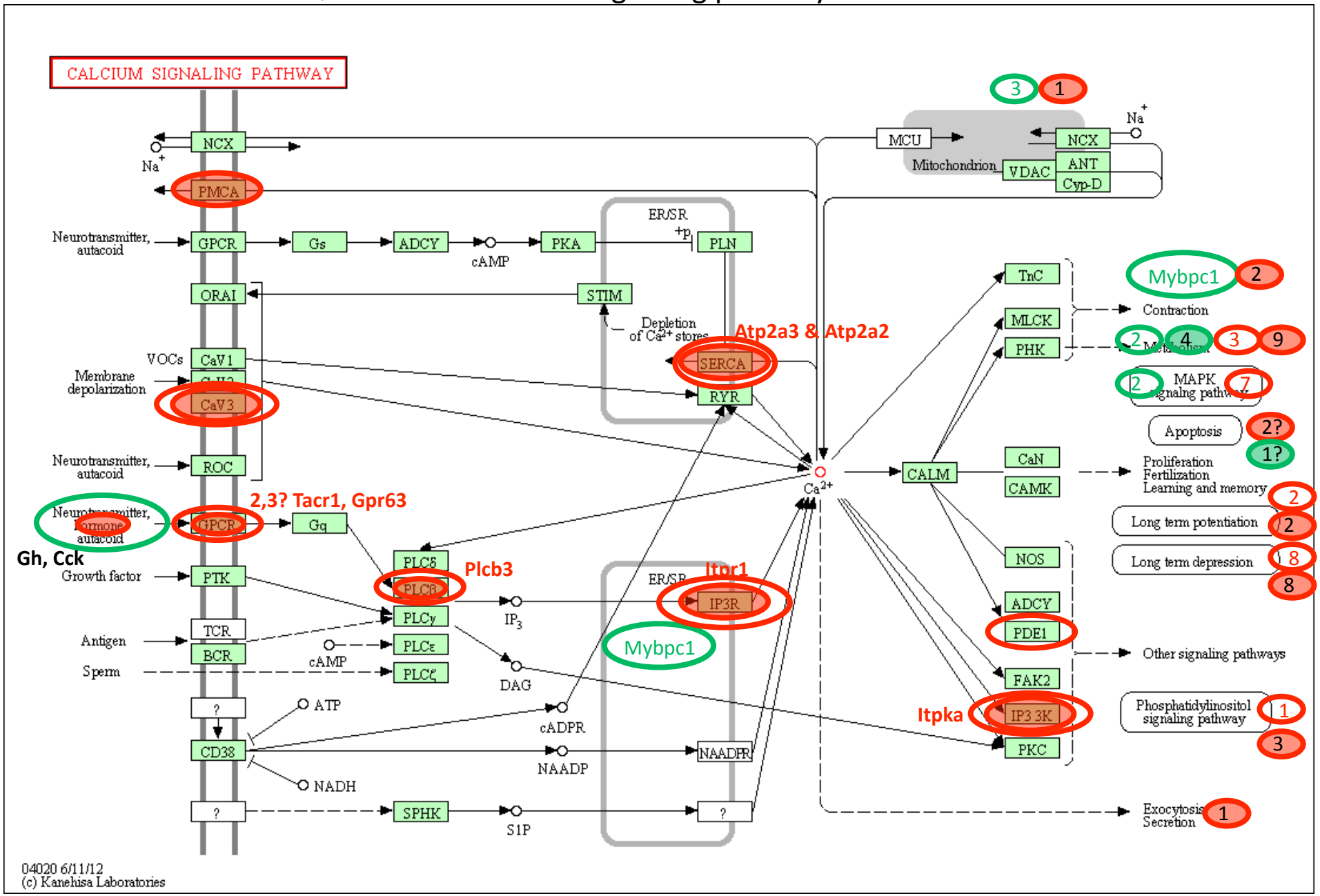
KO animals are represented by an X.

RNA sequencing analysis: FDR>10 for everything but 4 week KO (FDR>0)

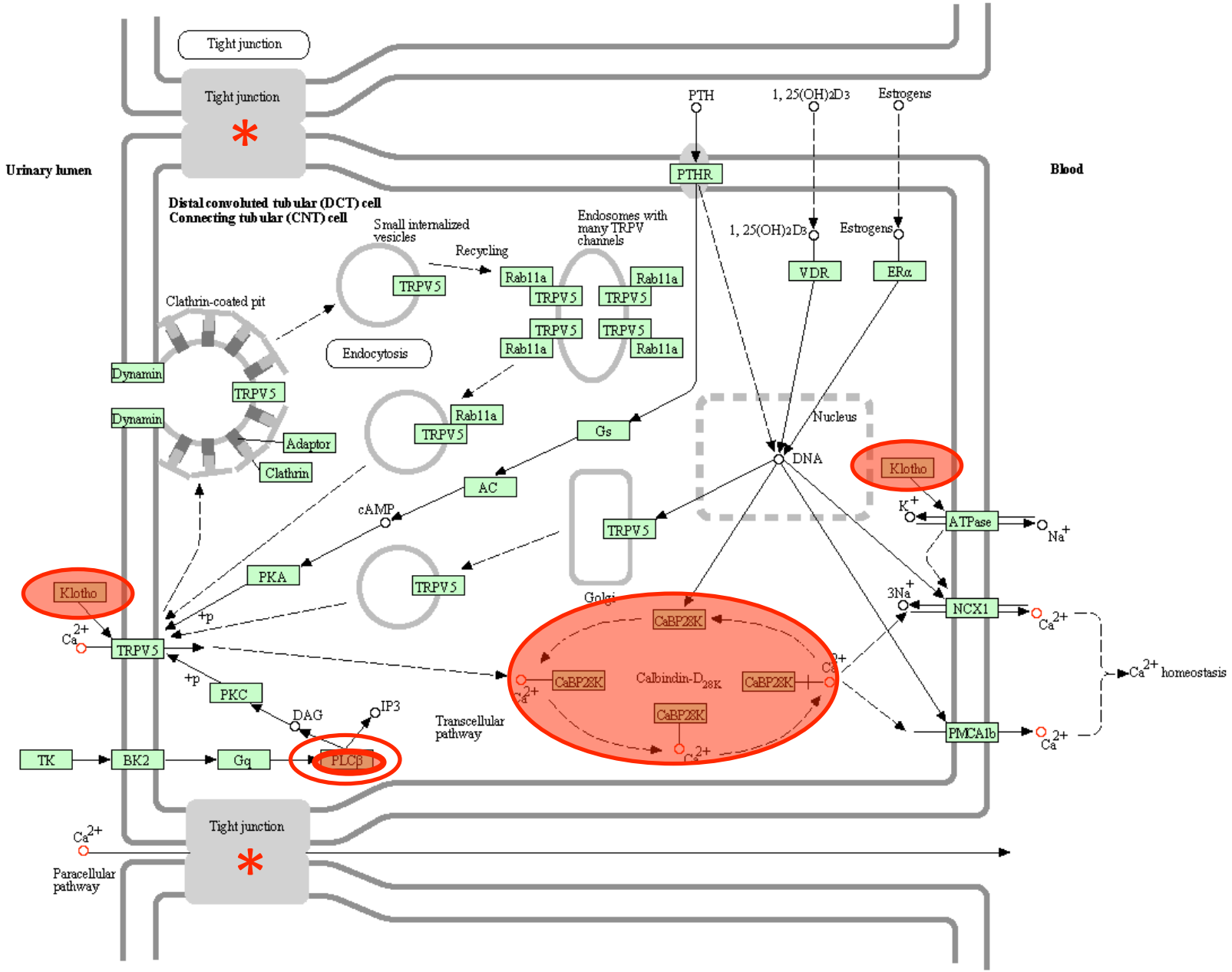
Q127 effects on Ca++ signaling pathway at 4 weeks

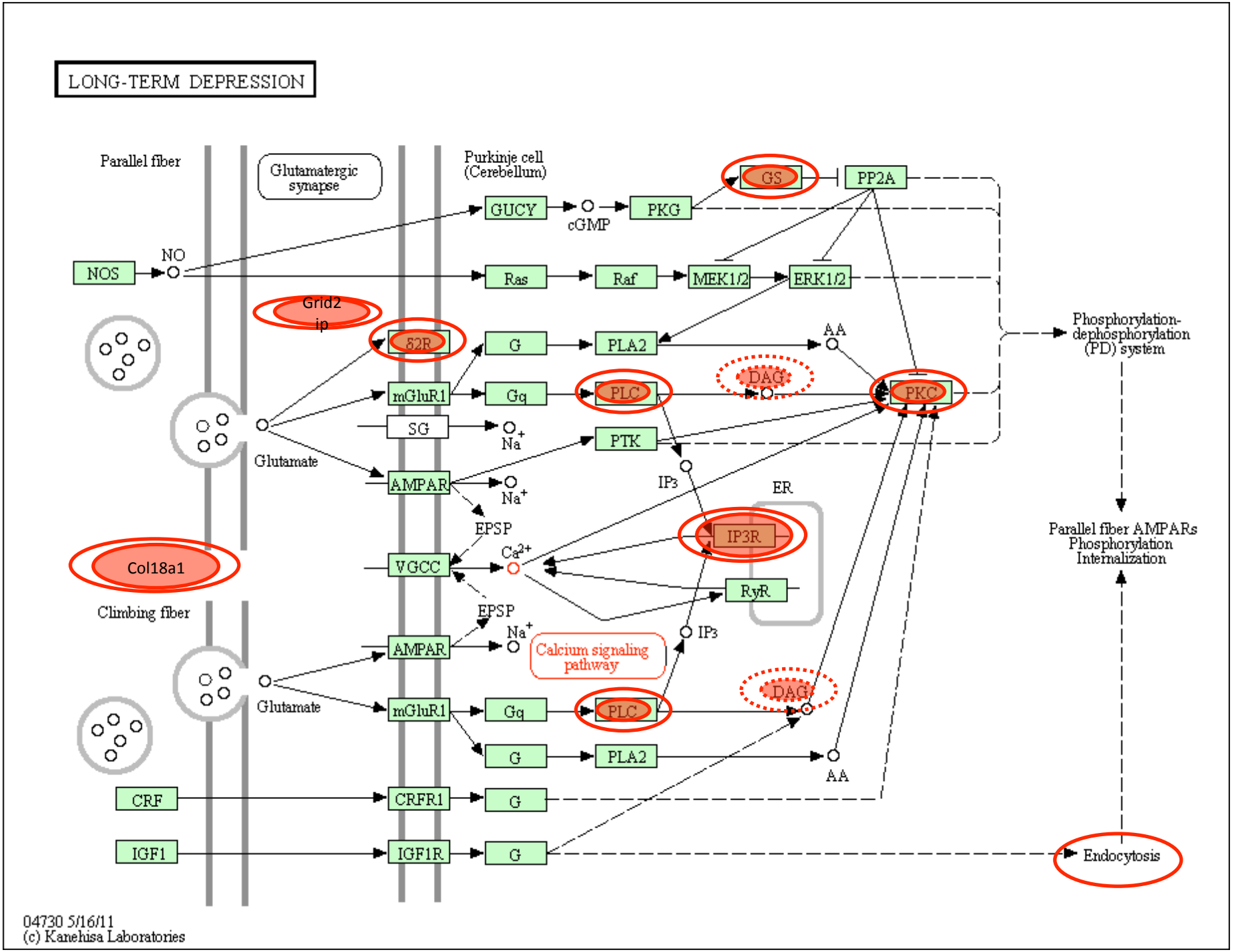


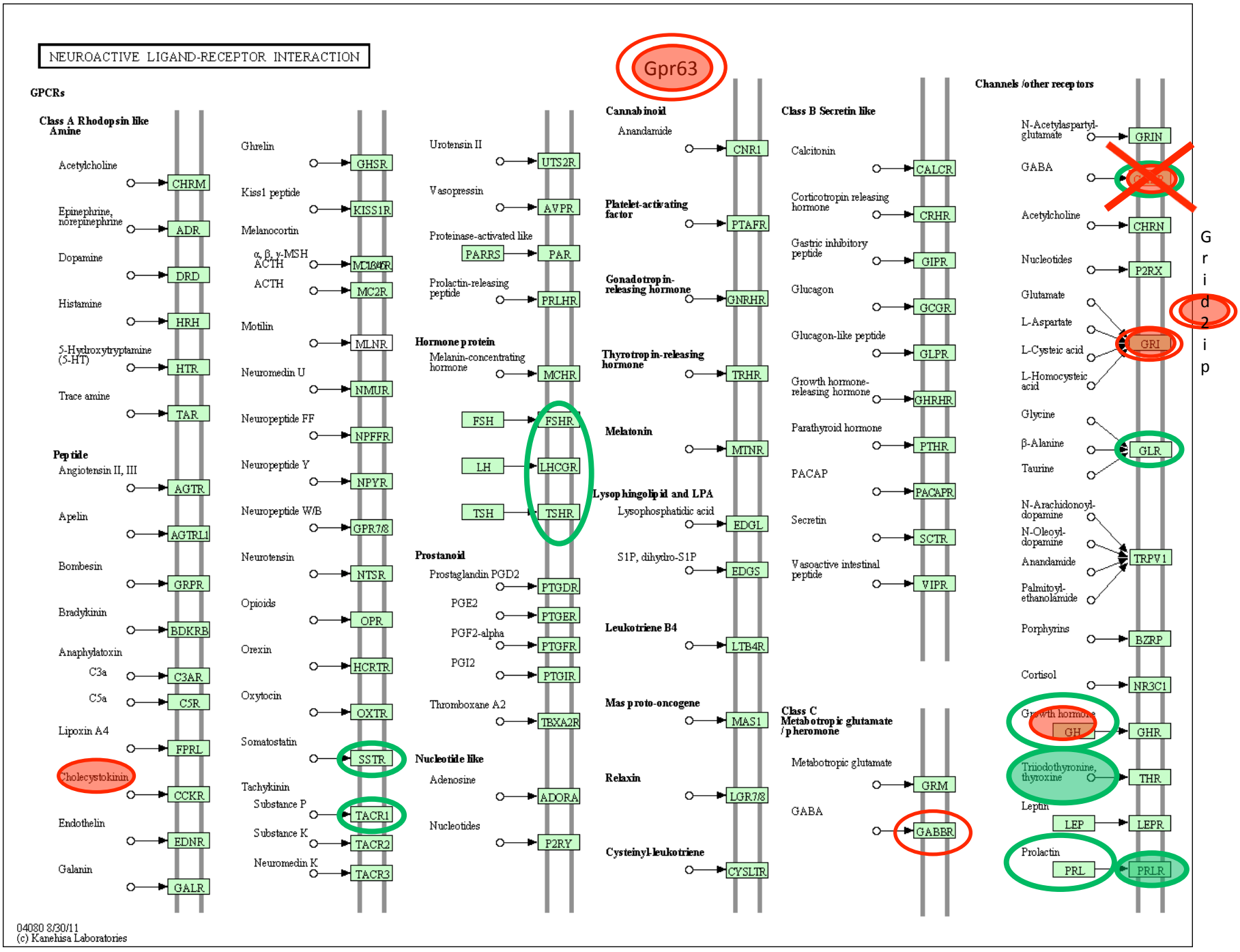
Q127 effects on Ca++ signaling pathway at 8 weeks

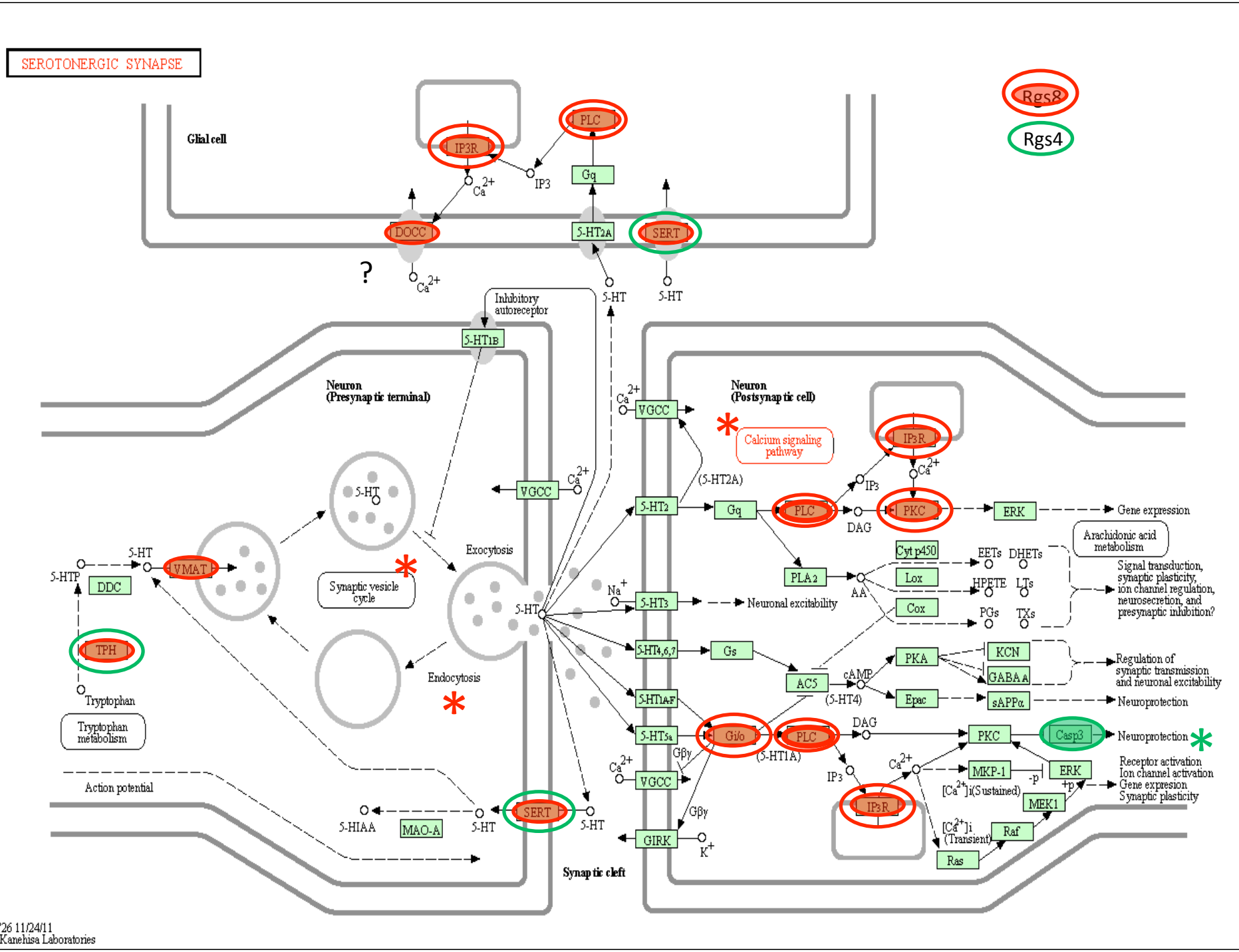


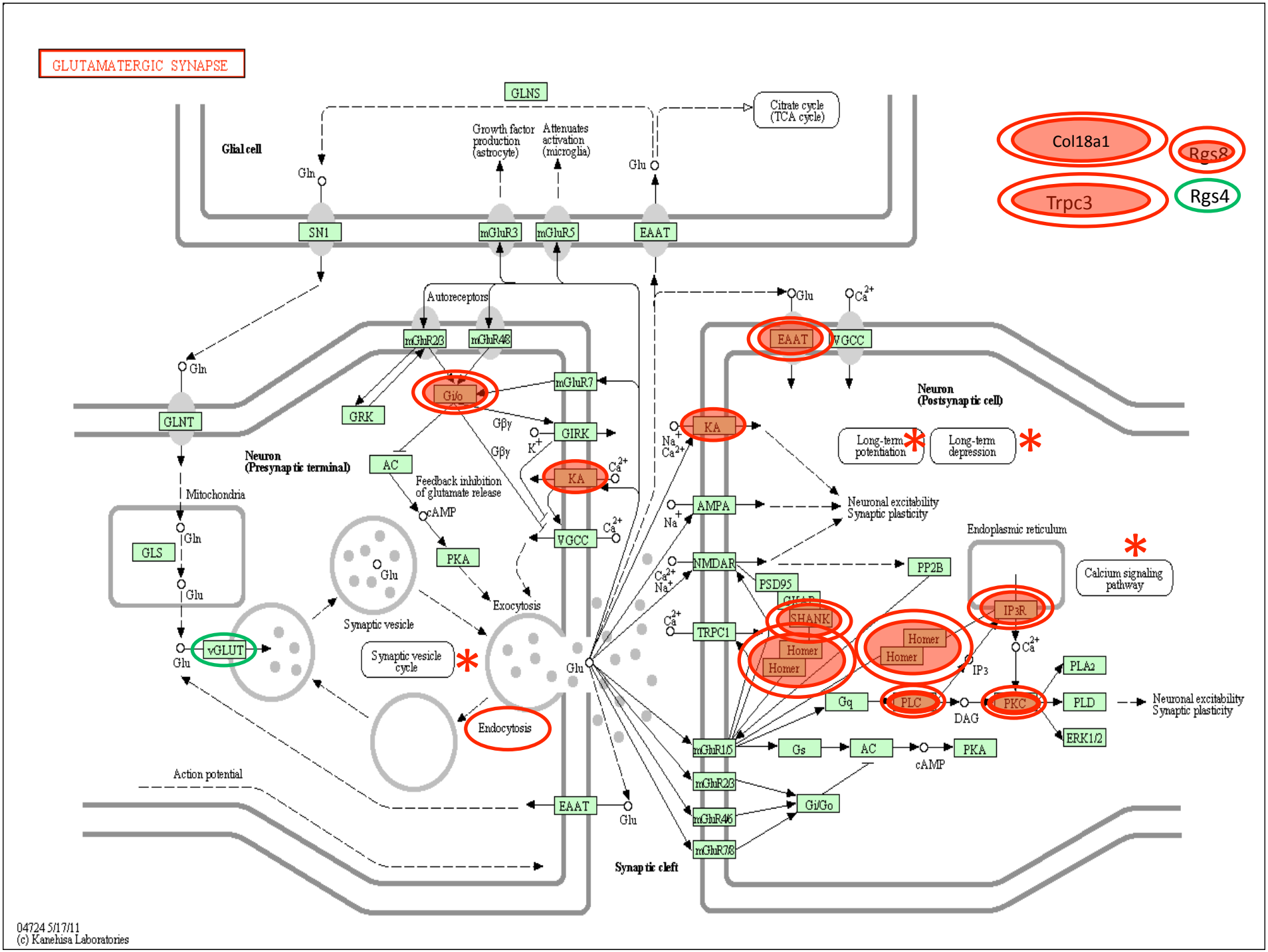
ENDOCRINE AND OTHER FACTOR - REGULATED CALCIUM REABSORPTION

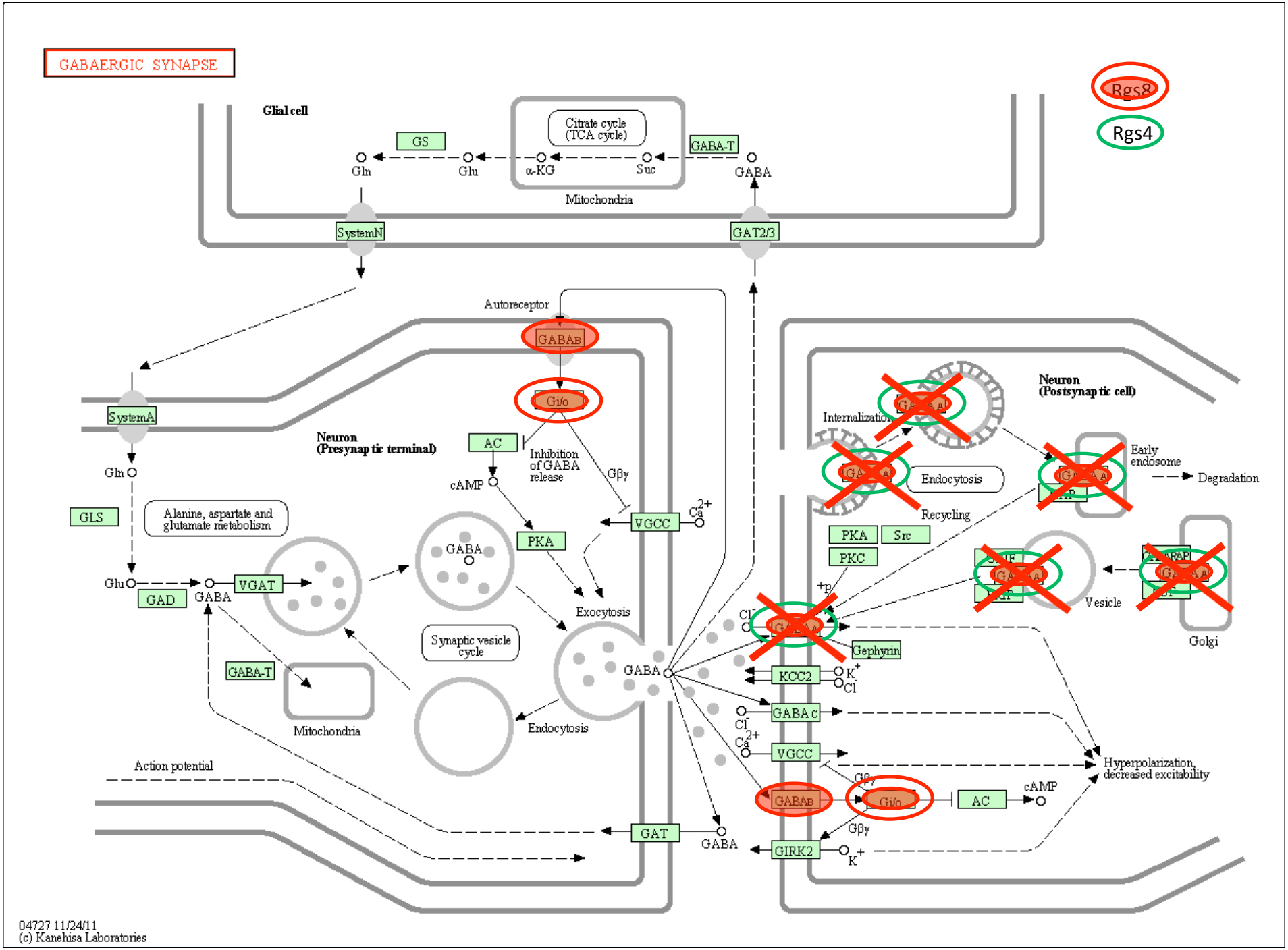


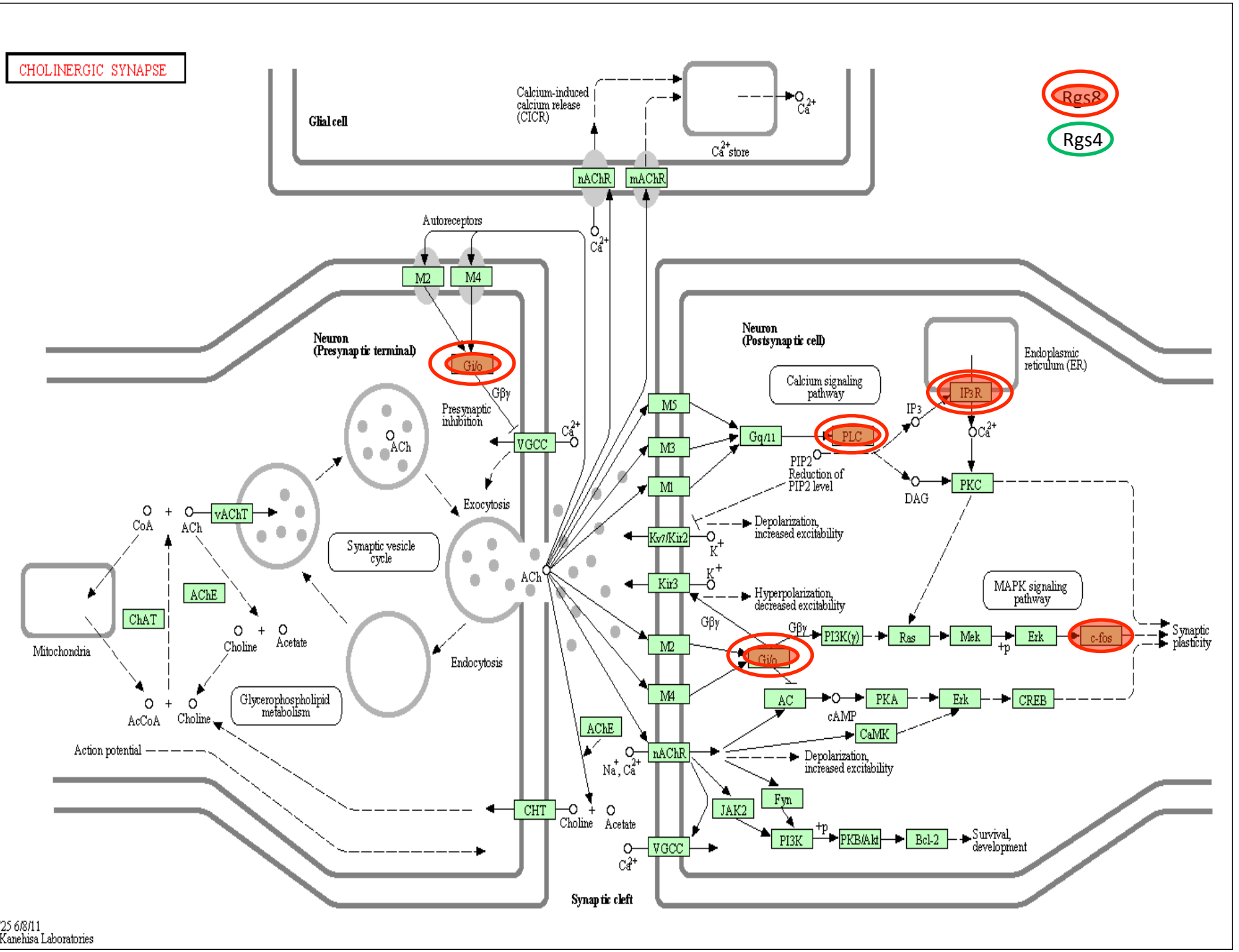

LONG-TERM DEPRESSION
Parallel fiber
Glutamatergic synapse
Purkinje cell (Cerebellum)
GUCY
cGMP
PKG
GS
PP2A
NOS
NO
Ras
Raf
MEK1/2
ERK1/2
Grid2 ip
δ2R
G
PLA2
AA
mGluR1
Gq
PLC
DAG
PKC
SG
Na+
PTK
Glutamate
AMPAR
IP3
ER
EPSP
IP3R
Col18a1
VGCC
Ca2+
RyR
Climbing fiber
Calcium signaling pathway
CRF
CRFR1
IGF1
IGF1R
Phosphorylation-dephosphorylation (PD) system
Parallel fiber AMPARs Phosphorylation Internalization
Endocytosis
04730 5/16/11
(c) Kanehisa Laboratories

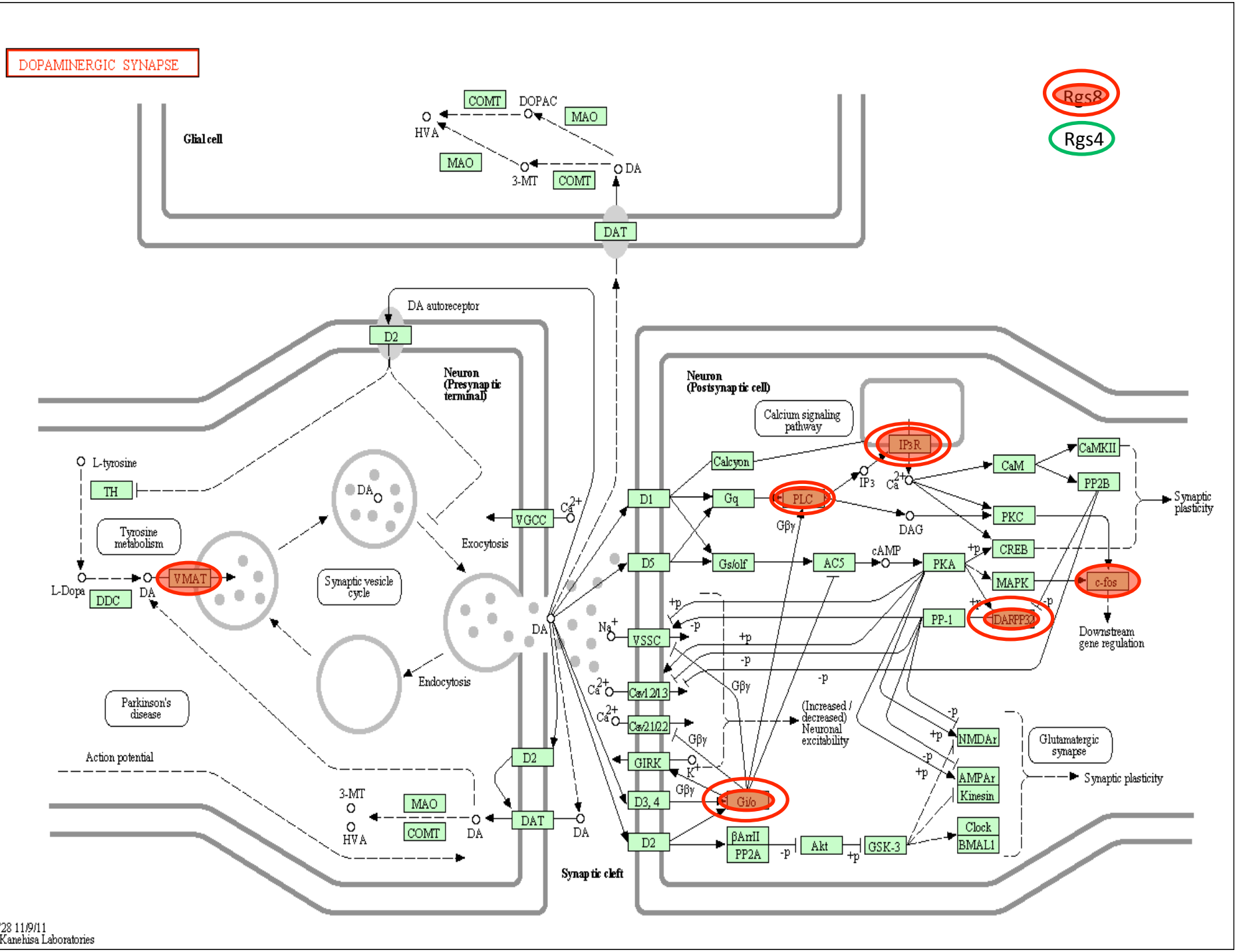

NEUROACTIVE LIGAND-RECEPTOR INTERACTION
Gpr63
Grid2ip
GPCRs
Class A Rhodopsin like
Amine
Acetylcholine
CHRM
Epinephrine, norepinephrine
ADR
Dopamine
DRD
Histamine
HRH
5-Hydroxytryptamine (5-HT)
HTR
Trace amine
TAR
Peptide
Angiotensin II, III
AGTR
Apelin
AGTRL1
Bombesin
GRPR
Bradykinin
BDKRB
Anaphylatoxin
C3a
C3AR
C5a
C5R
Lipoxin A4
FPRL
Cholecystokinin
CCKR
Endothelin
EDNR
Galanin
GALR
Ghrelin
GHSR
Kiss1 peptide
KISS1R
Melanocortin
α, β, γ-MSH
ACTH
MC1/4R
ACTH
MC2R
Motilin
MLNR
Neuromedin U
NMUR
Neuropeptide FF
NPFFR
Neuropeptide Y
NPYR
Neuropeptide W/B
GPR7/8
Neurotensin
NTSR
Opioids
OPR
Orexin
HCRTR
Oxytocin
OXTR
Somatostatin
SSTR
Tachykinin
Substance P
TACR1
Substance K
TACR2
Neuromedin K
TACR3
Urotensin II
UTS2R
Vasopressin
AVPR
Proteinase-activated like
PARRS
PAR
Prolactin-releasing peptide
PRLHR
Hormone protein
Melanin-concentrating hormone
MCHR
FSH
FSHR
LH
LHCGR
TSH
TSHR
Prostanoid
Prostaglandin PGD2
PTGDR
PGE2
PTGER
PGF2-alpha
PTGFR
PGI2
PTGIR
Thromboxane A2
TBXA2R
Nucleotide like
Adenosine
ADORA
Nucleotides
P2RY
Cannabinoid
Anandamide
CNR1
Platelet-activating factor
PTAFR
Gonadotropin-releasing hormone
GNRHR
Thyrotropin-releasing hormone
TRHR
Melatonin
MTNR
Lysophingolipid and LPA
Lysophosphatidic acid
EDGL
S1P, dihydro-S1P
EDGS
Leukotriene B4
LTB4R
Mas proto-oncogene
MAS1
Relaxin
LGR7/8
Cysteinyl-leukotriene
CYSLTR
Class B Secretin like
Calcitonin
CALCR
Corticotropin releasing hormone
CRHR
Gastric inhibitory peptide
GIPR
Glucagon
GCGR
Glucagon-like peptide
GLPR
Growth hormone-releasing hormone
GHRHR
Parathyroid hormone
PTHR
PACAP
PACAPR
Secretin
SCTR
Vasoactive intestinal peptide
VIPR
Class C
Metabotropic glutamate
/pheromone
Metabotropic glutamate
GRM
GABA
GABBR
Channels /other receptors
N-Acetylaspartyl-glutamate
GRIN
GABA
Acetylcholine
CHRN
Nucleotides
P2RX
Glutamate
L-Aspartate
L-Cysteic acid
L-Homocysteic acid
GRI
Glycine
β-Alanine
Taurine
GLR
N-Arachidonoyl-dopamine
N-Oleoyl-dopamine
Anandamide
Palmitoyl-ethanolamide
TRPV1
Porphyrins
BZRP
Cortisol
NR3C1
Growth hormone
GH
GHR
Triiodothyronine, thyroxine
THR
Leptin
LEP
LEPR
Prolactin
PRL
PRLR
04080 8/30/11
(c) Kanehisa Laboratories

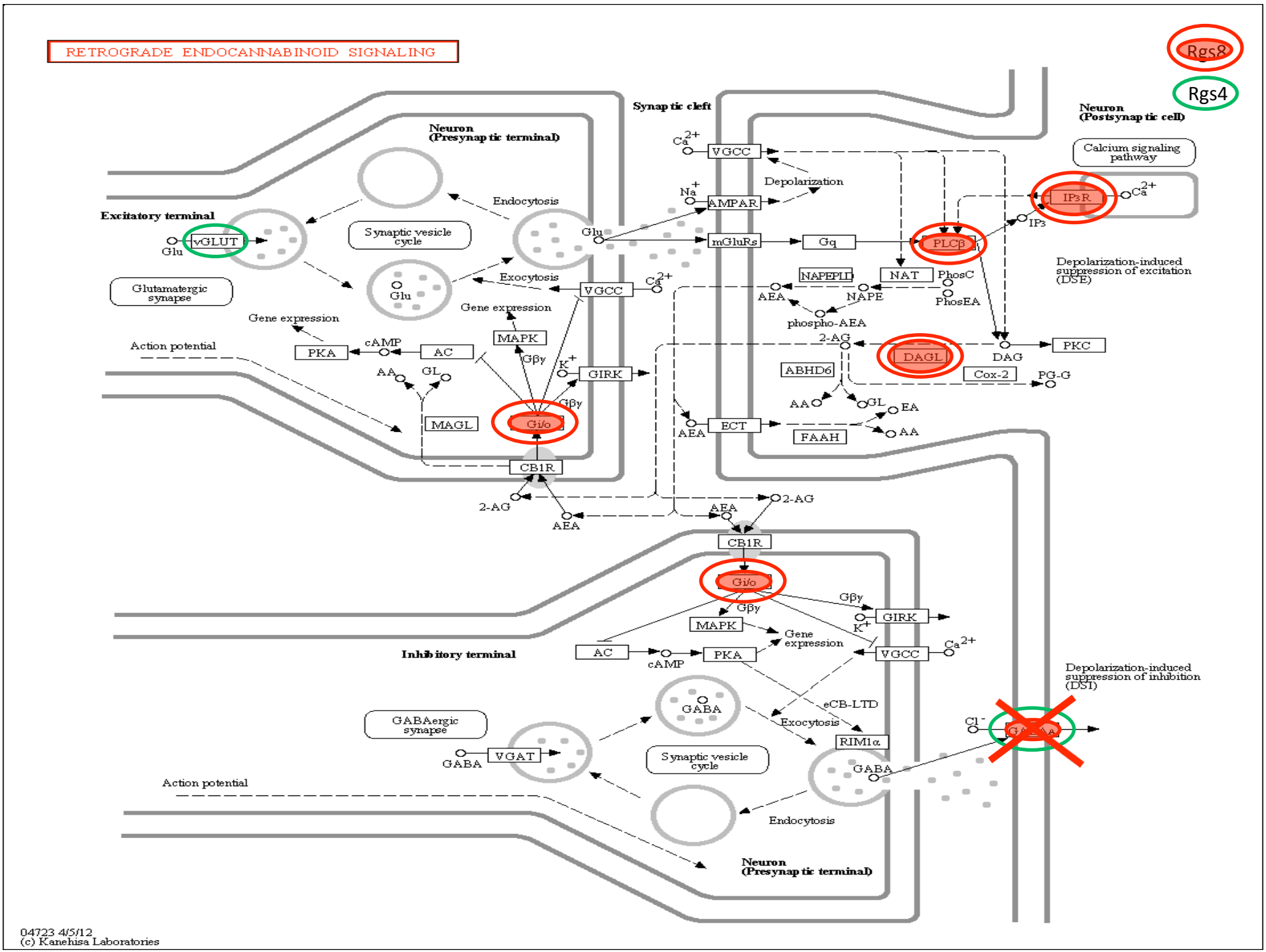


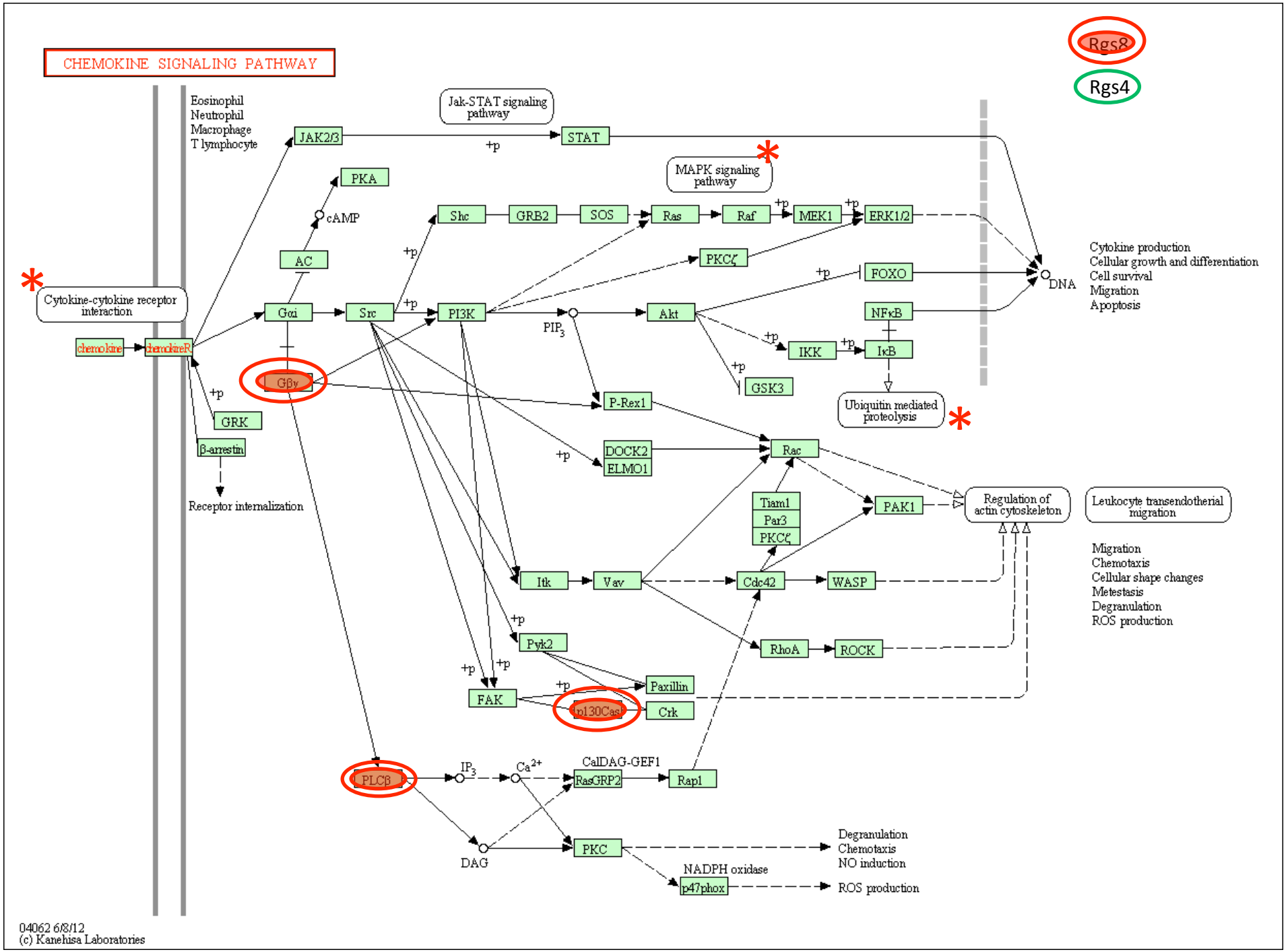

GLUTAMATERGIC SYNAPSE
Col18a1
Rgs8
Trpc3
Rgs4
GLNS
Citrate cycle (TCA cycle)
Glial cell
Growth factor production (astrocyte)
Attenuates activation (microglia)
Gln
Glu
SN1
mGluR3
mGluR5
EAAT
Autoreceptors
mGluR2/3
mGluR4/8
mGluR7
Gi/o
GRK
Gβγ
GIRK
K+
AC
Feedback inhibition of glutamate release
cAMP
PKA
KA
VGCC
Ca2+
Neuron (Presynaptic terminal)
GLNT
Mitochondria
GLS
vGLUT
Synaptic vesicle
Synaptic vesicle cycle
Exocytosis
Endocytosis
Action potential
Synaptic cleft
Neuron (Postsynaptic cell)
Na+
AMPA
NMDAR
TRPC1
Neuronal excitability Synaptic plasticity
Long-term potentiation
Long-term depression
PP2B
PSD95
SHANK
Homer
Endoplasmic reticulum
IP3R
IP3
Calcium signaling pathway
Gq
PLC
DAG
PKC
PLA2
PLD
ERK1/2
Gs
mGluR1/5
Gi/Go
mGluR6/7/8
04724 5/17/11
(c) Kanehisa Laboratories


GABAERGIC SYNAPSE
Rgs8
Rgs4
Glial cell
GS
Gln
Glu
Citrate cycle (TCA cycle)
α-KG
Suc
GABA-T
GABA
Mitochondria
SystemN
GAT2/3
Autoreceptor
GABAB
Gi/o
SystemA
Neuron (Presynaptic terminal)
AC
Inhibition of GABA release
Gβγ
cAMP
Gln
GLS
Alanine, aspartate and glutamate metabolism
PKA
VGCC
Ca2+
Glu
GAD
GABA
VGAT
GABA
Exocytosis
Synaptic vesicle cycle
GABA-T
Mitochondria
Endocytosis
Action potential
GAT
GABA
Neuron (Postsynaptic cell)
Internalization
Endocytosis
Recycling
Early endosome
Degradation
PKA
Src
PKC
+p
Vesicle
Golgi
Cl-
Gephyrin
GABAA
KCC2
K+
Cl-
GABAc
Cl-
Ca2+
VGCC
Hyperpolarization, decreased excitability
GABAB
Gi/o
AC
cAMP
Gβγ
GIRK2
K+
04727 11/24/11
(c) Kanehisa Laboratories




DOPAMINERGIC SYNAPSE
Rgs8
Rgs4
Glial cell
COMT
DOPAC
MAO
HVA
MAO
3-MT
COMT
DA
DAT
DA autoreceptor
D2
Neuron (Presynaptic terminal)
Neuron (Postsynaptic cell)
Calcium signaling pathway
L-tyrosine
TH
Tyrosine metabolism
L-Dopa
DDC
DA
VMAT
Synaptic vesicle cycle
Exocytosis
Endocytosis
VGCC
Ca2+
Parkinson's disease
Action potential
3-MT
MAO
HVA
COMT
DA
DAT
DA
D2
Synaptic cleft
DA
D1
D5
D2
D3, 4
Na+
VSSC
Ca2+
Cav1.2/1.3
Ca2+
Cav2.1/2.2
GIRK
K+
Gβγ
Calcyon
Gq
Gs/olf
Gi/o
βArrII
PP2A
IP3R
PLC
IP3
Ca2+
DAG
AC5
cAMP
PKA
PP-1
DARPP32
CaM
CaMKII
PP2B
PKC
CREB
MAPK
c-fos
Synaptic plasticity
Downstream gene regulation
(Increased / decreased) Neuronal excitability
NMDAr
AMPAr
Kinesin
Glutamatergic synapse
Synaptic plasticity
Clock
BMAL1
Akt
GSK-3
+p
-p
04728 11/9/11
(c) Kanehisa Laboratories


RETROGRADE ENDOCANNABINOID SIGNALING
Rgs8
Rgs4
Synaptic cleft
Neuron (Presynaptic terminal)
Neuron (Postsynaptic cell)
Excitatory terminal
Glutamatergic synapse
Synaptic vesicle cycle
Endocytosis
Exocytosis
Glu
vGLUT
Action potential
Gene expression
PKA
cAMP
AC
MAPK
Gβγ
K+
GIRK
AA
GL
MAGL
Gi/o
CB1R
2-AG
AEA
VGCC
Ca2+
Depolarization
Na+
AMPAR
mGluRs
Gq
PLCβ
IP3
IP3R
Calcium signaling pathway
Depolarization-induced suppression of excitation (DSE)
NAPEPLD
NAT
PhosC
PhosEA
NAPE
phospho-AEA
DAGL
DAG
PKC
ABHD6
Cox-2
PG-G
ECT
FAAH
EA
Inhibitory terminal
GABAergic synapse
GABA
VGAT
Cl-
GABAA
eCB-LTD
RIM1α
Depolarization-induced suppression of inhibition (DSI)
04723 4/5/12
(c) Kanehisa Laboratories


CHEMOKINE SIGNALING PATHWAY
Rgs8
Rgs4
Eosinophil
Neutrophil
Macrophage
T lymphocyte
Jak-STAT signaling pathway
JAK2/3
STAT
+p
MAPK signaling pathway
PKA
cAMP
AC
Shc
GRB2
SOS
Ras
Raf
MEK1
ERK1/2
PKCζ
FOXO
DNA
Cytokine production
Cellular growth and differentiation
Cell survival
Migration
Apoptosis
Cytokine-cytokine receptor interaction
chemokine
chemokineR
Gαi
Src
PI3K
PIP3
Akt
NFκB
IKK
IκB
GSK3
Gβγ
Ubiquitin mediated proteolysis
GRK
β-arrestin
Receptor internalization
P-Rex1
DOCK2
ELMO1
Rac
Tiam1
Par3
PKCζ
PAK1
Regulation of actin cytoskeleton
Leukocyte transendothelial migration
Migration
Chemotaxis
Cellular shape changes
Metastasis
Degranulation
ROS production
Itk
Vav
Cdc42
WASP
RhoA
ROCK
Pyk2
FAK
Paxillin
p130Cas
Crk
PLCβ
IP3
Ca2+
CalDAG-GEF1
RasGRP2
Rap1
DAG
PKC
Degranulation
Chemotaxis
NO induction
NADPH oxidase
p47phox
ROS production
04062 6/8/12
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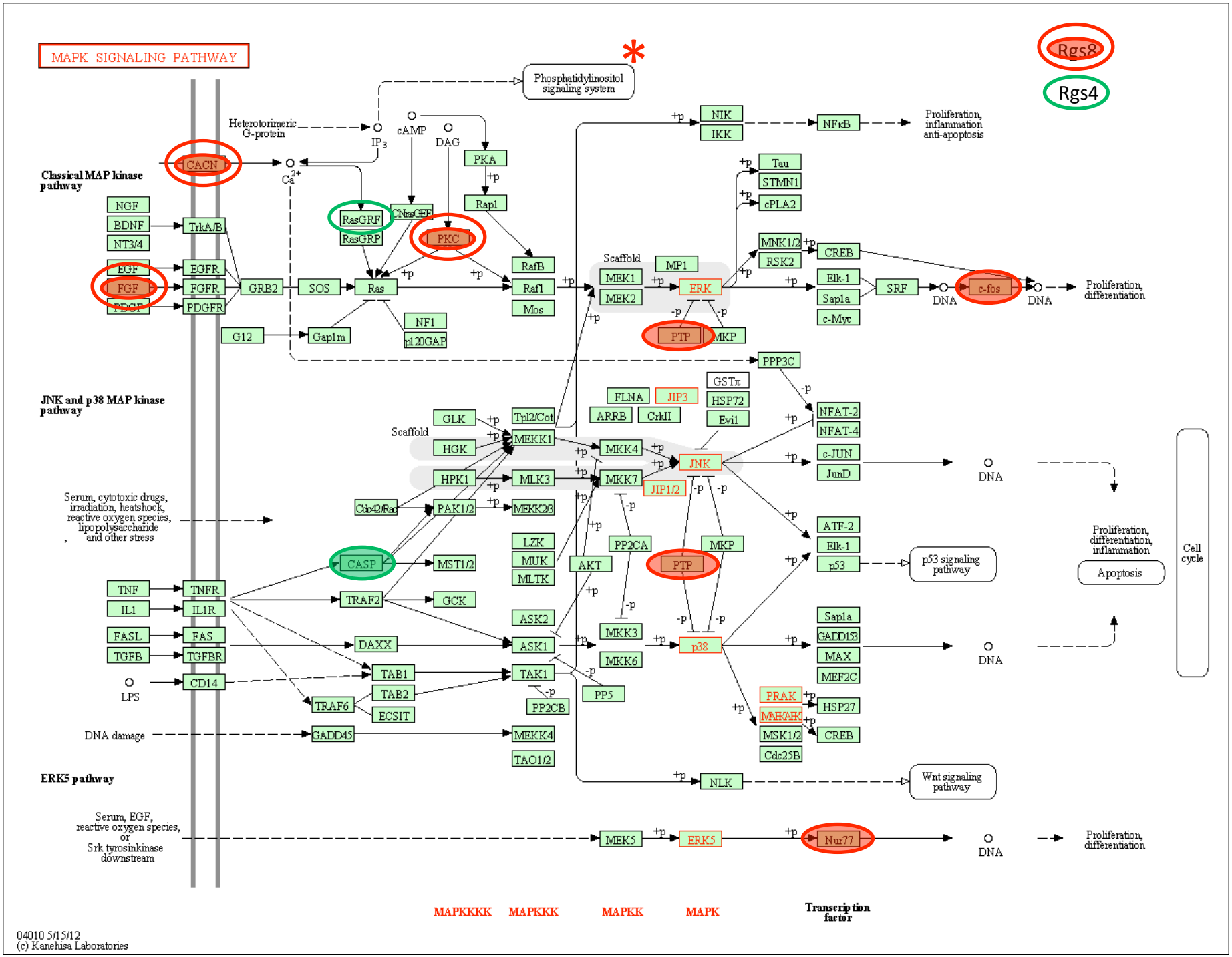
MAPK SIGNALING PATHWAY
Rgs8
Rgs4
Phosphatidylinositol signaling system
Heterotorimeric G-protein
IP3
cAMP
DAG
Ca2+
CACN
PKA
Rap1
RasGRF
RasGRP
CNasGEF
PKC
Classical MAP kinase pathway
NGF
BDNF
NT3/4
EGF
FGF
PDGF
TrkA/B
EGFR
FGFR
PDGFR
GRB2
SOS
Ras
RafB
Raf1
Mos
G12
Gap1m
NF1
p120GAP
Scaffold
MP1
MEK1
MEK2
ERK
PTP
MKP
NIK
IKK
NFκB
Proliferation, inflammation anti-apoptosis
Tau
STMN1
cPLA2
MNK1/2
RSK2
CREB
Elk-1
Sap1a
c-Myc
SRF
c-fos
DNA
Proliferation, differentiation
PPP3C
JNK and p38 MAP kinase pathway
GLK
HGK
HPK1
Cdc42/Rac
PAK1/2
Tpl2/Cot
MEKK1
MLK3
MEKK2/3
LZK
MUK
MLTK
ASK2
ASK1
TAK1
PP2CB
MKK4
MKK7
MKK3
MKK6
PP5
JIP1/2
JIP3
FLNA
ARRB
CrkII
GSTπ
HSP72
Evi1
JNK
p38
PP2CA
AKT
NFAT-2
NFAT-4
c-JUN
JunD
ATF-2
Elk-1
p53
p53 signaling pathway
Sap1a
GADD153
MAX
MEF2C
PRAK
MAPKAPK
MSK1/2
Cdc25B
HSP27
CREB
Proliferation, differentiation, inflammation
Apoptosis
Cell cycle
Serum, cytotoxic drugs, irradiation, heatshock, reactive oxygen species, lipopolysaccharide and other stress
CASP
MST1/2
TNF
IL1
FASL
TGFB
LPS
TNFR
IL1R
FAS
TGFBR
CD14
TRAF2
GCK
DAXX
TAB1
TAB2
ECSIT
TRAF6
DNA damage
GADD45
MEKK4
TAO1/2
ERK5 pathway
Serum, EGF, reactive oxygen species, or Src tyrosinkinase downstream
MEK5
ERK5
Nur77
NLK
Wnt signaling pathway
MAPKKKK
MAPKKK
MAPKK
MAPK
Transcription factor
04010 5/15/12
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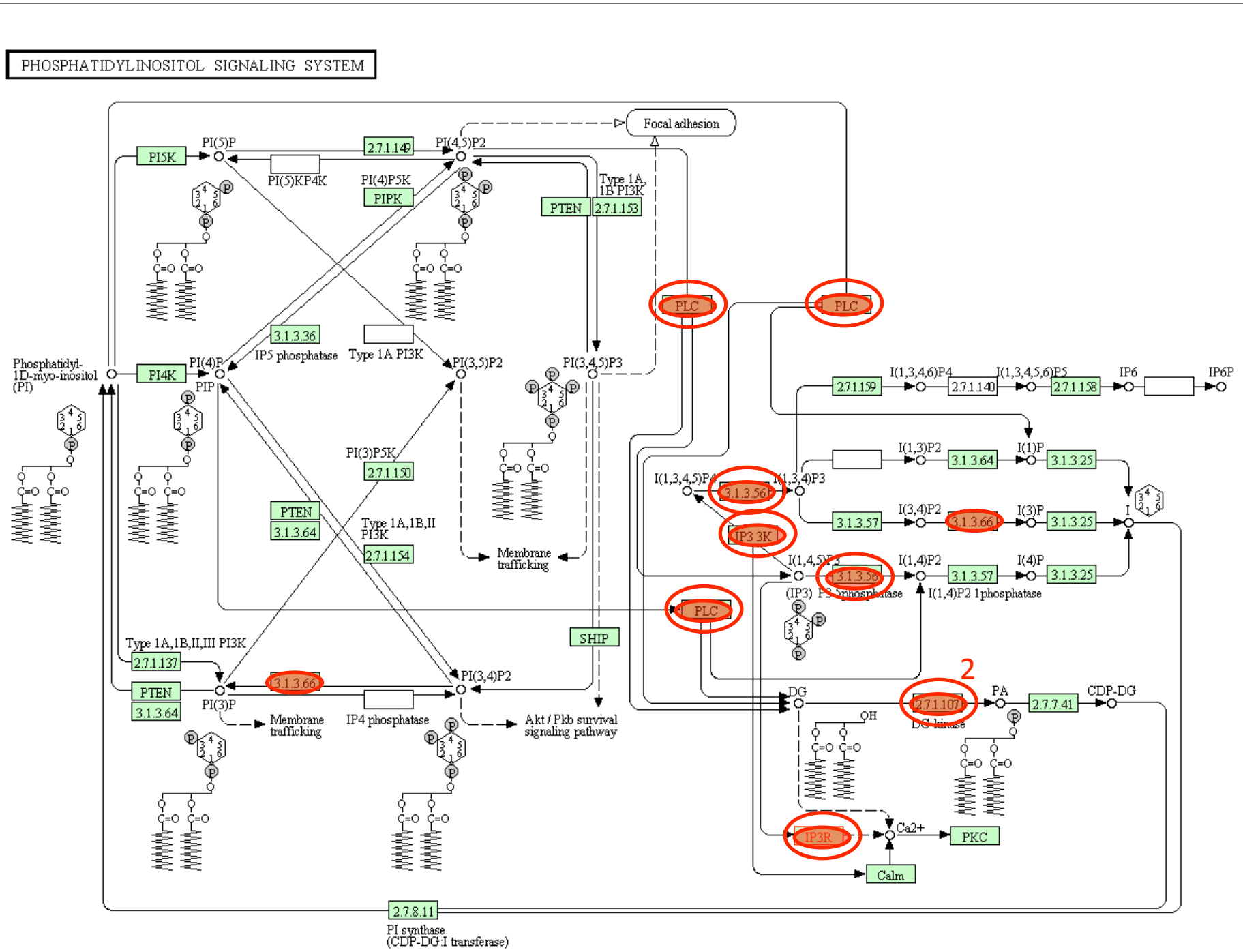
PHOSPHATIDYLINOSITOL SIGNALING SYSTEM
Focal adhesion
PI5K
PI(5)P
2.7.1.149
PI(4,5)P2
PI(5)KP4K
PI(4)P5K
PIPK
Type 1A, 1B PI3K
PTEN
2.7.1.153
PLC
PLC
3.1.3.36
IP5 phosphatase
Type 1A PI3K
Phosphatidyl-1D-myo-inositol (PI)
PI4K
PI(4)P
PIP
PI(3,5)P2
PI(3,4,5)P3
2.7.1.159
I(1,3,4,6)P4
2.7.1.140
I(1,3,4,5,6)P5
2.7.1.158
IP6
IP6P
I(1,3)P2
3.1.3.64
I(1)P
3.1.3.25
I(1,3,4,5)P4
3.1.3.56
I(1,3,4)P3
3.1.3.57
I(3,4)P2
3.1.3.66
I(3)P
3.1.3.25
I
PI(3)P5K
2.7.1.150
PTEN
3.1.3.64
Type 1A,1B,II PI3K
2.7.1.154
Membrane trafficking
IP3 3K
I(1,4,5)P3
3.1.3.56
I(1,4)P2
3.1.3.57
I(4)P
3.1.3.25
(IP3) P3 3phosphatase
I(1,4)P2 1phosphatase
PLC
SHIP
Type 1A,1B,II,III PI3K
2.7.1.137
PTEN
3.1.3.64
3.1.3.66
PI(3)P
PI(3,4)P2
Membrane trafficking
IP4 phosphatase
Akt / Pkb survival signaling pathway
DG
2
2.7.1.107
DG kinase
PA
2.7.7.41
CDP-DG
OH
IP3R
Ca2+
PKC
Calm
2.7.8.11
PI synthase (CDP-DG:I transferase)
04070 12/20/11
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- **Regulator of G-protein signaling 8** is a protein that in humans is encoded by the *RGS8* gene.[1][2]
- This gene is a member of the regulator of G protein signaling (RGS) family and encodes a protein with a single RGS domain. Regulator of G protein signaling (RGS) proteins are regulatory and structural components of G protein-coupled receptor complexes. They accelerate transit through the cycle of GTP binding and hydrolysis to GDP, thereby terminating signal transduction, but paradoxically, also accelerate receptor-stimulated activation.[2]
- **Regulator of G protein signaling 4** or **RGS4** is a protein which regulates G protein signaling.[1] A number of studies associate the RGS4 gene with schizophrenia,[2][3][4][5] while some fail to detect an association.[6]

- RGS4 is also of interest as one of the three main RGS proteins (along with RGS9 and RGS17) involved in terminating signalling by the mu opioid receptor,[7] and may be important in the development of tolerance to opioid drugs.[8][9][10][11][12]
- Regulator of G protein signaling (RGS) family members are regulatory molecules that act as GTPase activating proteins (GAPs) for G alpha subunits of heterotrimeric G proteins. RGS proteins are able to deactivate G protein subunits of the Gi alpha, Go alpha and Gq alpha subtypes. They drive G proteins into their inactive GDP-bound forms. Regulator of G protein signaling 4 belongs to this family. All RGS proteins share a conserved 120-amino acid sequence termed the RGS domain. Regulator of G protein signaling 4 protein is 37% identical to RGS1 and 97% identical to rat Rgs4. This protein negatively regulates signaling upstream or at the level of the heterotrimeric G protein and is localized in the cytoplasm.[1]

- Include LTP pathway, focal adhesion