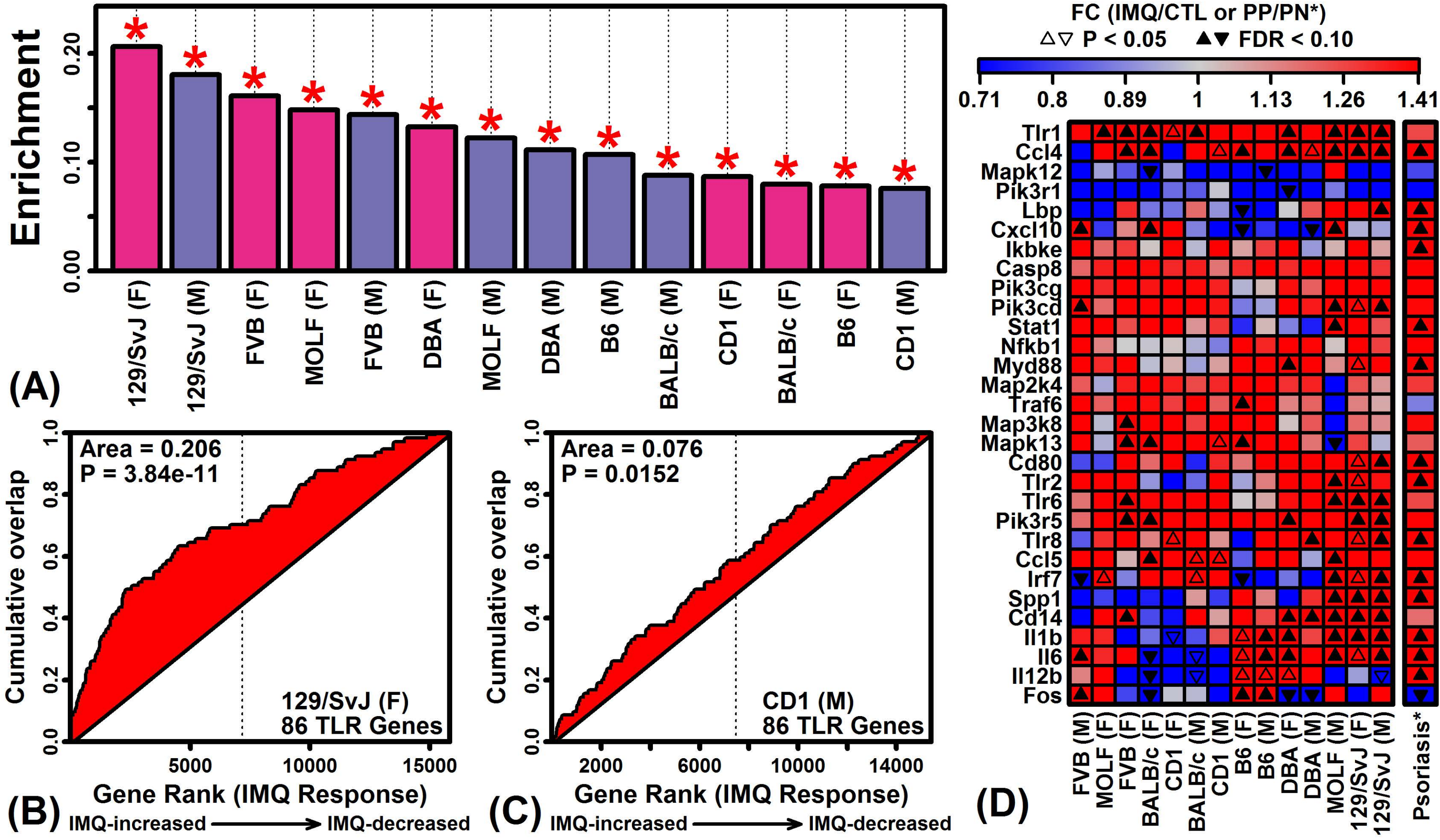
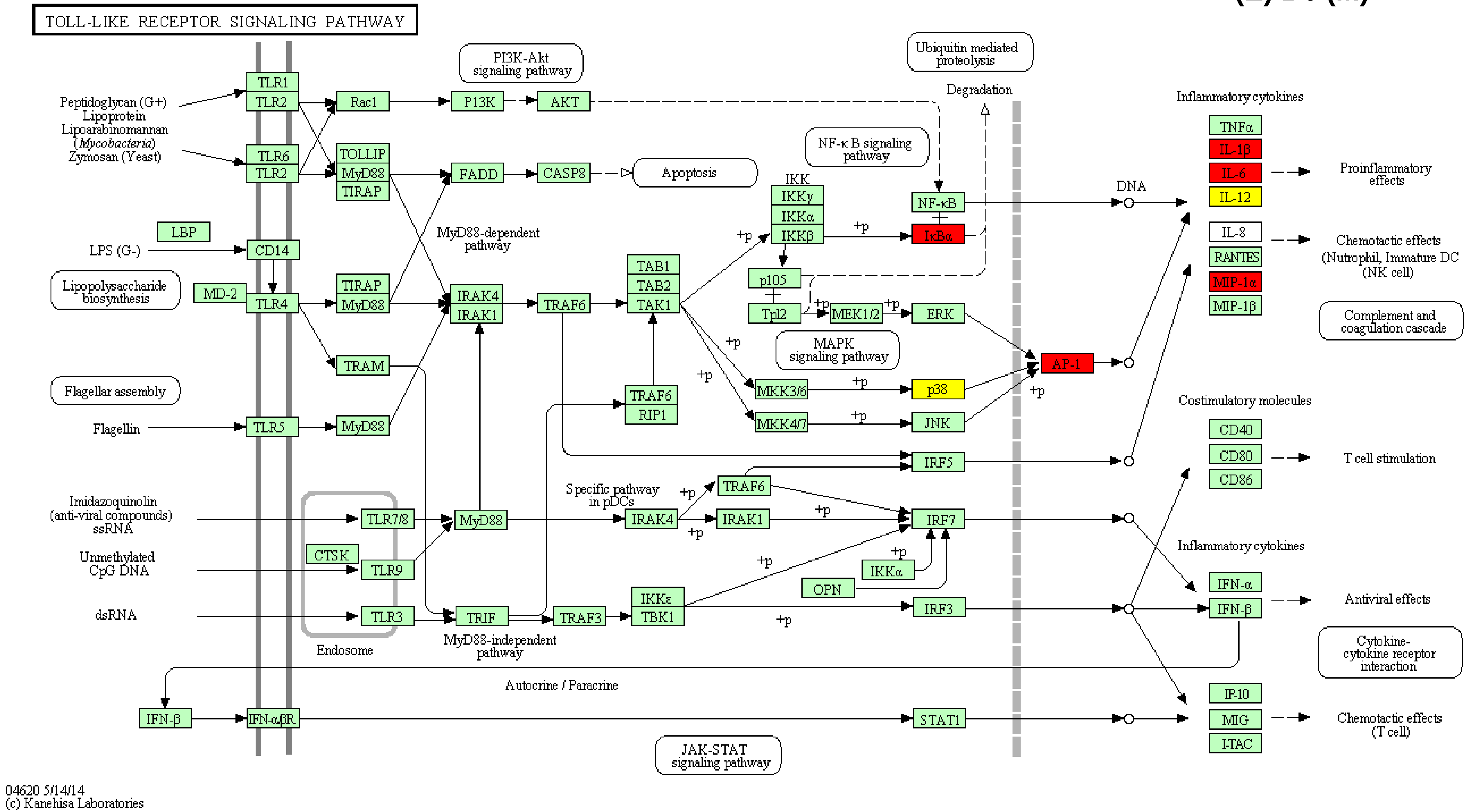
Additional File 12. Genes associated with toll-like receptor (TLR) signaling are disproportionately elevated by IMQ in all strains. (A) TLR gene set enrichment analysis (GSEA). GSEA was performed using 101 TLR-associated genes (KEGG database; pathway ID mmu04620). Enrichment greater than zero indicates bias of TLR genes towards IMQ-increased expression (asterisk: FDR < 0.05, Wilcoxon rank sum test). (B) 129/SvJ females (GSEA analysis). Genes were ranked based upon IMQ response (horizontal axis) and cumulative overlap with the ranked gene list was evaluated (vertical axis). The area between the cumulative overlap curve and diagonal (red) corresponds to the enrichment statistic in part (A). 86 of 101 TLR genes with detectable expression were included in the analysis. (C) CD1 males (GSEA analysis). (D) TLR pathway genes most frequently altered across strains. (E - R) KEGG TLR pathway maps (red: IMQ-increased; yellow: IMQ-decreased).


(A)
Enrichment
0.00
0.10
0.20
129/SvJ (F)
129/SvJ (M)
FVB (F)
MOLF (F)
FVB (M)
DBA (F)
MOLF (M)
DBA (M)
B6 (M)
BALB/c (M)
CD1 (F)
BALB/c (F)
B6 (F)
CD1 (M)
(B)
Area = 0.206
P = 3.84e-11
129/SvJ (F)
86 TLR Genes
Cumulative overlap
0.0
0.2
0.4
0.6
0.8
1.0
5000
10000
15000
Gene Rank (IMQ Response)
IMQ-increased → IMQ-decreased
(C)
Area = 0.076
P = 0.0152
CD1 (M)
86 TLR Genes
Cumulative overlap
0.0
0.2
0.4
0.6
0.8
1.0
2000
6000
10000
14000
Gene Rank (IMQ Response)
IMQ-increased → IMQ-decreased
(D)
FC (IMQ/CTL or PP/PN*)
△▽ P < 0.05
▲▼ FDR < 0.10
0.71
0.8
0.89
1
1.13
1.26
1.41
Tlr1
Ccl4
Mapk12
Pik3r1
Lbp
Cxcl10
Ikbke
Casp8
Pik3cg
Pik3cd
Stat1
Nfkb1
Myd88
Map2k4
Traf6
Map3k8
Mapk13
Cd80
Tlr2
Tlr6
Pik3r5
Tlr8
Ccl5
Irf7
Spp1
Cd14
Il1b
Il6
Il12b
Fos
FVB (M)
MOLF (F)
FVB (F)
BALB/c (F)
CD1 (F)
BALB/c (M)
CD1 (M)
B6 (F)
B6 (M)
DBA (F)
DBA (M)
MOLF (M)
129/SvJ (F)
129/SvJ (M)
Psoriasis*

(E) B6 (M)


TOLL-LIKE RECEPTOR SIGNALING PATHWAY
Peptidoglycan (G+)
Lipoprotein
Lipoarabinomannan
(Mycobacteria)
Zymosan (Yeast)
TLR1
TLR2
TLR6
TLR2
Rac1
PI3K-Akt signaling pathway
PI3K
AKT
TOLLIP
MyD88
TIRAP
FADD
CASP8
Apoptosis
LBP
LPS (G-)
CD14
Lipopolysaccharide biosynthesis
MD-2
TLR4
TIRAP
MyD88
MyD88-dependent pathway
IRAK4
IRAK1
TRAF6
TAB1
TAB2
TAK1
TRAM
Flagellar assembly
Flagellin
TLR5
MyD88
TRAF6
RIP1
Ubiquitin mediated proteolysis
Degradation
NF-κB signaling pathway
IKK
IKKγ
IKKα
IKKβ
+p
+p
NF-κB
IκBα
p105
Tpl2
+p
MEK1/2
+p
ERK
MAPK signaling pathway
+p
+p
MKK3/6
+p
p38
MKK4/7
+p
JNK
AP-1
+p
DNA
Inflammatory cytokines
TNFα
IL-1β
IL-6
IL-12
Proinflammatory effects
IL-8
RANTES
MIP-1α
MIP-1β
Chemotactic effects
(Nutrophil, Immature DC
(NK cell)
Complement and coagulation cascade
Costimulatory molecules
CD40
CD80
CD86
T cell stimulation
IRF5
Imidazoquinolin
(anti-viral compounds)
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TLR7/8
MyD88
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TRAF6
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IRAK1
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CTSK
TLR9
+p
IKKα
+p
OPN
dsRNA
TLR3
Endosome
TRIF
MyD88-independent pathway
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IKKε
TBK1
+p
IRF3
Inflammatory cytokines
IFN-α
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Cytokine-cytokine receptor interaction
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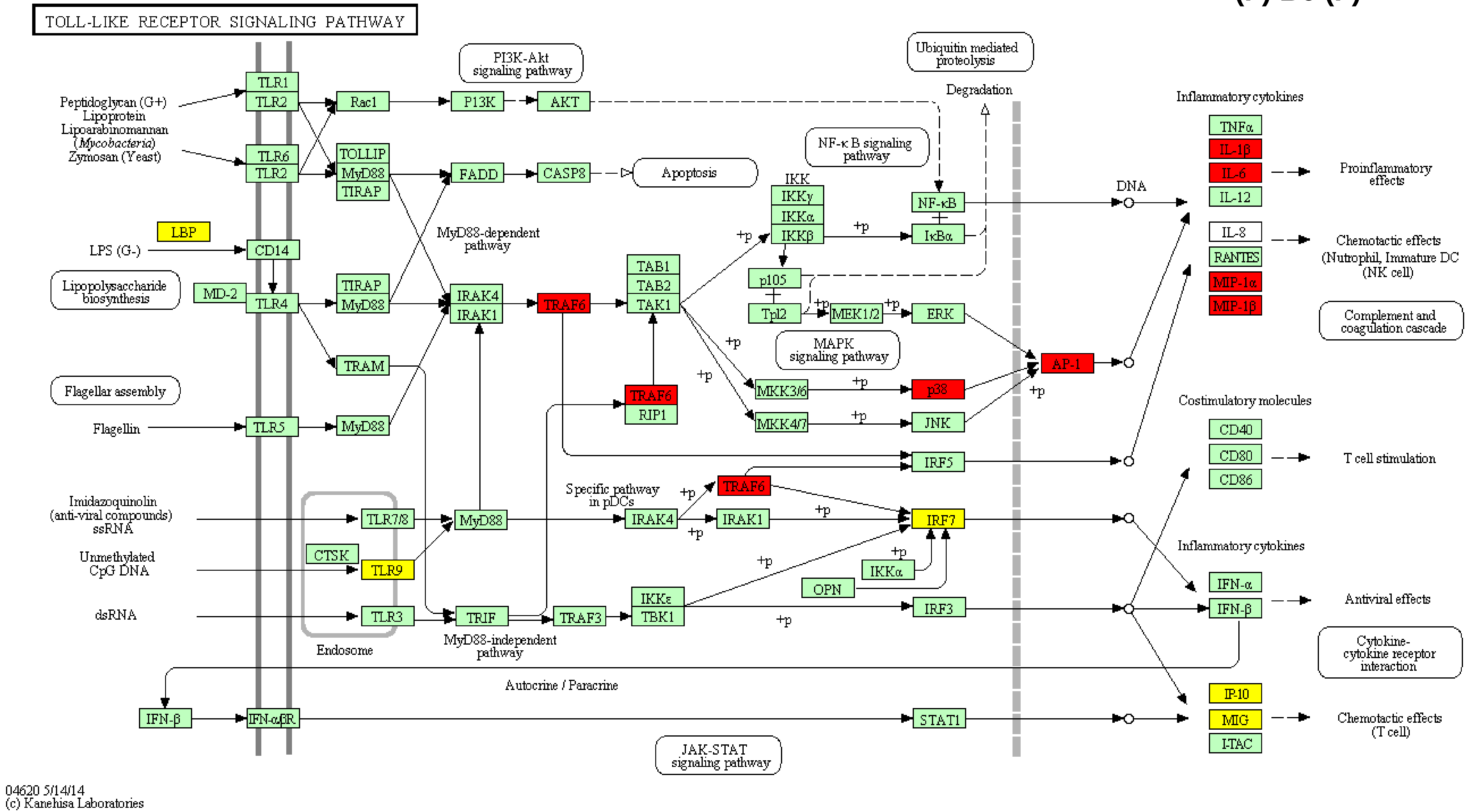
IFN-β
IFN-α/βR
STAT1
JAK-STAT signaling pathway
IP-10
MIG
I-TAC
Chemotactic effects
(T cell)
04620 5/14/14
(c) Kanehisa Laboratories

(F) B6 (F)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(T cell)
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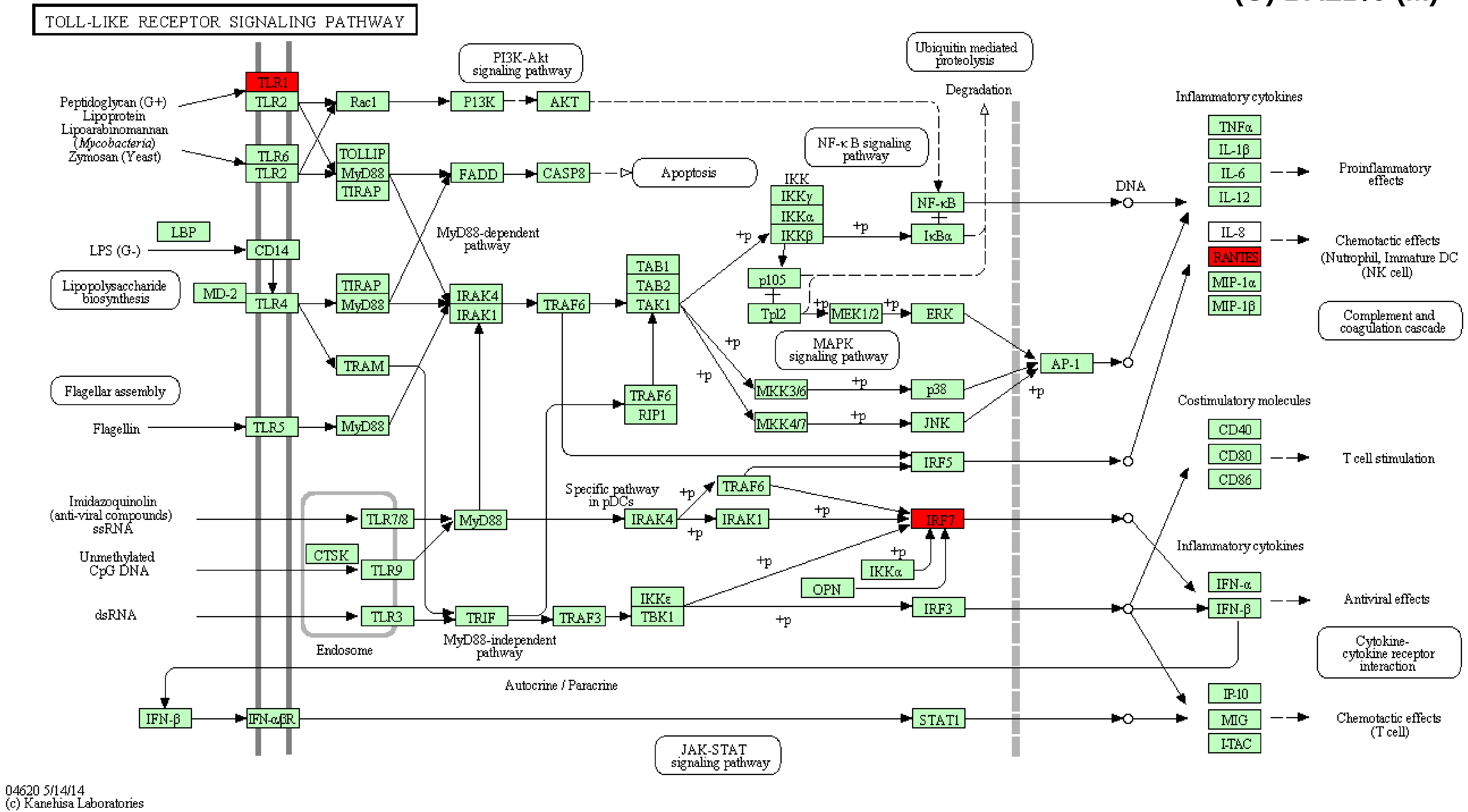
(c) Kanehisa Laboratories

(G) BALB/c (M)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MKK4/7
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RANTES
MIP-1α
MIP-1β
Chemotactic effects (Nutrophil, Immature DC (NK cell)
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CD80
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T cell stimulation
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IFN-α
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Antiviral effects
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MIG
I-TAC
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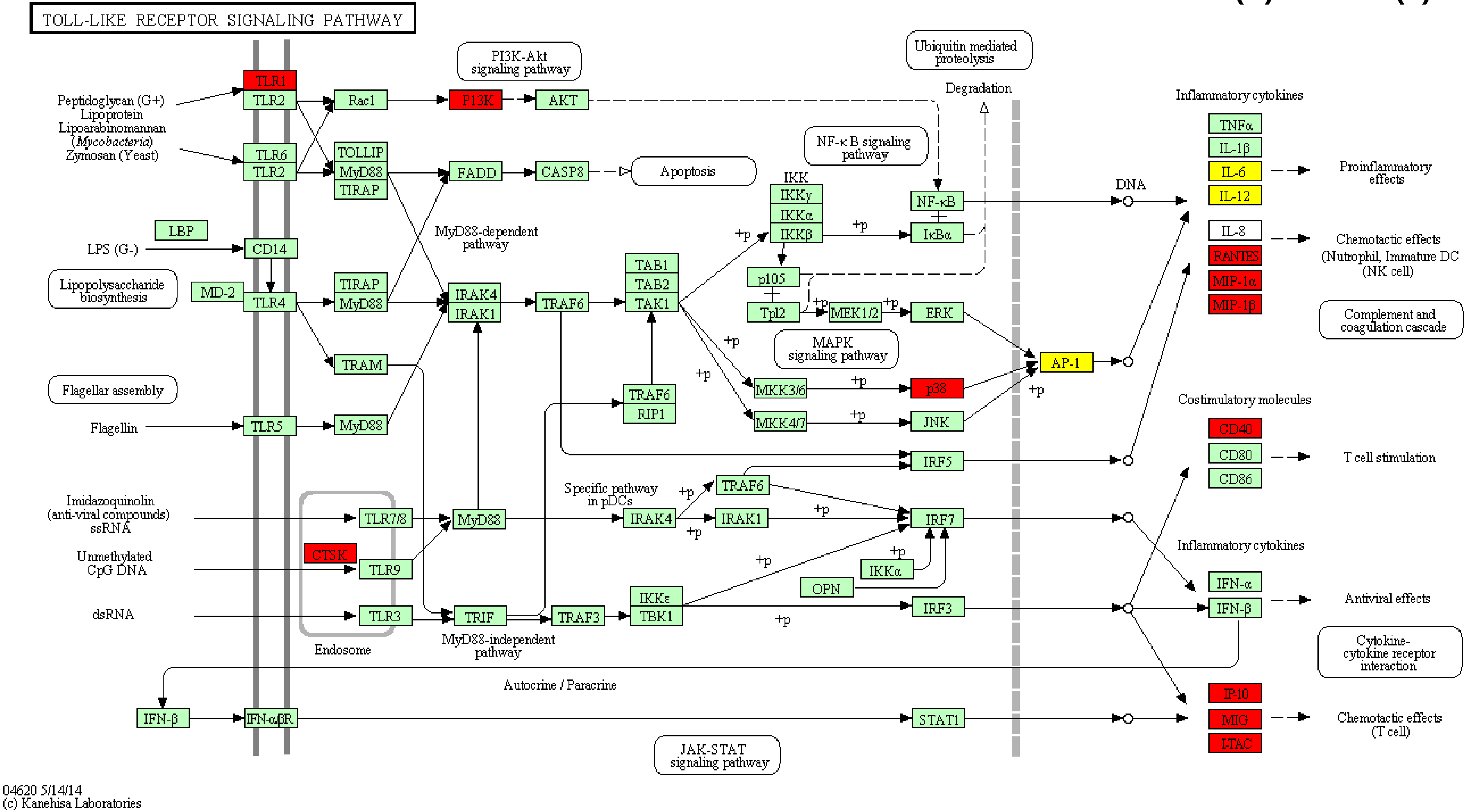
04620 5/14/14
(c) Kanehisa Laboratories

(H) BALB/c (F)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Lipoarabinomannan
(*Mycobacteria*)
Zymosan (Yeast)
TLR1
TLR2
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CD14
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TAB2
TAK1
p105
Tpl2
MEK1/2
ERK
MAPK signaling pathway
TRAM
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Flagellar assembly
Flagellin
TLR5
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TRAF6
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CTSK
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IKKα
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IFN-α
IFN-β
Antiviral effects
dsRNA
TLR3
Endosome
TRIF
MyD88-independent pathway
TRAF3
IKKε
TBK1
IRF3
Cytokine-cytokine receptor interaction
Autocrine / Paracrine
IFN-β
IFN-α/βR
STAT1
JAK-STAT signaling pathway
IP-10
MIG
I-TAC
Chemotactic effects
(T cell)
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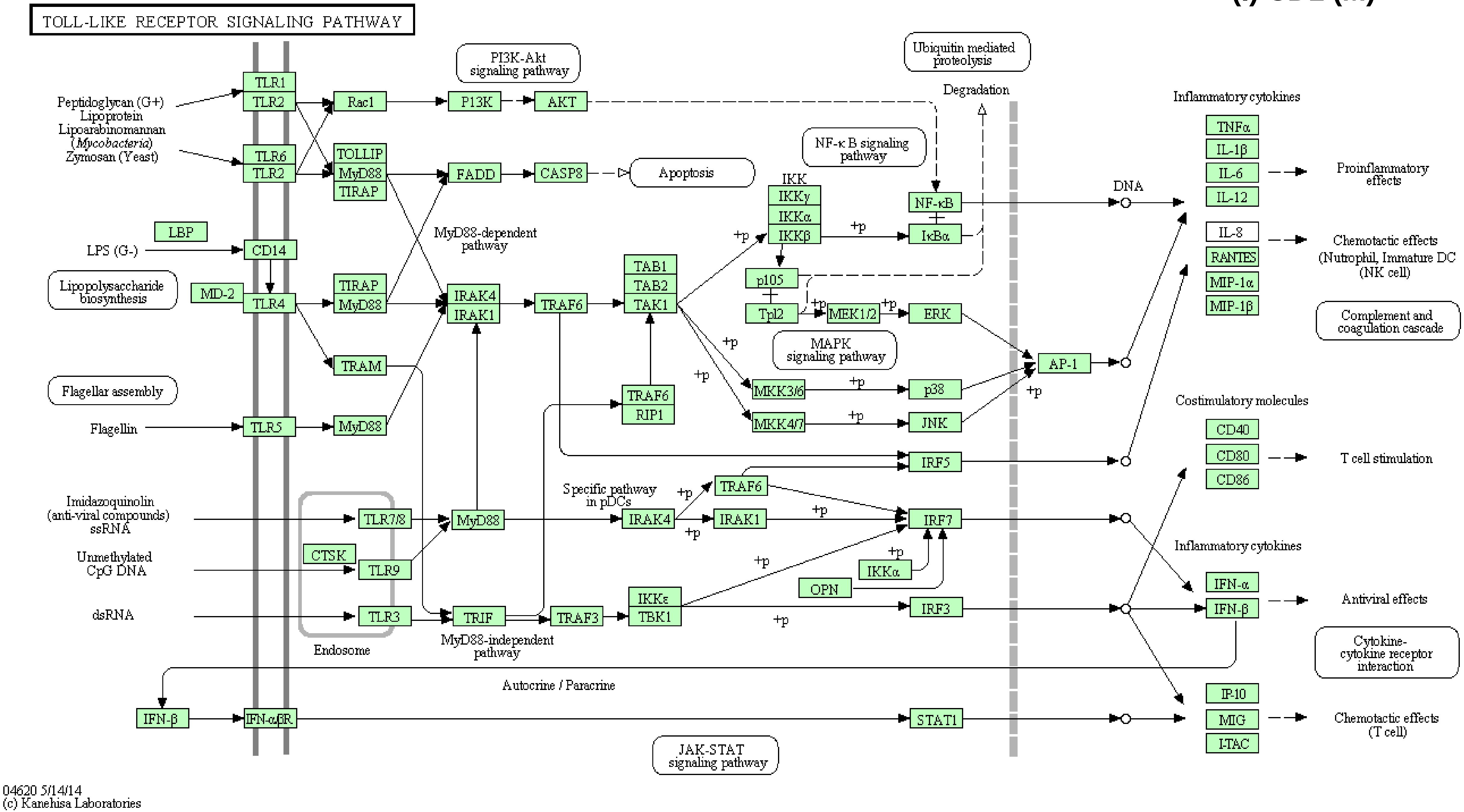
(c) Kanehisa Laboratories

(I) CD1 (M)


TOLL-LIKE RECEPTOR SIGNALING PATHWAY
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Lipoprotein
Lipoarabinomannan
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Zymosan (Yeast)
TLR1
TLR2
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TLR2
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PI3K-Akt signaling pathway
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IKKα
IKKβ
NF-κB
IκBα
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LBP
LPS (G-)
CD14
Lipopolysaccharide biosynthesis
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MyD88
MyD88-dependent pathway
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CD40
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Antiviral effects
Cytokine-cytokine receptor interaction
IP-10
MIG
I-TAC
Chemotactic effects
(T cell)
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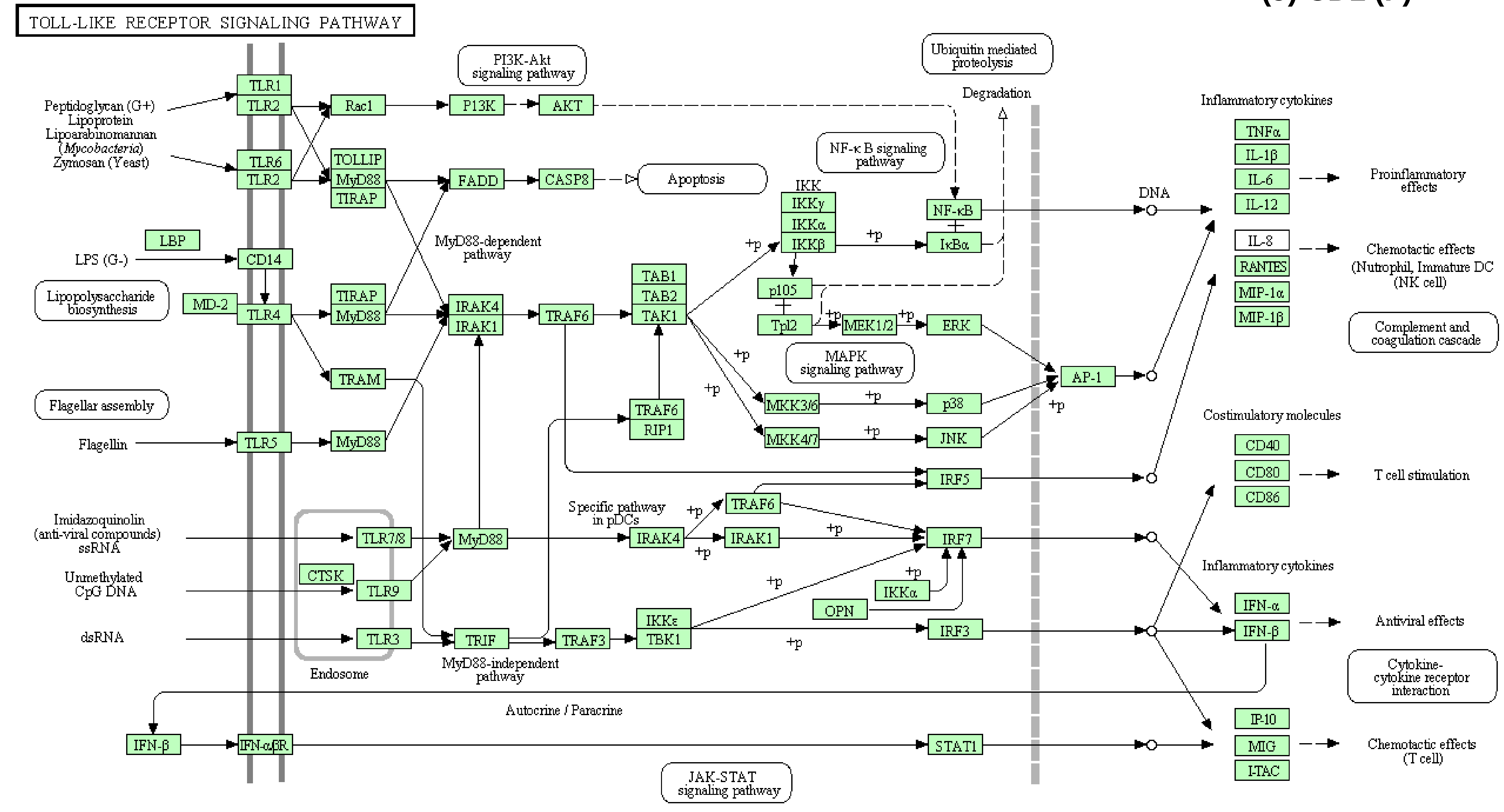
(c) Kanehisa Laboratories

(J) CD1 (F)



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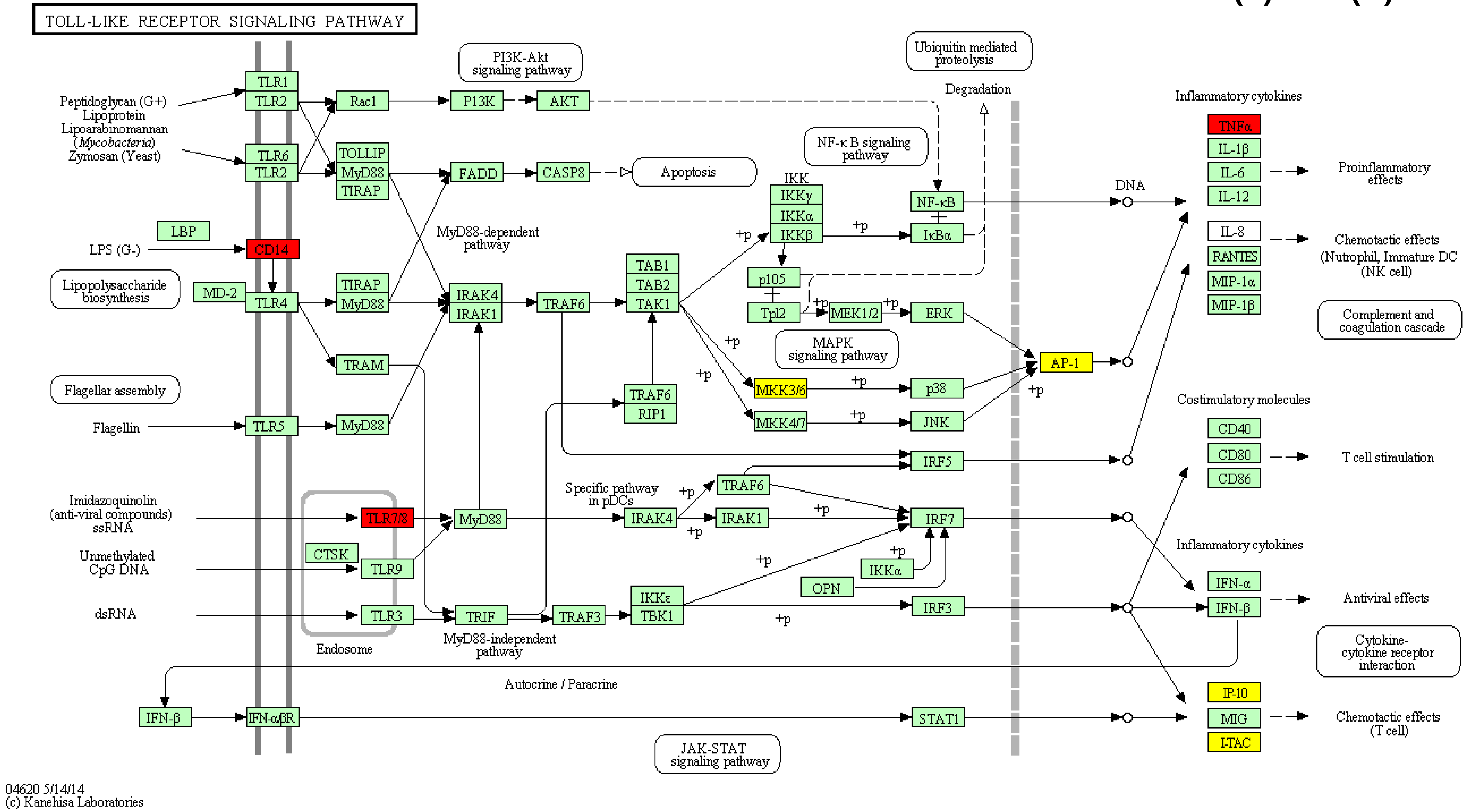
(K) DBA (M)


TOLL-LIKE RECEPTOR SIGNALING PATHWAY
Peptidoglycan (G+)
Lipoprotein
Lipoarabinomannan
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TLR1
TLR2
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TLR2
Rac1
PI3K-Akt signaling pathway
PI3K
AKT
TOLLIP
MyD88
TIRAP
FADD
CASP8
Apoptosis
Ubiquitin mediated proteolysis
Degradation
NF-κB signaling pathway
IKK
IKKγ
IKKα
IKKβ
NF-κB
IκBα
+p
LBP
LPS (G-)
CD14
MD-2
TLR4
Lipopolysaccharide biosynthesis
TIRAP
MyD88
MyD88-dependent pathway
IRAK4
IRAK1
TRAF6
TAB1
TAB2
TAK1
p105
Tpl2
MEK1/2
ERK
MAPK signaling pathway
TRAM
Flagellar assembly
Flagellin
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MyD88
TRAF6
RIP1
MKK3/6
p38
MKK4/7
JNK
AP-1
IRF5
DNA
Inflammatory cytokines
TNFα
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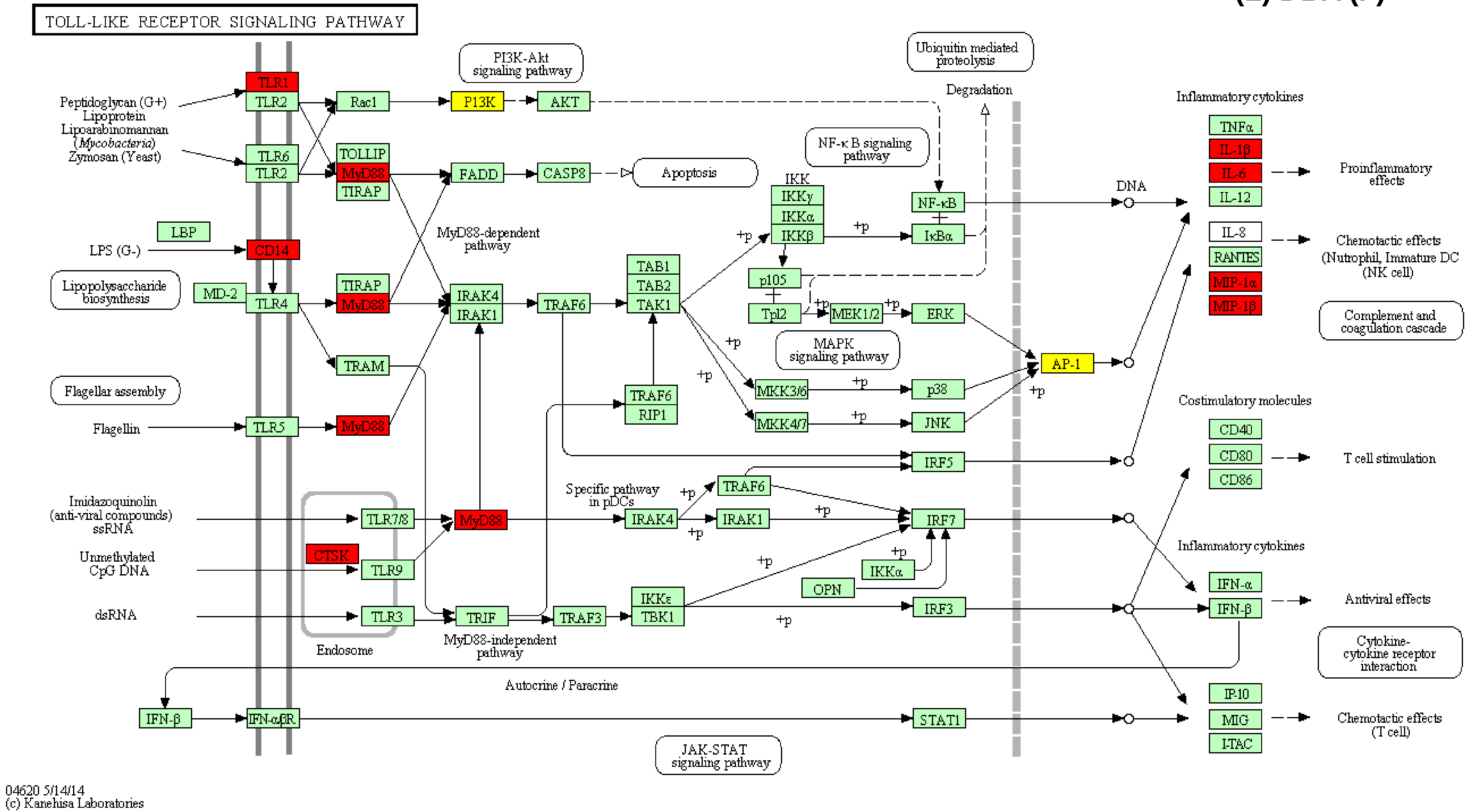
JAK-STAT signaling pathway
IP-10
MIG
I-TAC
Chemotactic effects (T cell)
04620 5/14/14
(c) Kanehisa Laboratories

(L) DBA (F)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PI3K-Akt signaling pathway
Ubiquitin mediated proteolysis
Degradation
Inflammatory cytokines
Peptidoglycan (G+)
Lipoprotein
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(Mycobacteria)
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Rac1
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Chemotactic effects
(T cell)
JAK-STAT signaling pathway
04620 5/14/14
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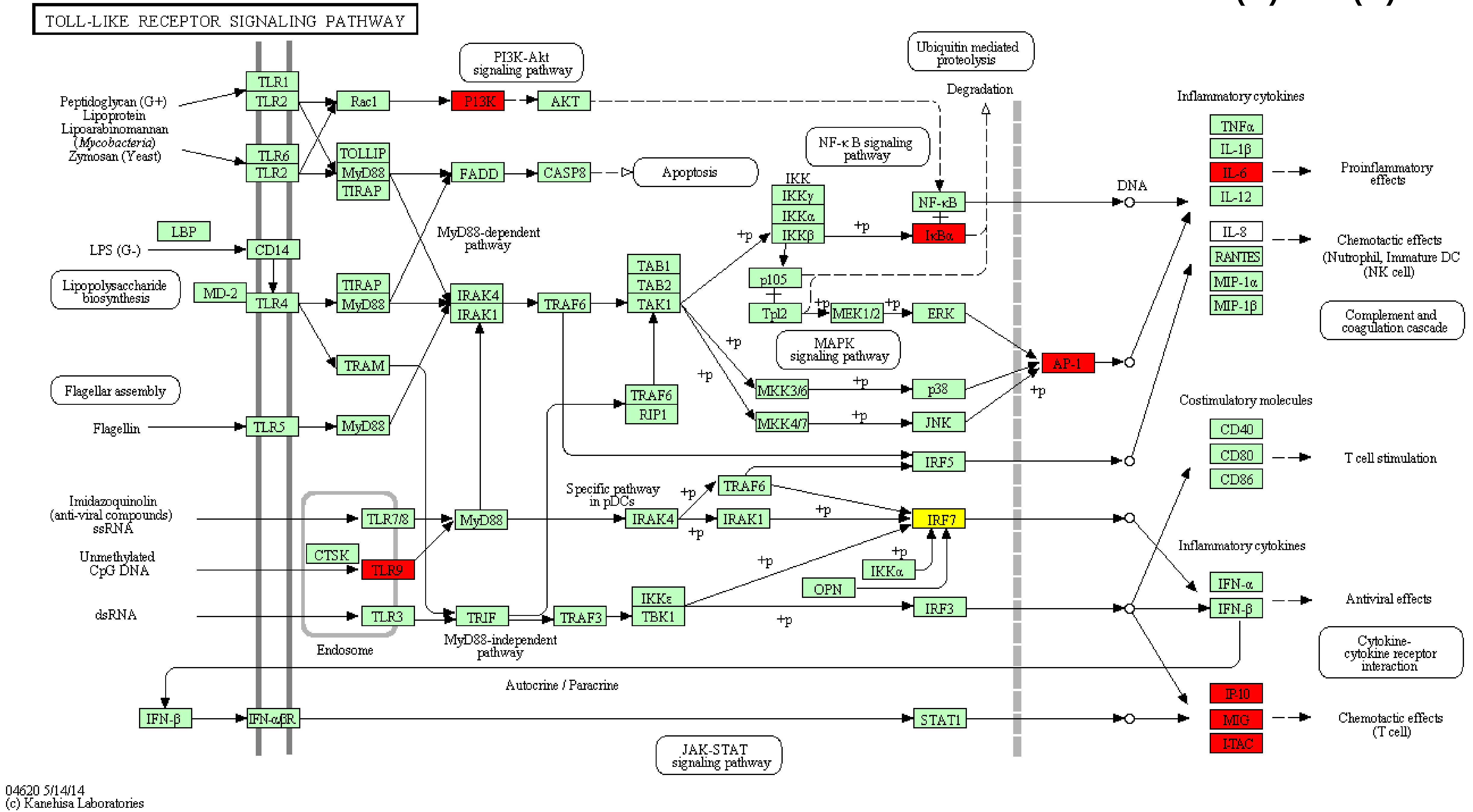
(M) FVB (M)



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IFN-α/βR
JAK-STAT signaling pathway
04620 5/14/14
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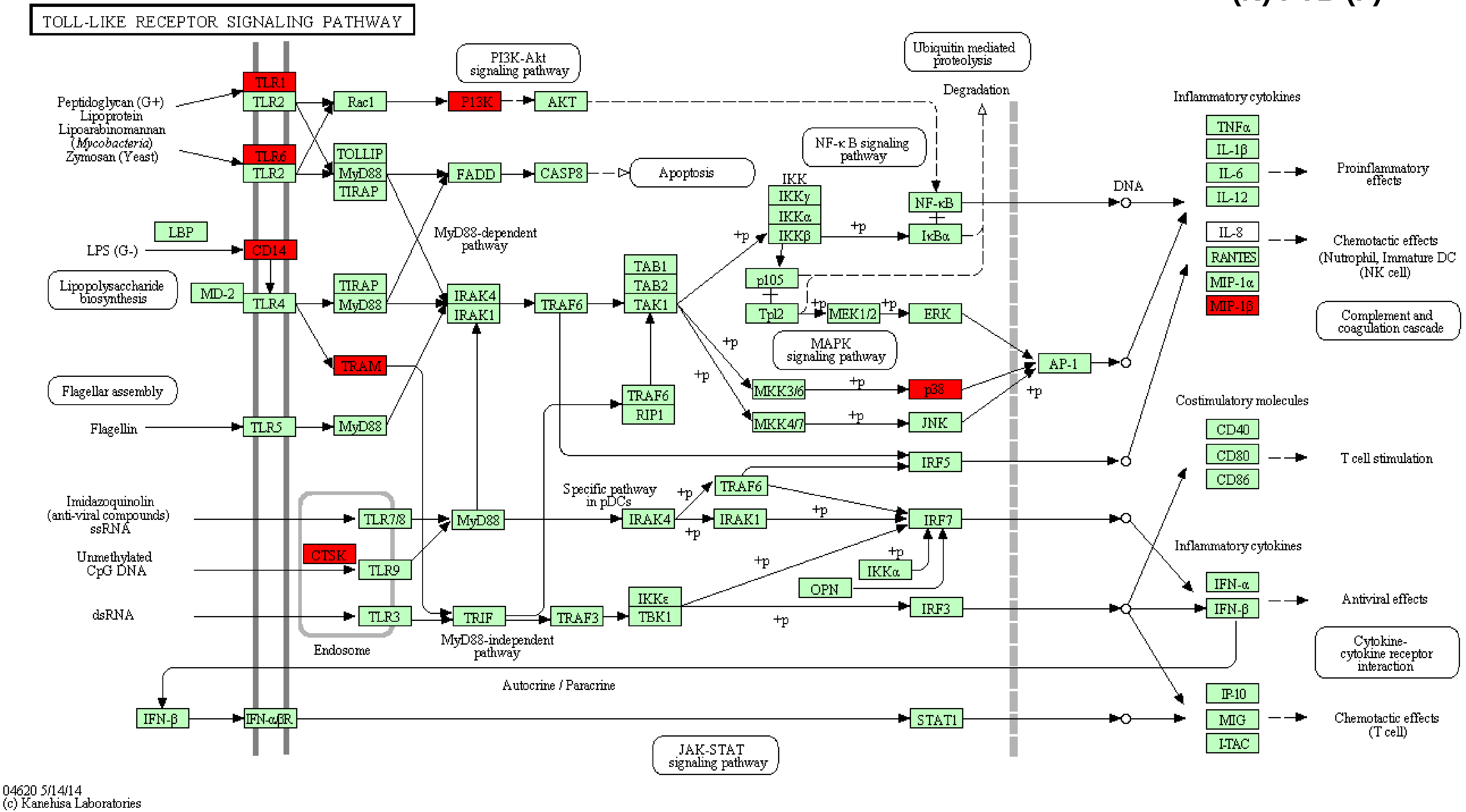
(N) FVB (F)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PI3K
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TIRAP
FADD
CASP8
Apoptosis
LBP
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IL-1β
IL-6
IL-12
Proinflammatory effects
IL-8
RANTES
MIP-1α
MIP-1β
Chemotactic effects
(Nutrophil, Immature DC (NK cell)
Complement and coagulation cascade
Costimulatory molecules
CD40
CD80
CD86
T cell stimulation
Imidazoquinolin
(anti-viral compounds)
ssRNA
Unmethylated CpG DNA
dsRNA
Endosome
TLR7/8
CTSK
TLR9
TLR3
MyD88
TRIF
MyD88-independent pathway
Specific pathway in pDCs
IRAK4
IRAK1
TRAF6
IRF7
IKKα
OPN
TRAF3
IKKε
TBK1
IRF3
Inflammatory cytokines
IFN-α
IFN-β
Antiviral effects
Cytokine-cytokine receptor interaction
Autocrine / Paracrine
IFN-β
IFN-α/βR
STAT1
JAK-STAT signaling pathway
IP-10
MIG
I-TAC
Chemotactic effects (T cell)
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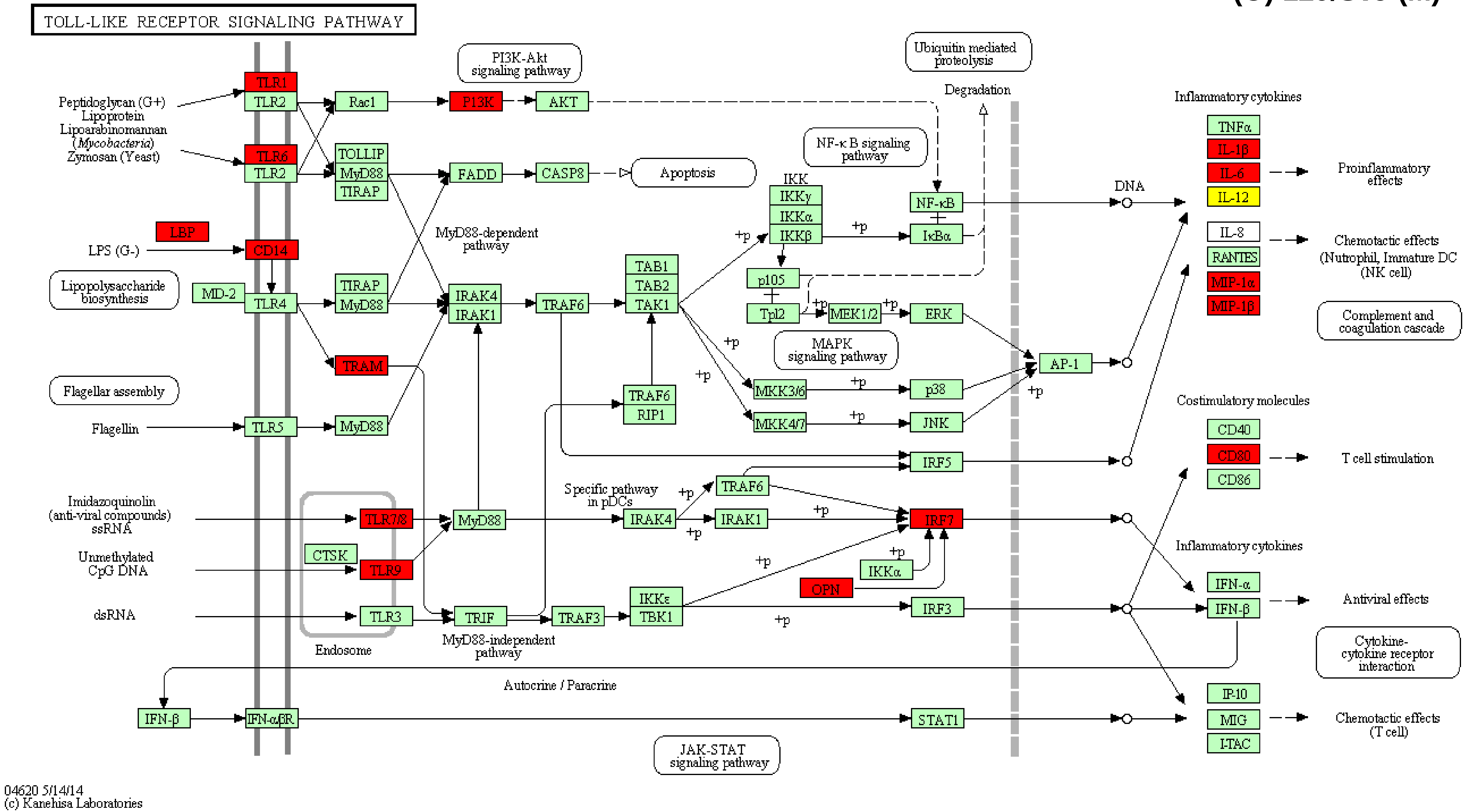
(O) 129/SvJ (M)


TOLL-LIKE RECEPTOR SIGNALING PATHWAY
Peptidoglycan (G+)
Lipoprotein
Lipoarabinomannan
(Mycobacteria)
Zymosan (Yeast)
TLR1
TLR2
TLR6
TLR2
LBP
LPS (G-)
CD14
Lipopolysaccharide biosynthesis
MD-2
TLR4
TRAM
Flagellar assembly
Flagellin
TLR5
MyD88
Rac1
PI3K-Akt signaling pathway
PI3K
AKT
TOLLIP
MyD88
TIRAP
FADD
CASP8
Apoptosis
TIRAP
MyD88
MyD88-dependent pathway
IRAK4
IRAK1
TRAF6
TAB1
TAB2
TAK1
TRAF6
RIP1
Ubiquitin mediated proteolysis
Degradation
NF-κB signaling pathway
IKK
IKKγ
IKKα
IKKβ
NF-κB
IκBα
p105
Tpl2
MEK1/2
ERK
MAPK signaling pathway
MKK3/6
p38
MKK4/7
JNK
AP-1
IRF5
+p
DNA
Inflammatory cytokines
TNFα
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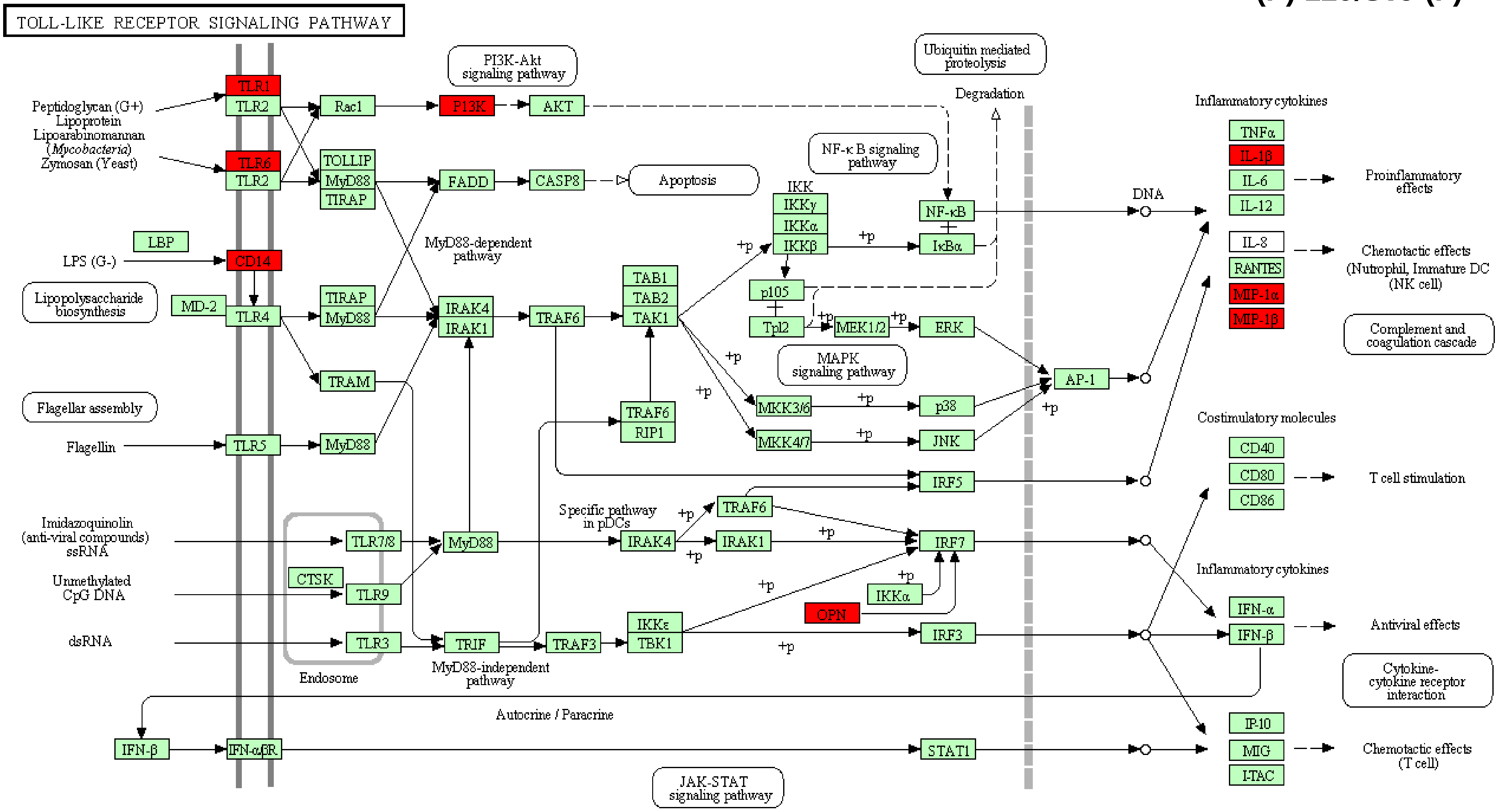
(P) 129/SvJ (F)



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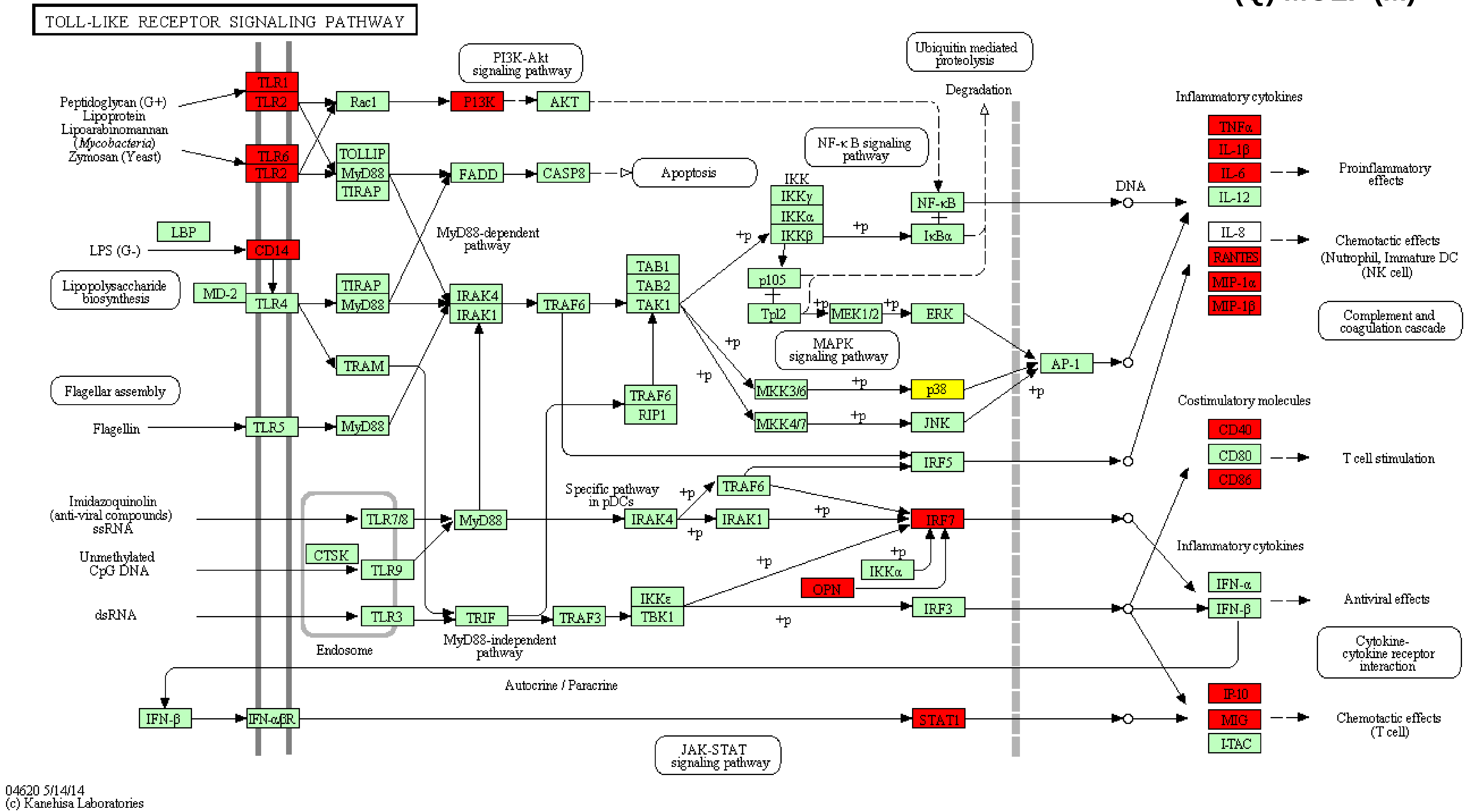
(Q) MOLF (M)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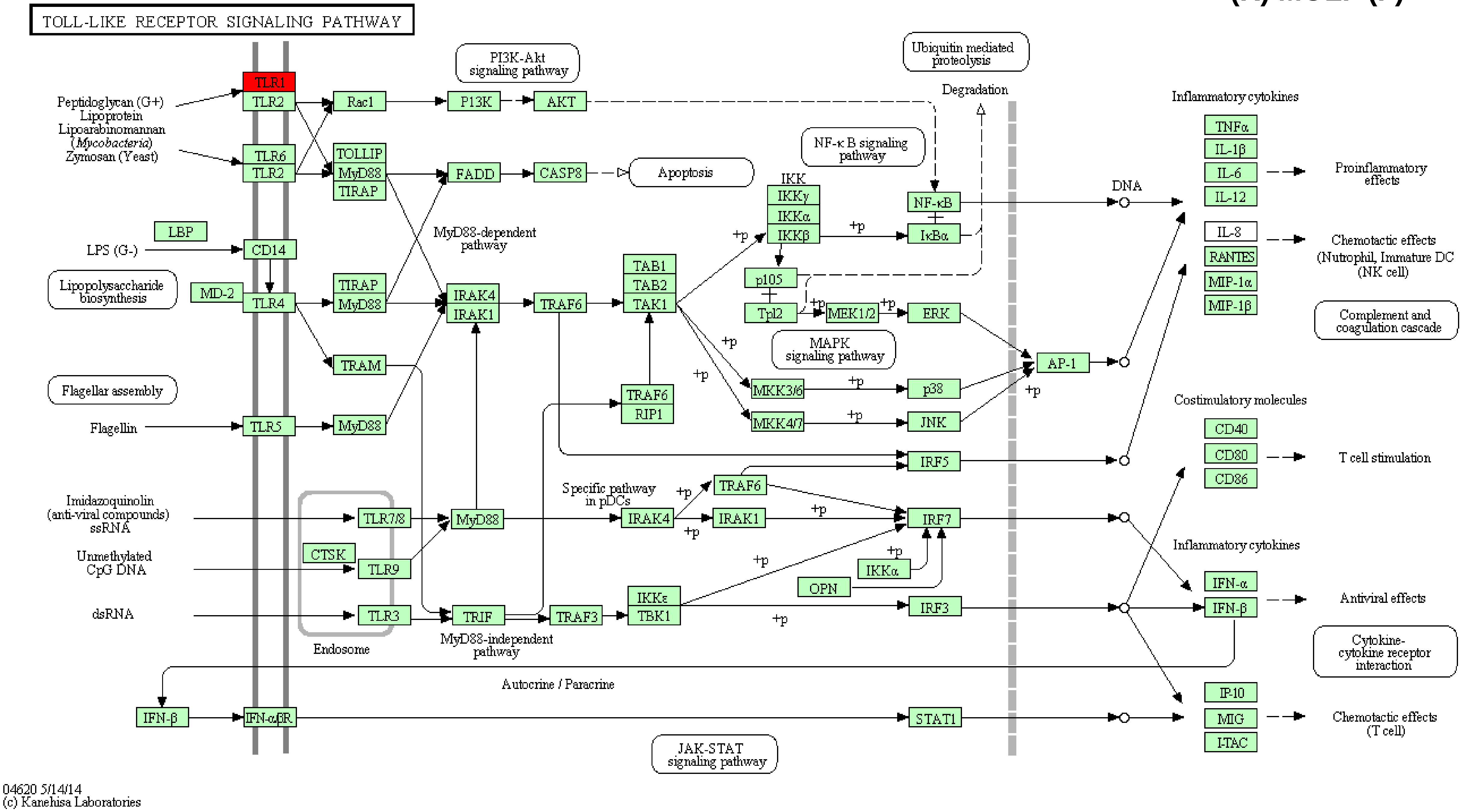
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