FIG. 1

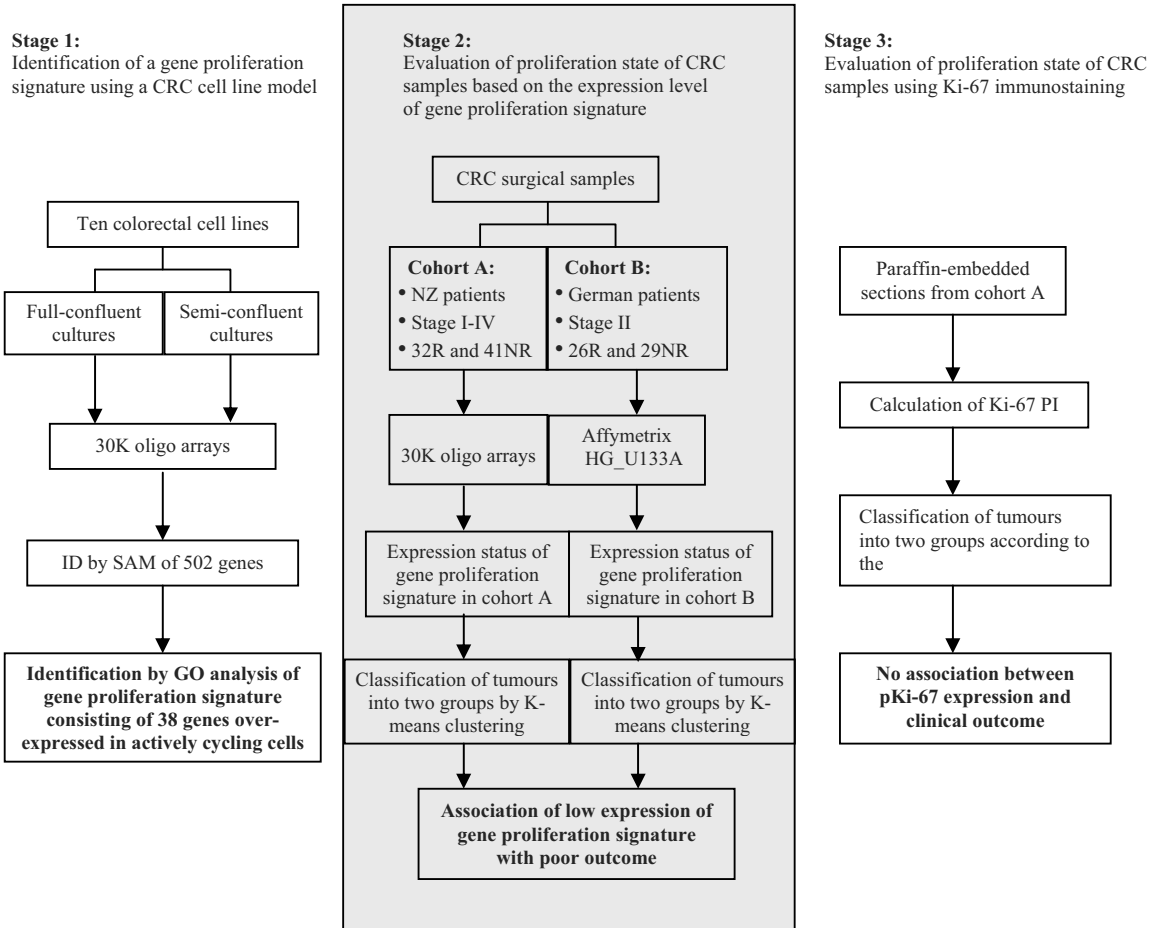

Stage 1:
Identification of a gene proliferation signature using a CRC cell line model
Ten colorectal cell lines
Full-confluent cultures
Semi-confluent cultures
30K oligo arrays
ID by SAM of 502 genes
Identification by GO analysis of gene proliferation signature consisting of 38 genes over-expressed in actively cycling cells
Stage 2:
Evaluation of proliferation state of CRC samples based on the expression level of gene proliferation signature
CRC surgical samples
Cohort A:
• NZ patients
• Stage I-IV
• 32R and 41NR
Cohort B:
• German patients
• Stage II
• 26R and 29NR
30K oligo arrays
Affymetrix HG_U133A
Expression status of gene proliferation signature in cohort A
Expression status of gene proliferation signature in cohort B
Classification of tumours into two groups by K-means clustering
Classification of tumours into two groups by K-means clustering
Association of low expression of gene proliferation signature with poor outcome
Stage 3:
Evaluation of proliferation state of CRC samples using Ki-67 immunostaining
Paraffin-embedded sections from cohort A
Calculation of Ki-67 PI
Classification of tumours into two groups according to the
No association between pKi-67 expression and clinical outcome

FIG. 2

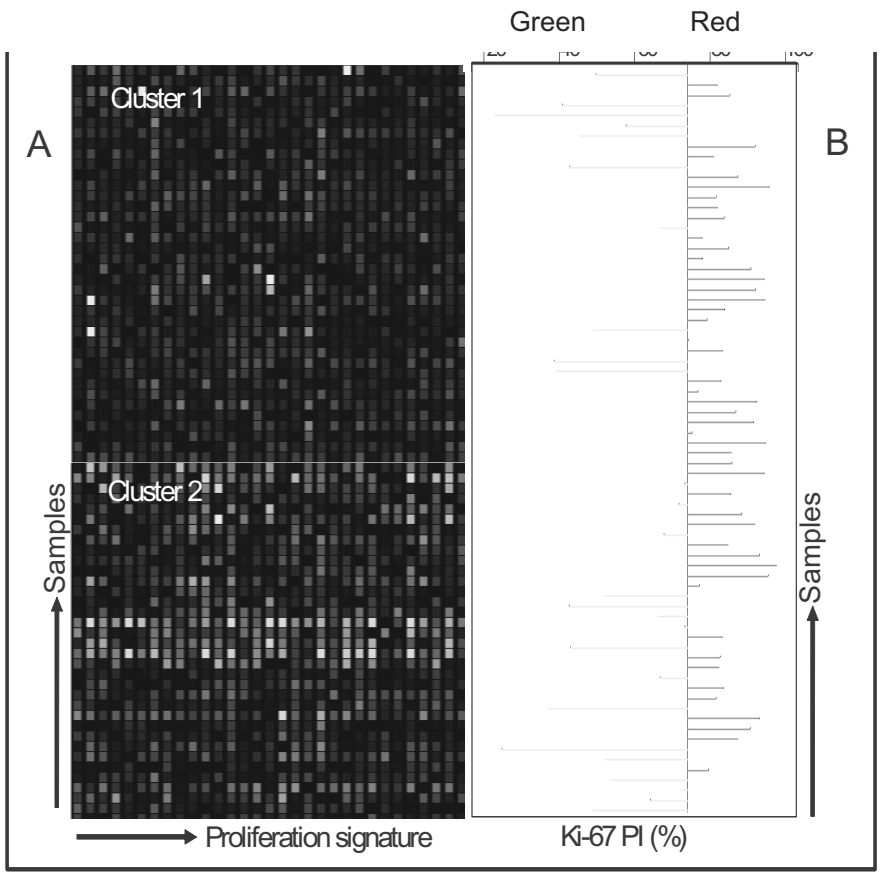

Predominantly
Red
Green
Red
A
B
Cluster 1
Cluster 2
Samples
Samples
Proliferation signature
Ki-67 PI (%)
Predominantly
Green

FIG. 3

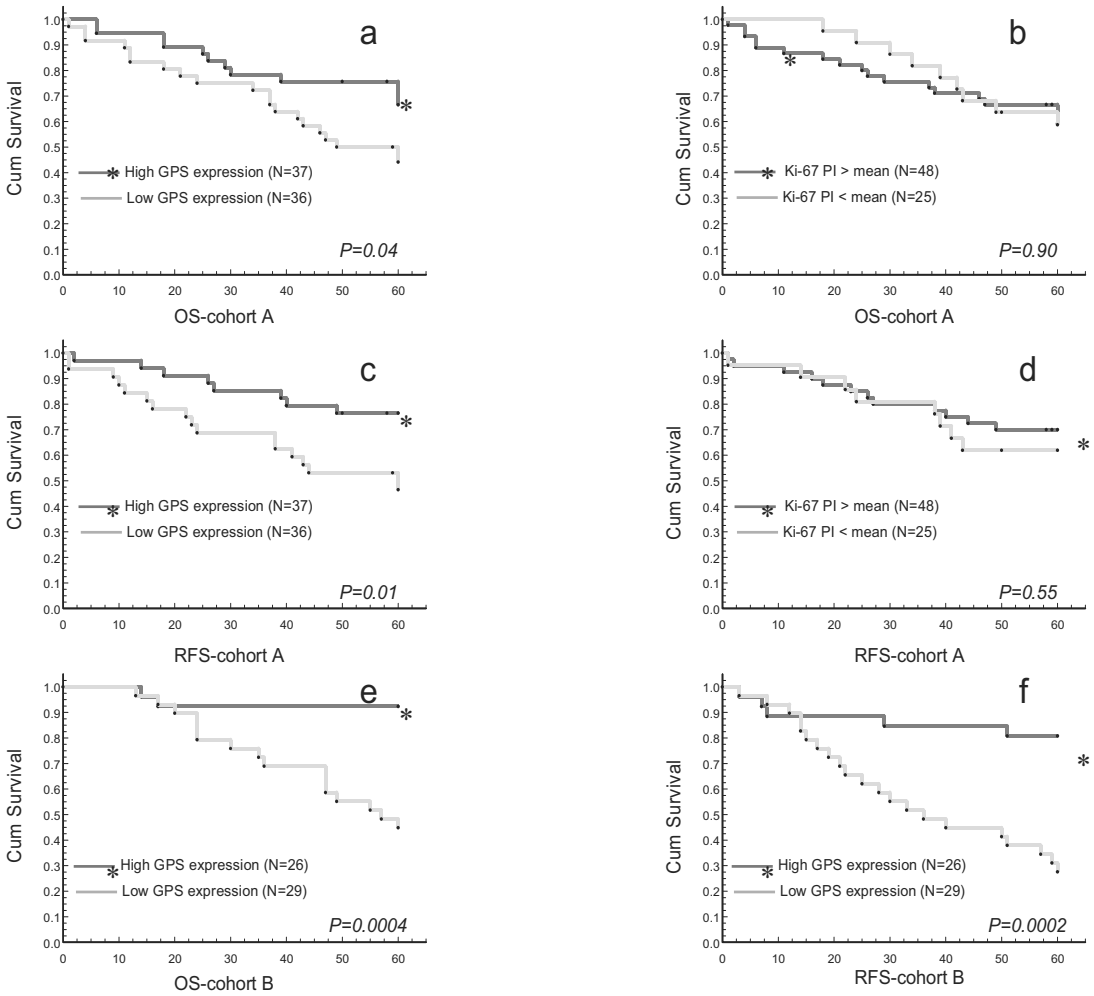

a
Cum Survival
High GPS expression (N=37)
Low GPS expression (N=36)
P=0.04
OS-cohort A
b
Ki-67 PI > mean (N=48)
Ki-67 PI < mean (N=25)
P=0.90
OS-cohort A
c
High GPS expression (N=37)
Low GPS expression (N=36)
P=0.01
RFS-cohort A
d
Ki-67 PI > mean (N=48)
Ki-67 PI < mean (N=25)
P=0.55
RFS-cohort A
e
High GPS expression (N=26)
Low GPS expression (N=29)
P=0.0004
OS-cohort B
f
High GPS expression (N=26)
Low GPS expression (N=29)
P=0.0002
RFS-cohort B

FIG. 4

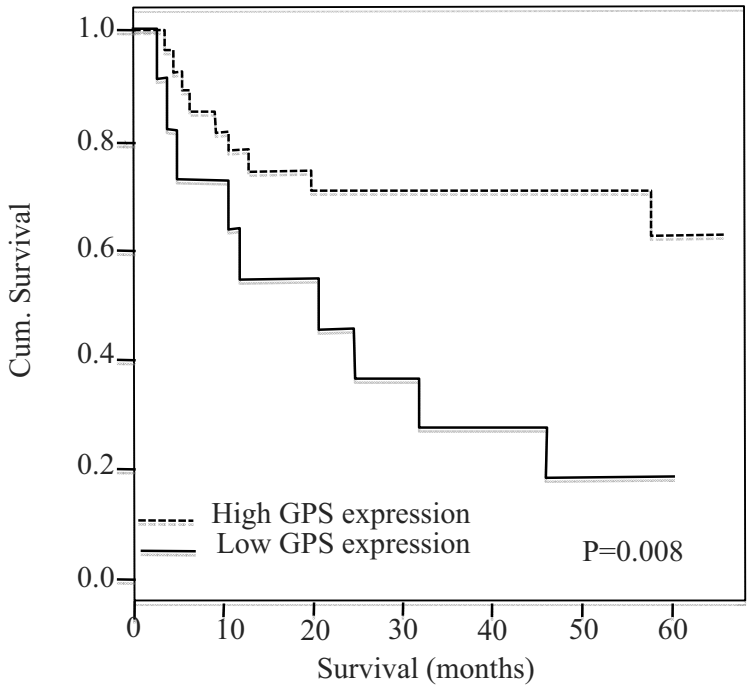
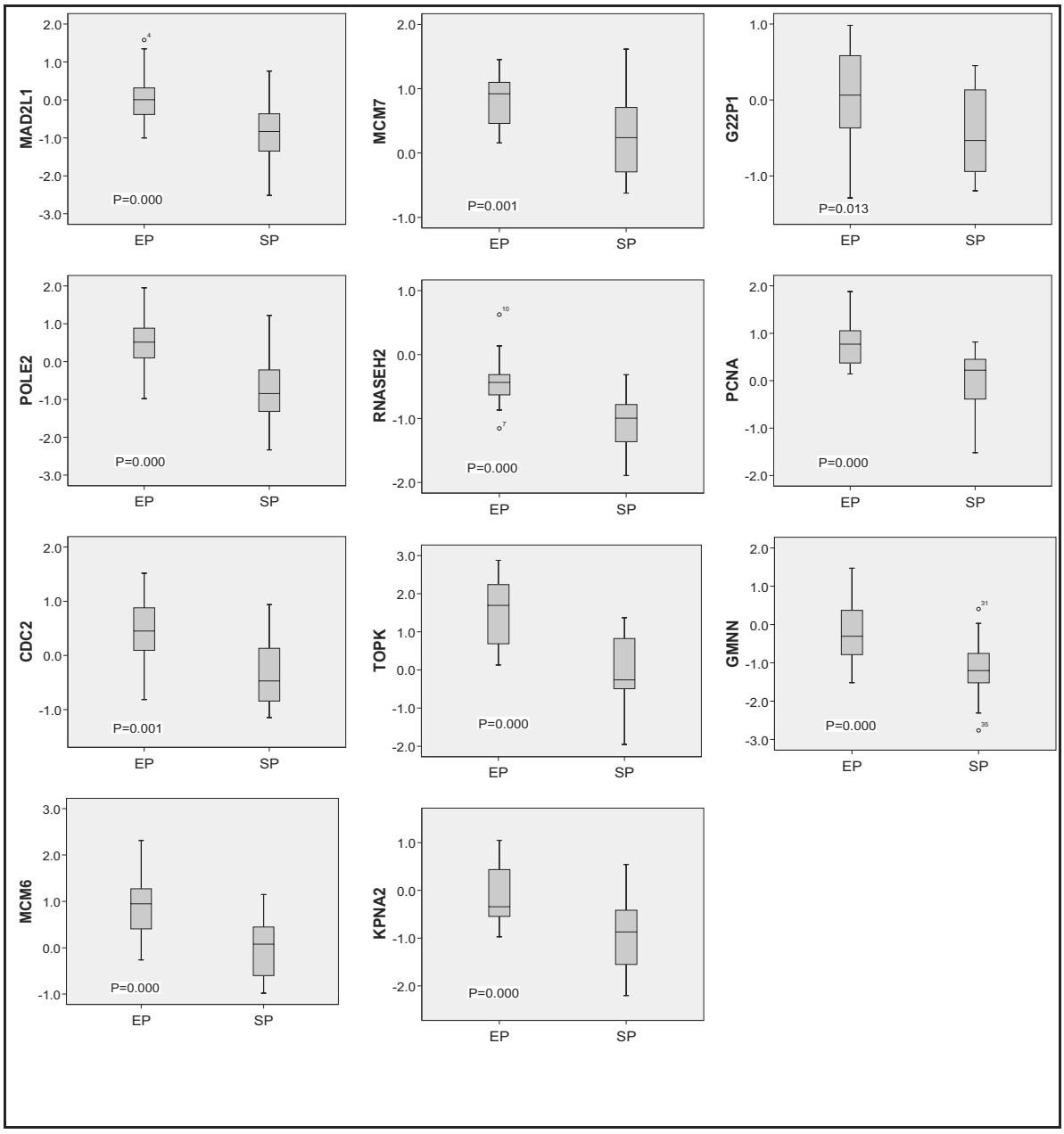

1.0
0.8
0.6
0.4
0.2
0.0
Cum. Survival
High GPS expression
Low GPS expression
P=0.008
0
10
20
30
40
50
60
Survival (months)

FIG. 5


MAD2L1
P=0.000
EP
SP
MCM7
P=0.001
EP
SP
G22P1
P=0.013
EP
SP
POLE2
P=0.000
EP
SP
RNASEH2
P=0.000
EP
SP
PCNA
P=0.000
EP
SP
CDC2
P=0.001
EP
SP
TOPK
P=0.000
EP
SP
GMNN
P=0.000
EP
SP
MCM6
P=0.000
EP
SP
KPNA2
P=0.000
EP
SP