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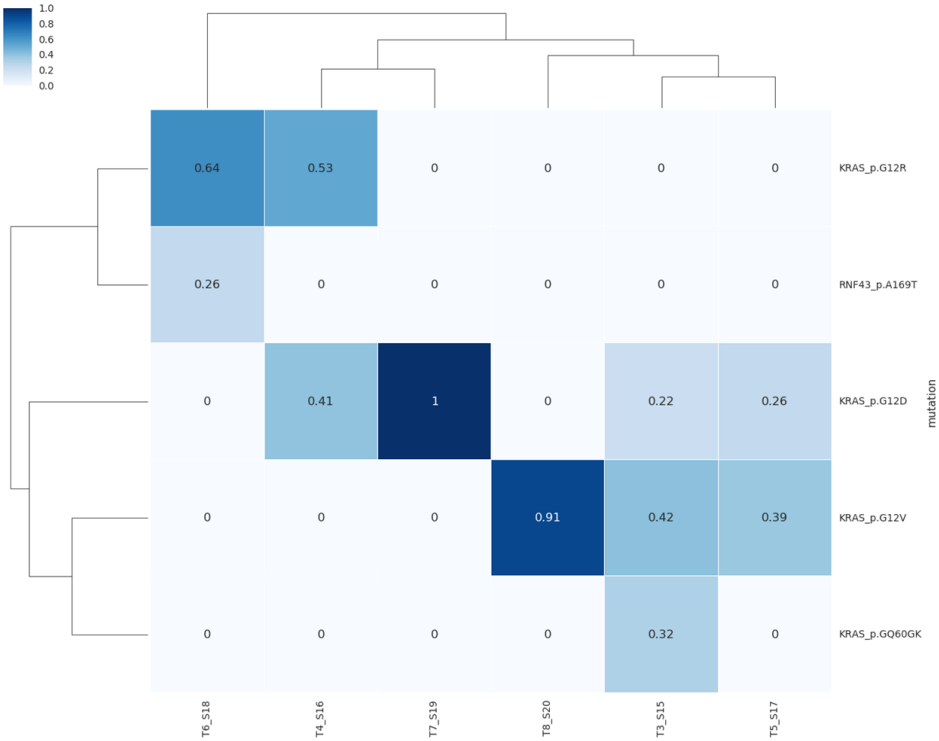
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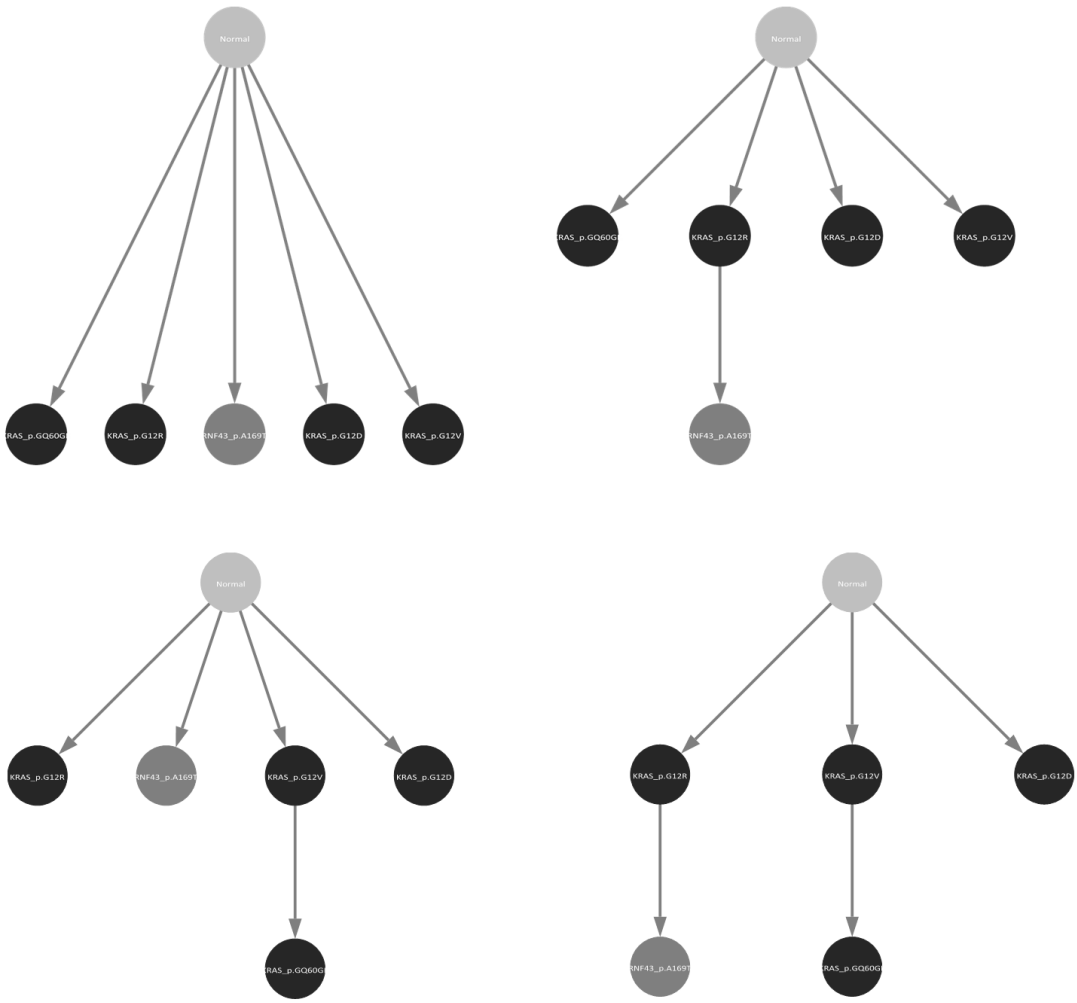
0 0.41 1 0 0.22 0.26 KRAS_p.G12D
0 0 0 0.91 0.42 0.39 KRAS_p.G12V
0 0 0 0 0.32 0 KRAS_p.GQ60GK
mutation
T6_S18
T4_S16
T7_S19
T8_S20
T3_S15
T5_S17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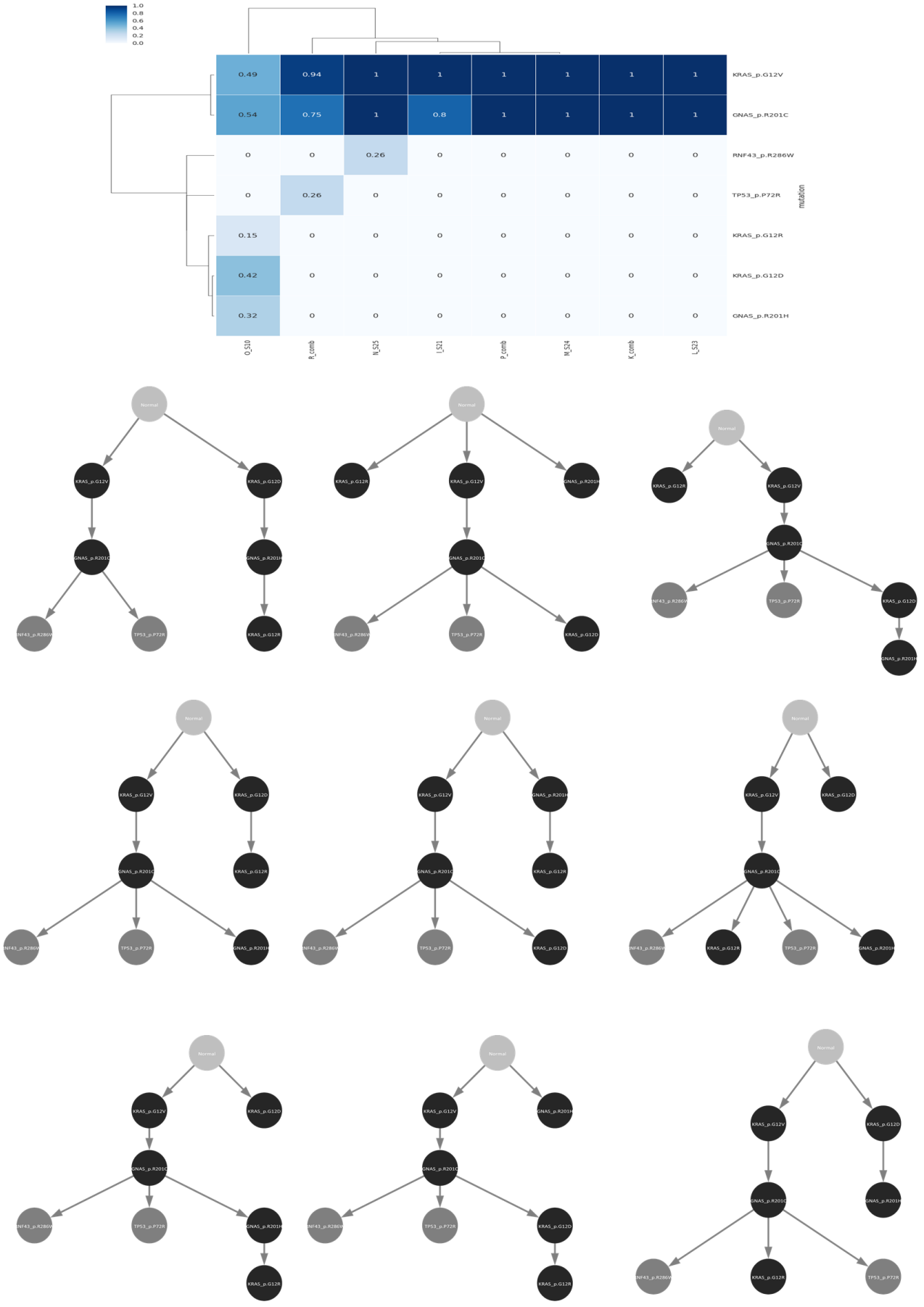
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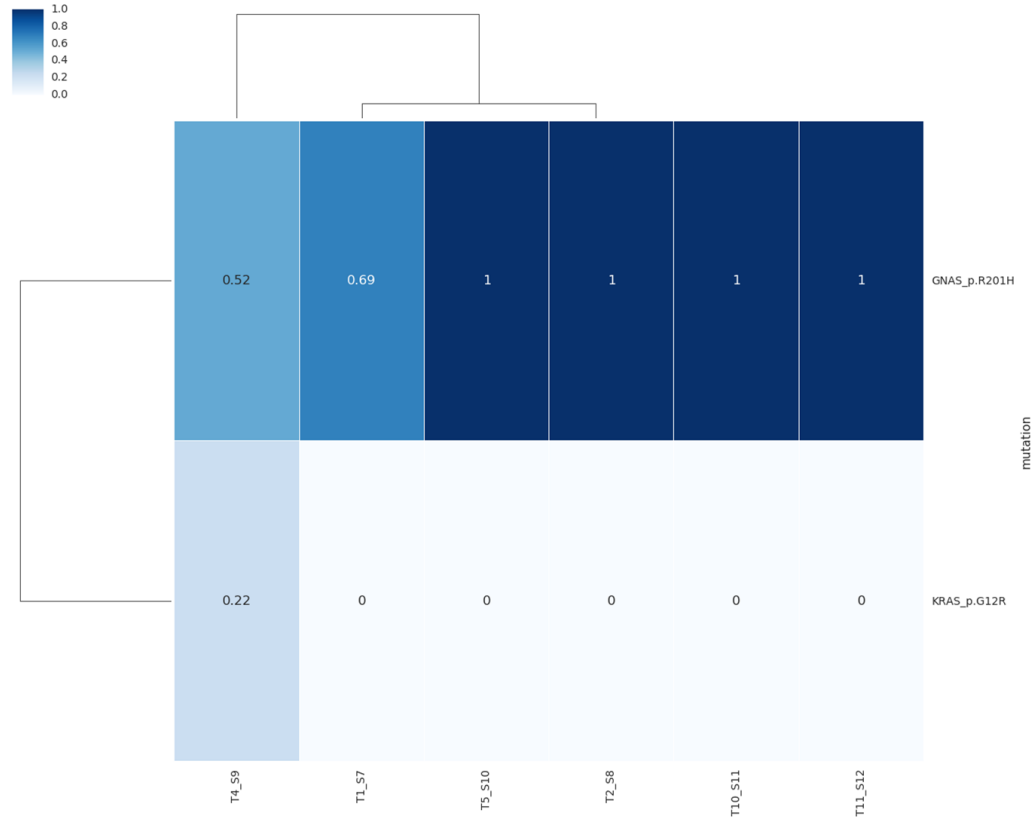
0.54 0.75 1 0.8 1 1 1 1 GNAS_p.R201C
0 0 0.26 0 0 0 0 0 RNF43_p.R286W
0 0.26 0 0 0 0 0 0 TP53_p.P72R
0.15 0 0 0 0 0 0 0 KRAS_p.G12R
0.42 0 0 0 0 0 0 0 KRAS_p.G12D
0.32 0 0 0 0 0 0 0 GNAS_p.R201H
mutation
Q_S10
R_comb
N_S25
I_S21
P_comb
M_S24
K_comb
L_S23
Normal
KRAS_p.G12V
KRAS_p.G12D
GNAS_p.R201C
GNAS_p.R201H
RNF43_p.R286W
TP53_p.P72R
KRAS_p.G12R

C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0
0
0
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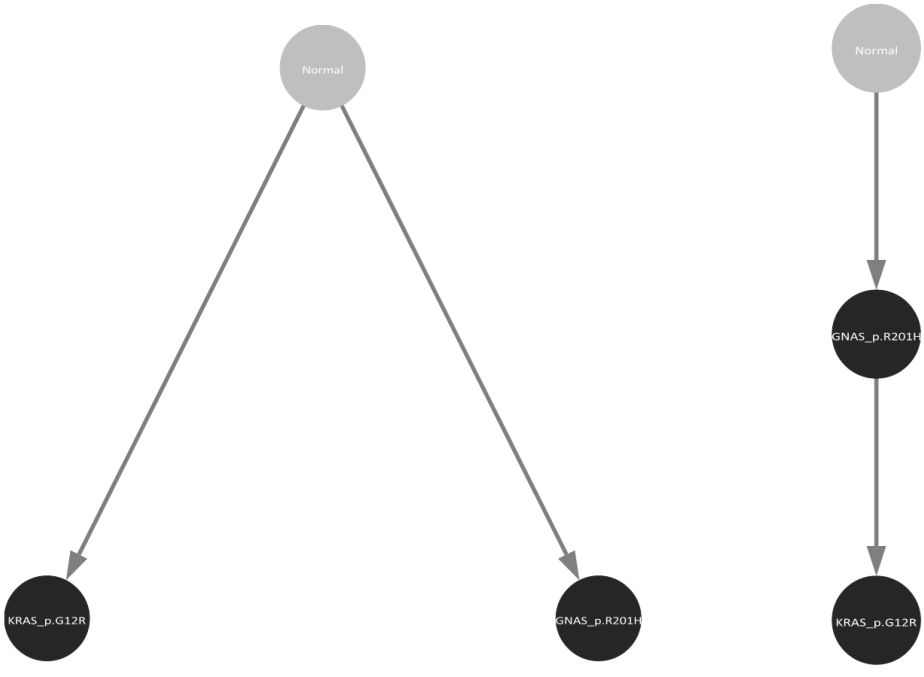
KRAS_p.G12R
mutation
T4_S9
T1_S7
T5_S10
T2_S8
T10_S11
T11_S12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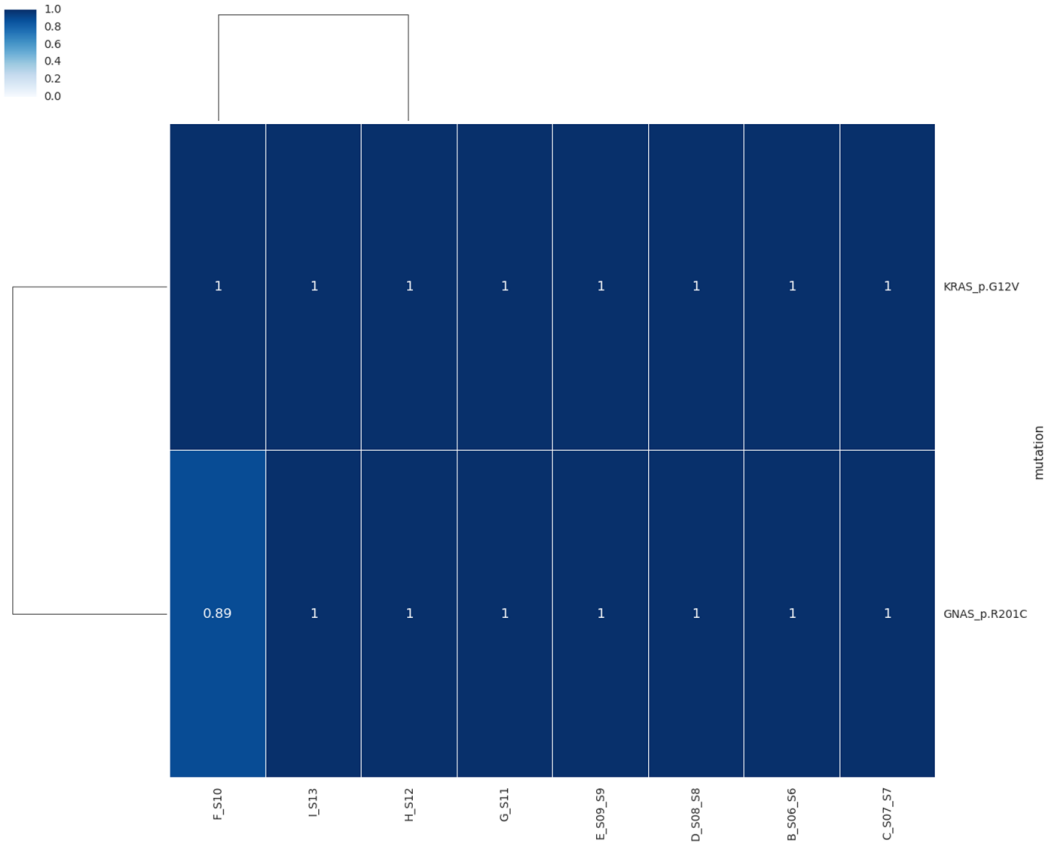
GNAS_p.R201H
Normal
GNAS_p.R201H
KRAS_p.G12R

D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0.4
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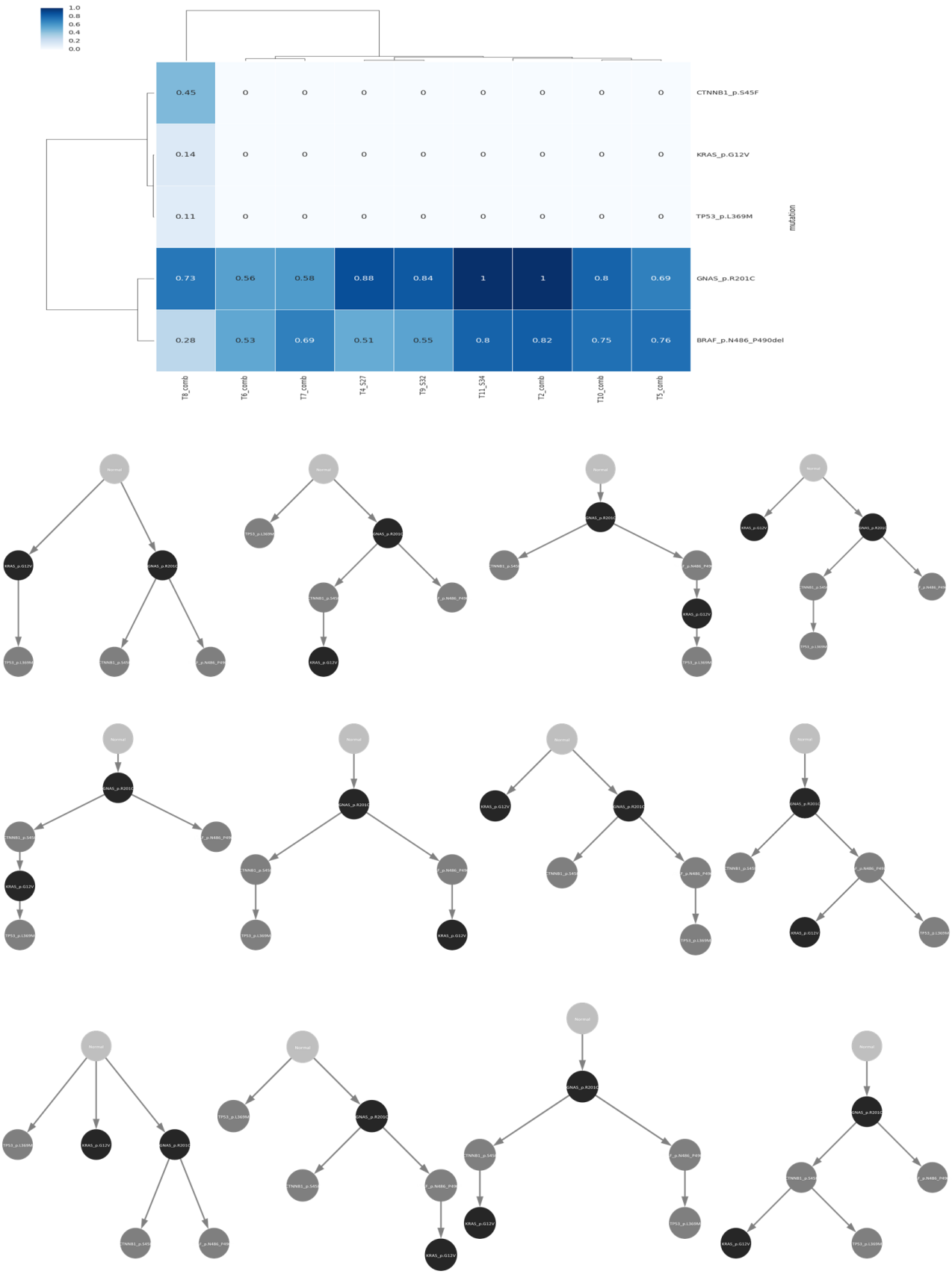
0.0
1
1
1
1
1
1
1
1
KRAS_p.G12V
0.89
1
1
1
1
1
1
1
GNAS_p.R201C
mutation
F_S10
I_S13
H_S12
G_S11
E_S09_S9
D_S08_S8
B_S06_S6
C_S07_S7

Normal
KRAS_p.G12V
GNAS_p.R201C

E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0.0
CTNNB1_p.S45F
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TP53_p.L369M
GNAS_p.R201C
BRAF_p.N486_P490del
mutation
T8_comb
T6_comb
T7_comb
T4_S27
T9_S32
T11_S34
T2_comb
T10_comb
T5_comb
0.45 0 0 0 0 0 0 0 0
0.14 0 0 0 0 0 0 0 0
0.11 0 0 0 0 0 0 0 0
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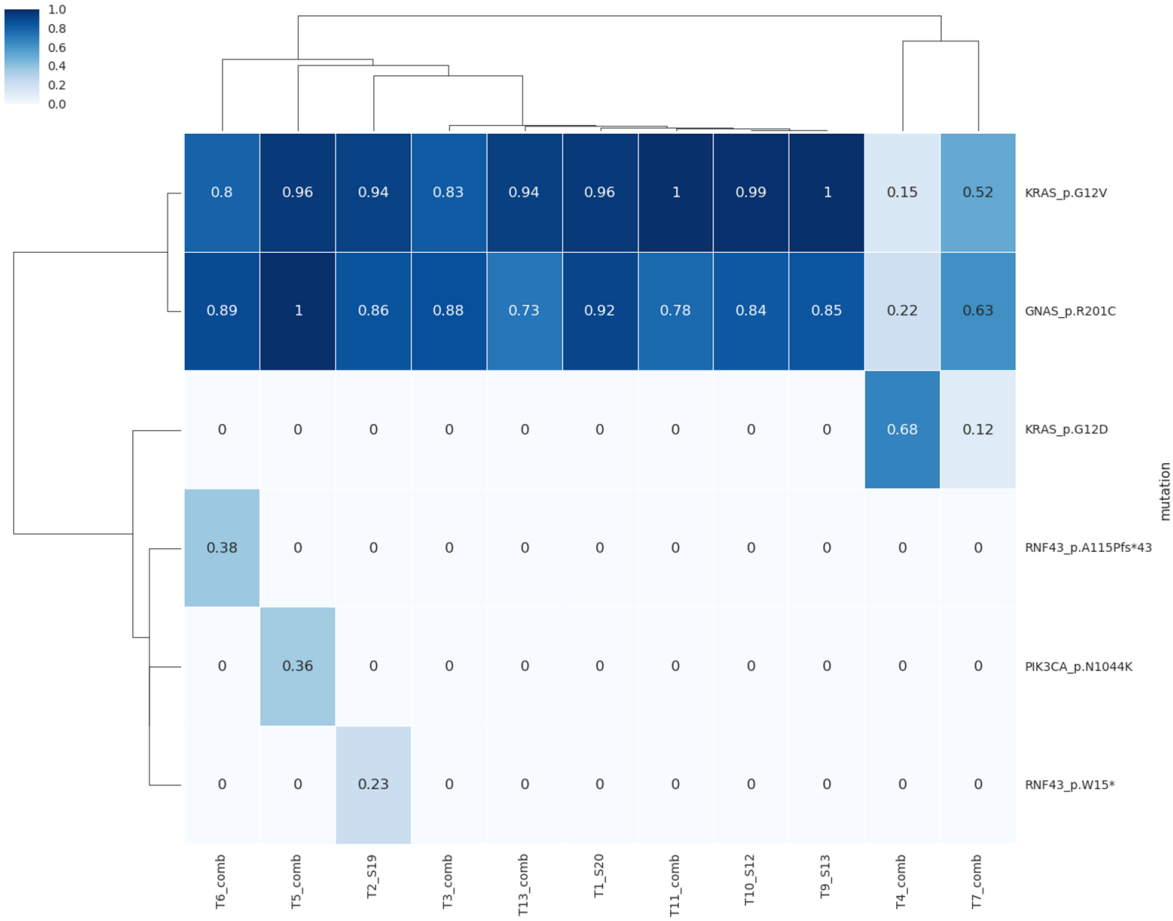
0.28 0.53 0.69 0.51 0.55 0.8 0.82 0.75 0.76
Normal

F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0.6
0.4
0.2
0.0
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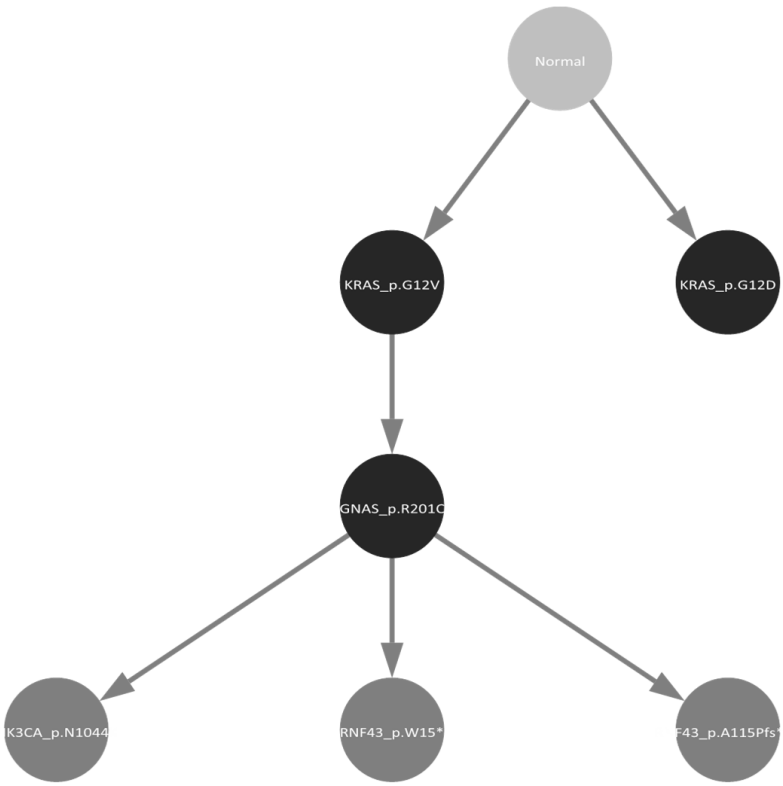
GNAS_p.R201C
KRAS_p.G12D
RNF43_p.A115Pfs*43
PIK3CA_p.N1044K
RNF43_p.W15*
mutation
T6_comb
T5_comb
T2_S19
T3_comb
T13_comb
T1_S20
T11_comb
T10_S12
T9_S13
T4_comb
T7_comb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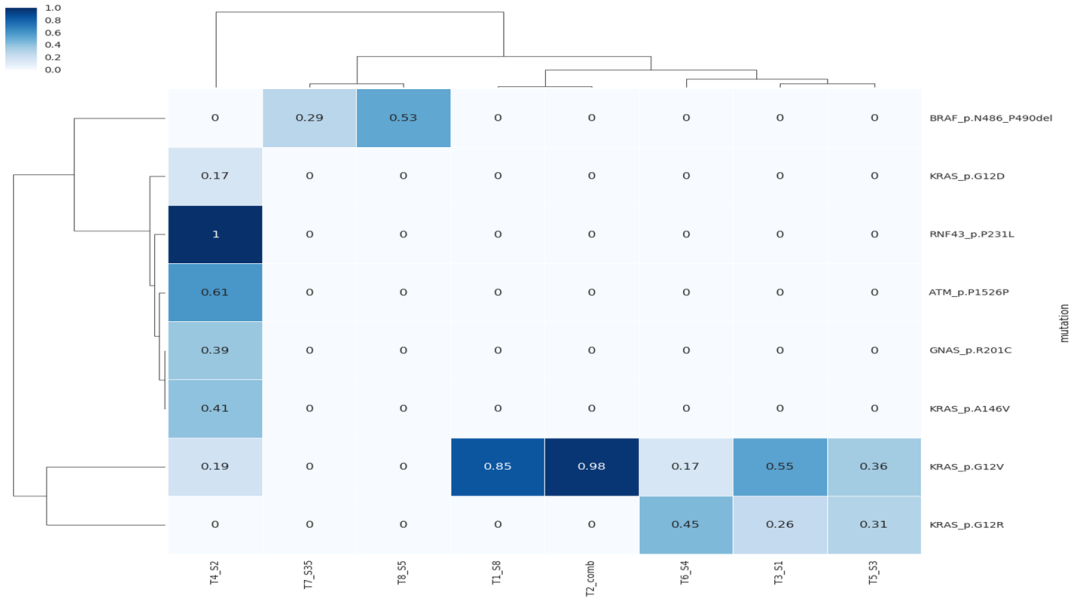
KRAS_p.G12D
GNAS_p.R201C
K3CA_p.N1044
RNF43_p.W15*
F43_p.A115Pfs*

G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0.4
0.2
0.0
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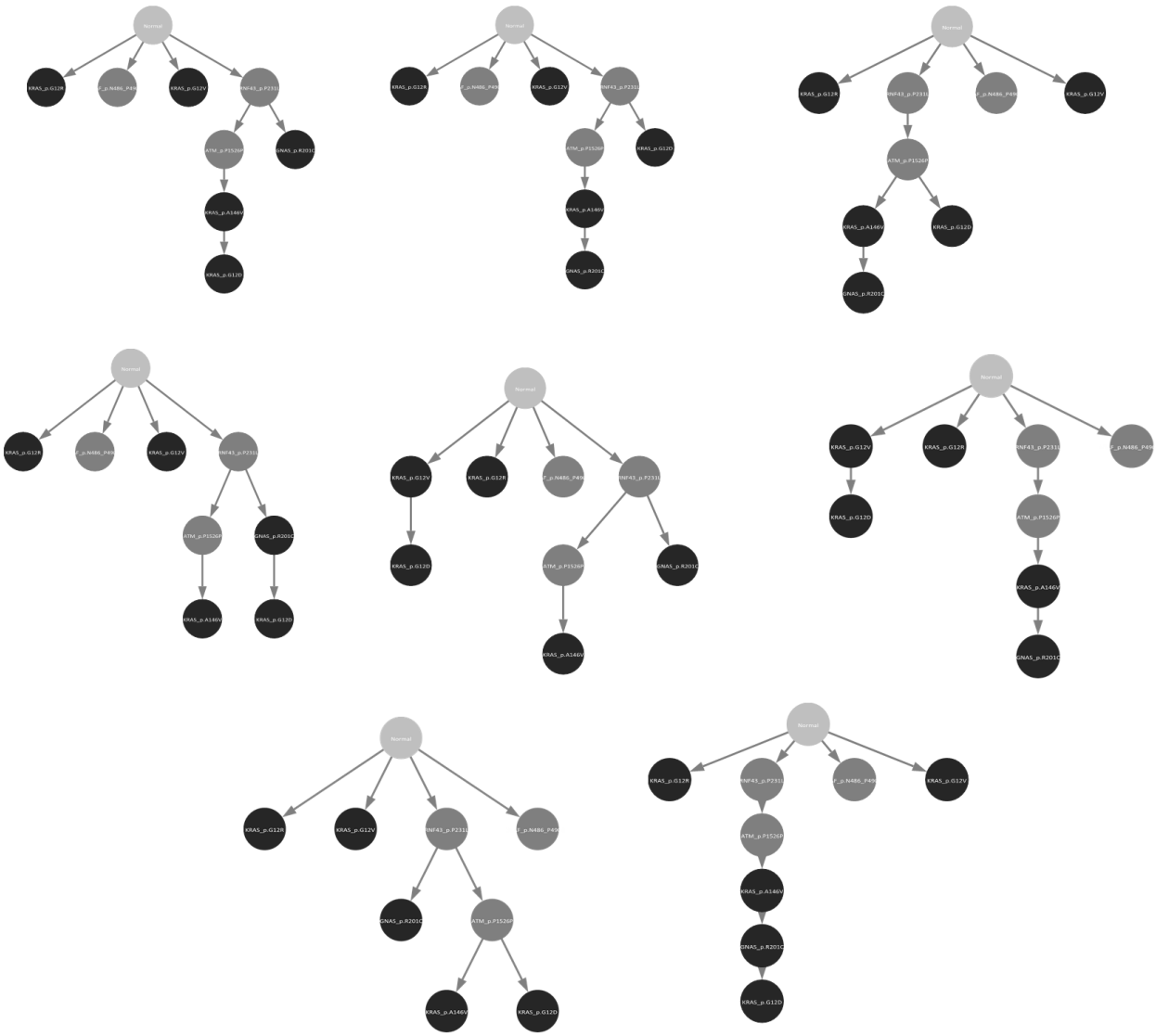
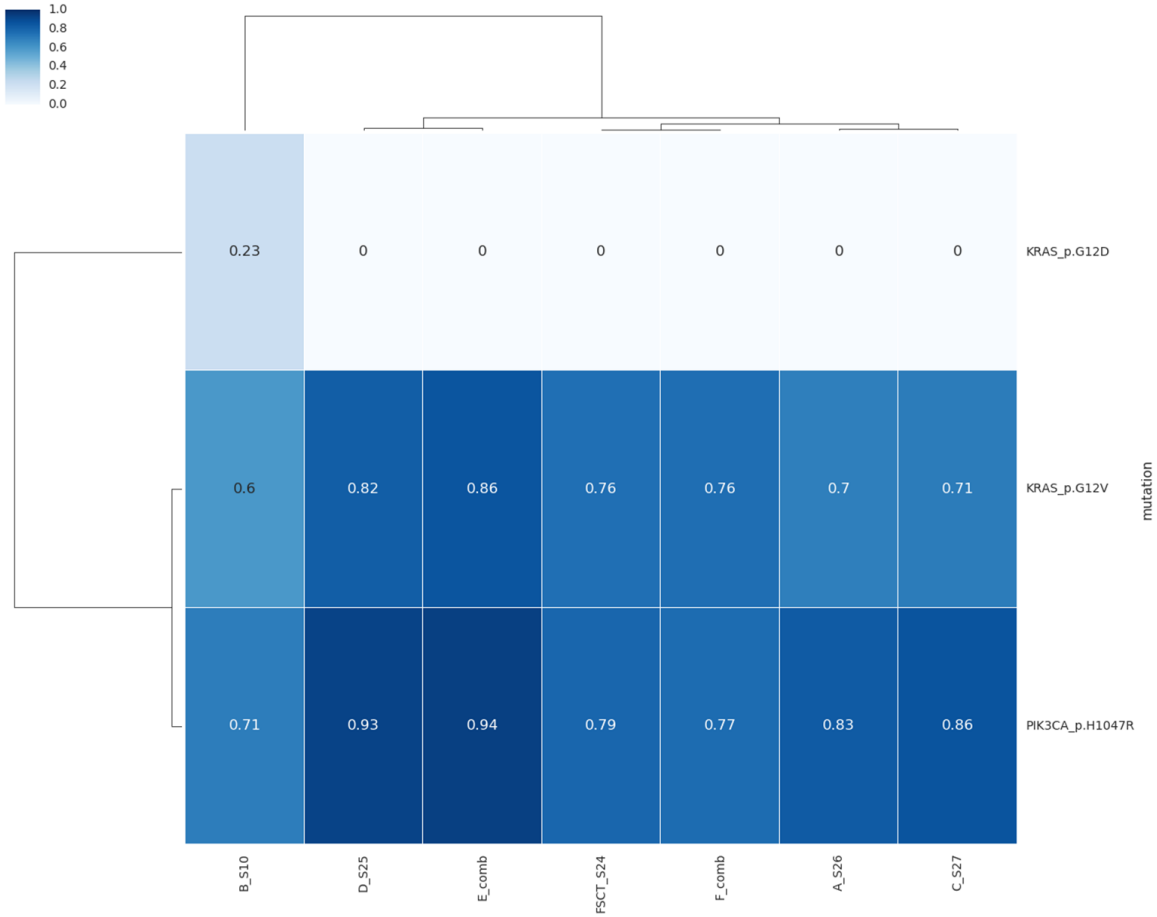
KRAS_p.G12D
RNF43_p.P231L
ATM_p.P1526P
GNAS_p.R201C
KRAS_p.A146V
KRAS_p.G12V
KRAS_p.G12R
mutation
T4_S2
T7_S35
T8_S5
T1_S8
T2_comb
T6_S4
T3_S1
T5_S3



H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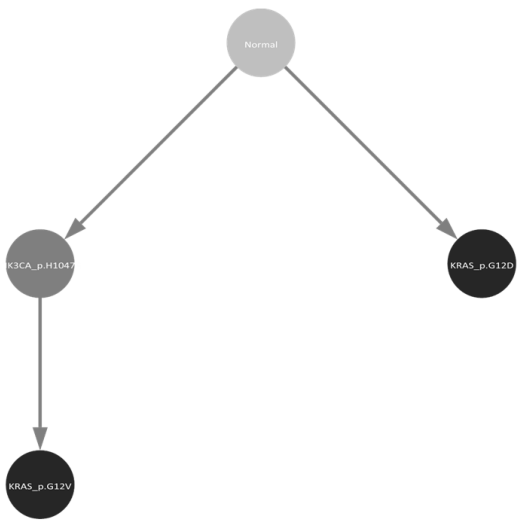
0.6
0.4
0.2
0.0
0.23
0
0
0
0
0
0
KRAS_p.G12D
0.6
0.82
0.86
0.76
0.76
0.7
0.71
KRAS_p.G12V
mutation
0.71
0.93
0.94
0.79
0.77
0.83
0.86
PIK3CA_p.H1047R
B_S10
D_S25
E_comb
FSCT_S24
F_comb
A_S26
C_S27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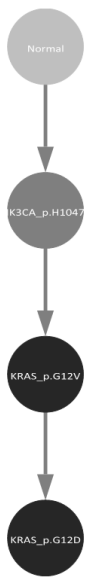
KRAS_p.G12D
KRAS_p.G12V


Normal
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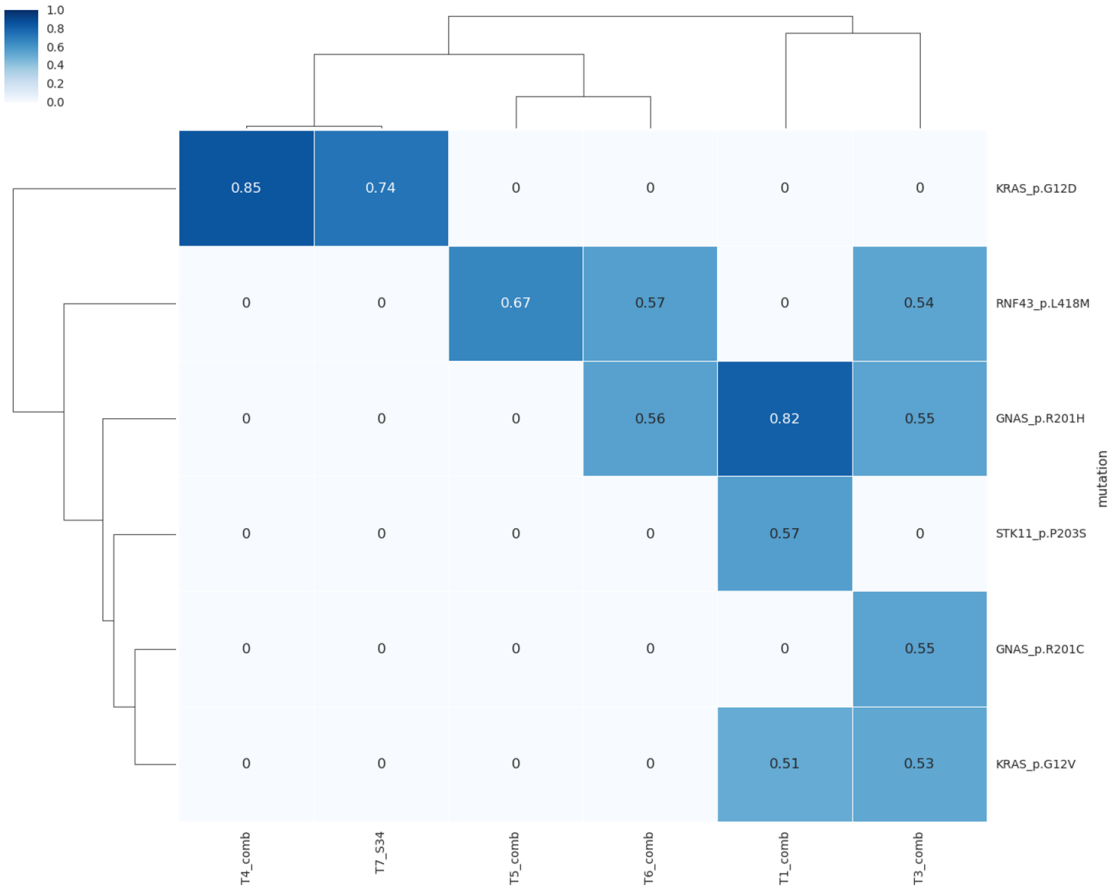
KRAS_p.G12V
KRAS_p.G12D

I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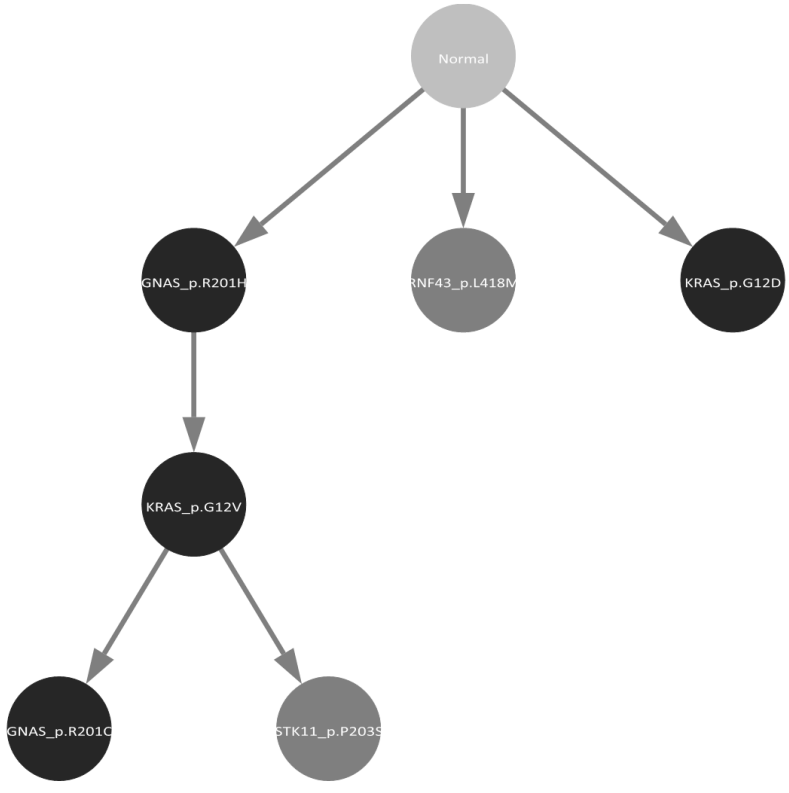
0.4
0.2
0.0
0.85 0.74 0 0 0 0 KRAS_p.G12D
0 0 0.67 0.57 0 0.54 RNF43_p.L418M
0 0 0 0.56 0.82 0.55 GNAS_p.R201H
0 0 0 0 0.57 0 STK11_p.P203S
0 0 0 0 0 0.55 GNAS_p.R201C
0 0 0 0 0.51 0.53 KRAS_p.G12V
mutation
T4_comb
T7_S34
T5_comb
T6_comb
T1_comb
T3_comb


Normal
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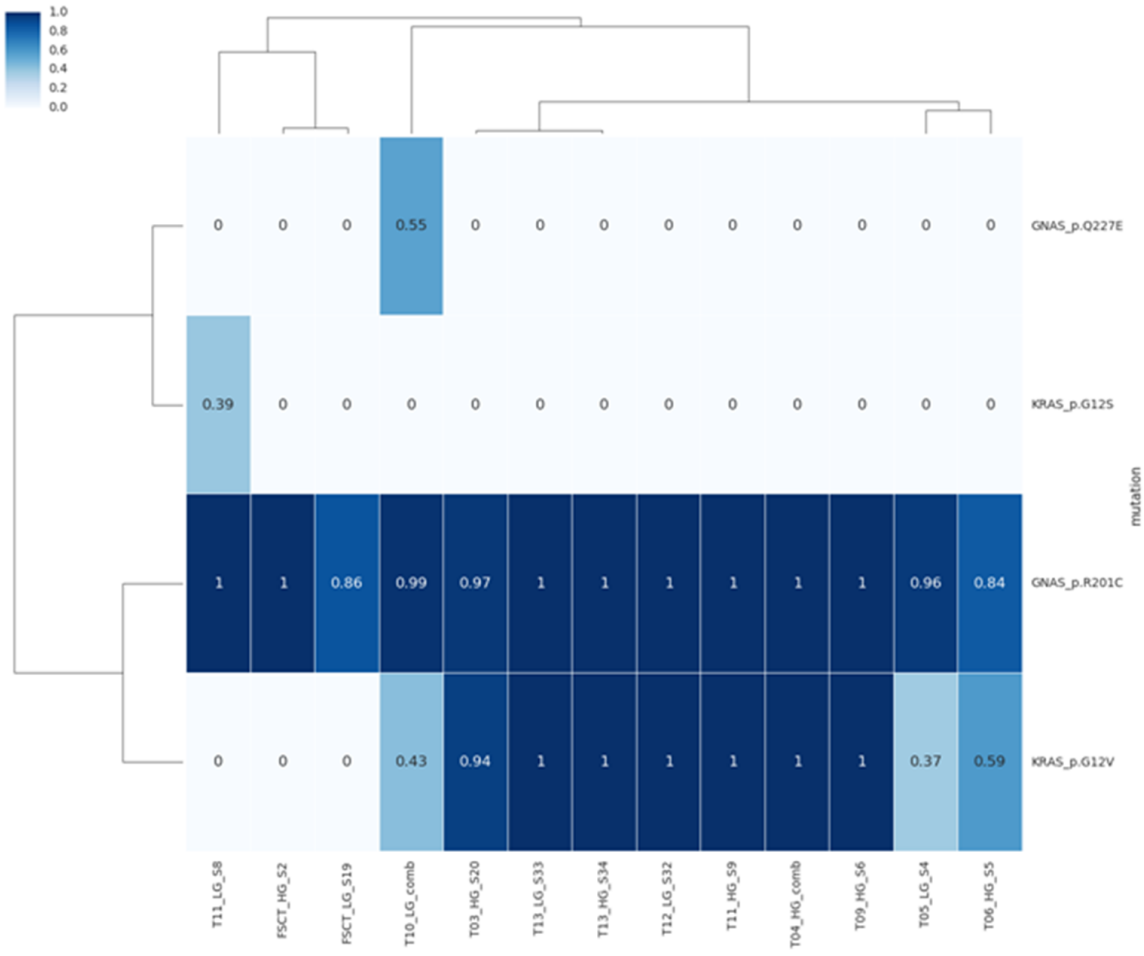
RNF43_p.L418M
KRAS_p.G12D
KRAS_p.G12V
GNAS_p.R201C
STK11_p.P203S

J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0.4
0.2
0.0
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KRAS_p.G12S
GNAS_p.R201C
KRAS_p.G12V
mutation
T11_LG_S8
FSCT_HG_S2
FSCT_LG_S19
T10_LG_comb
T03_HG_S20
T13_LG_S33
T13_HG_S34
T12_LG_S32
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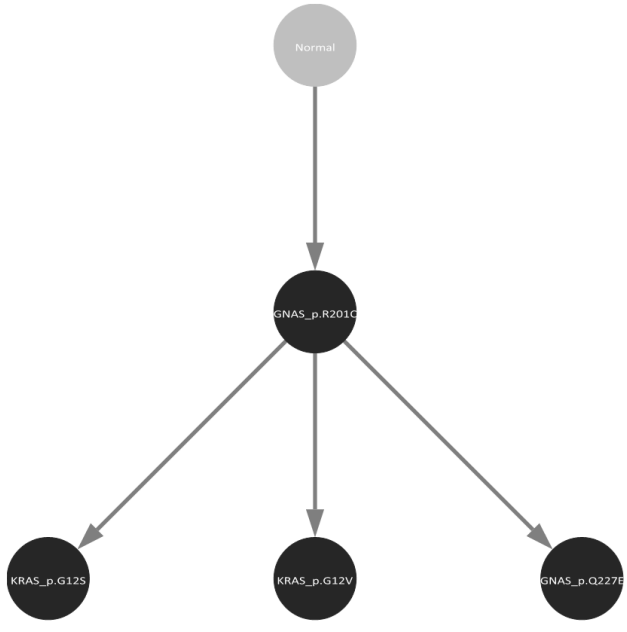
T05_LG_S4
T06_HG_S5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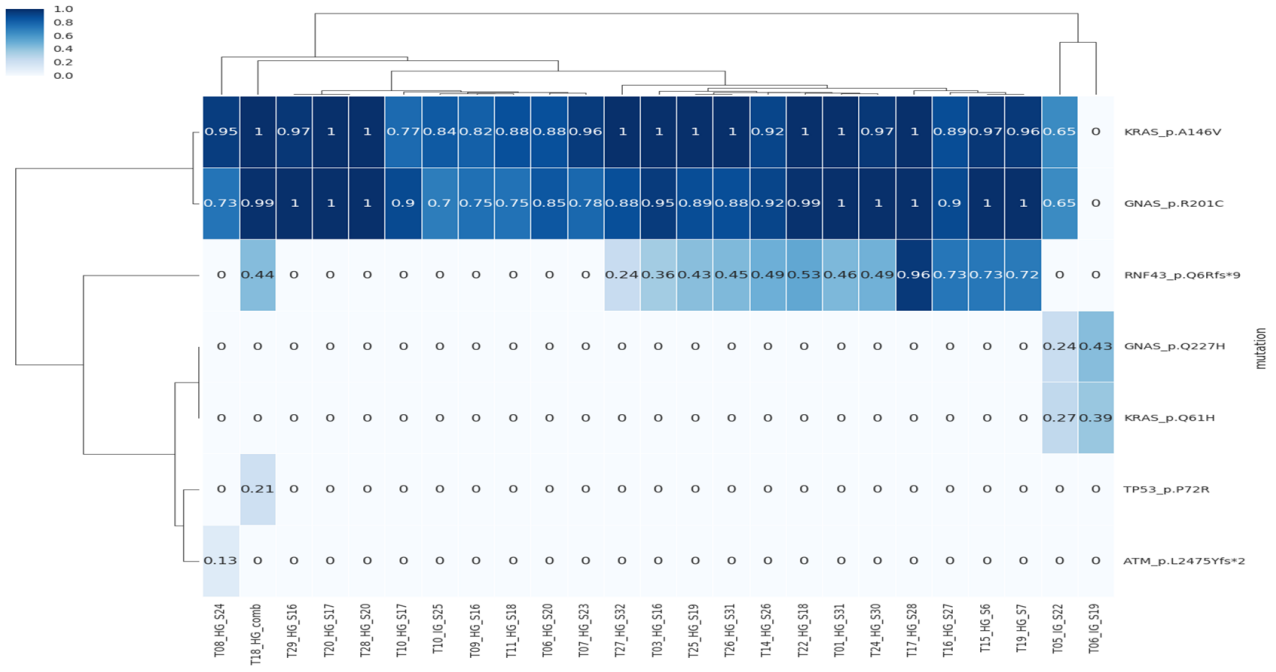
KRAS_p.G12S
KRAS_p.G12V
GNAS_p.Q227E

K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0.0
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GNAS_p.R201C
RNF43_p.Q6Rfs*9
GNAS_p.Q227H
KRAS_p.Q61H
TP53_p.P72R
ATM_p.L2475Yfs*2
mutation
T08_HG_S24
T18_HG_comb
T29_HG_S16
T20_HG_S17
T28_HG_S20
T10_HG_S17
T10_IG_S25
T09_HG_S16
T11_HG_S18
T06_HG_S20
T07_HG_S23
T27_HG_S32
T03_HG_S16
T25_HG_S19
T26_HG_S31
T14_HG_S26
T22_HG_S18
T01_HG_S31
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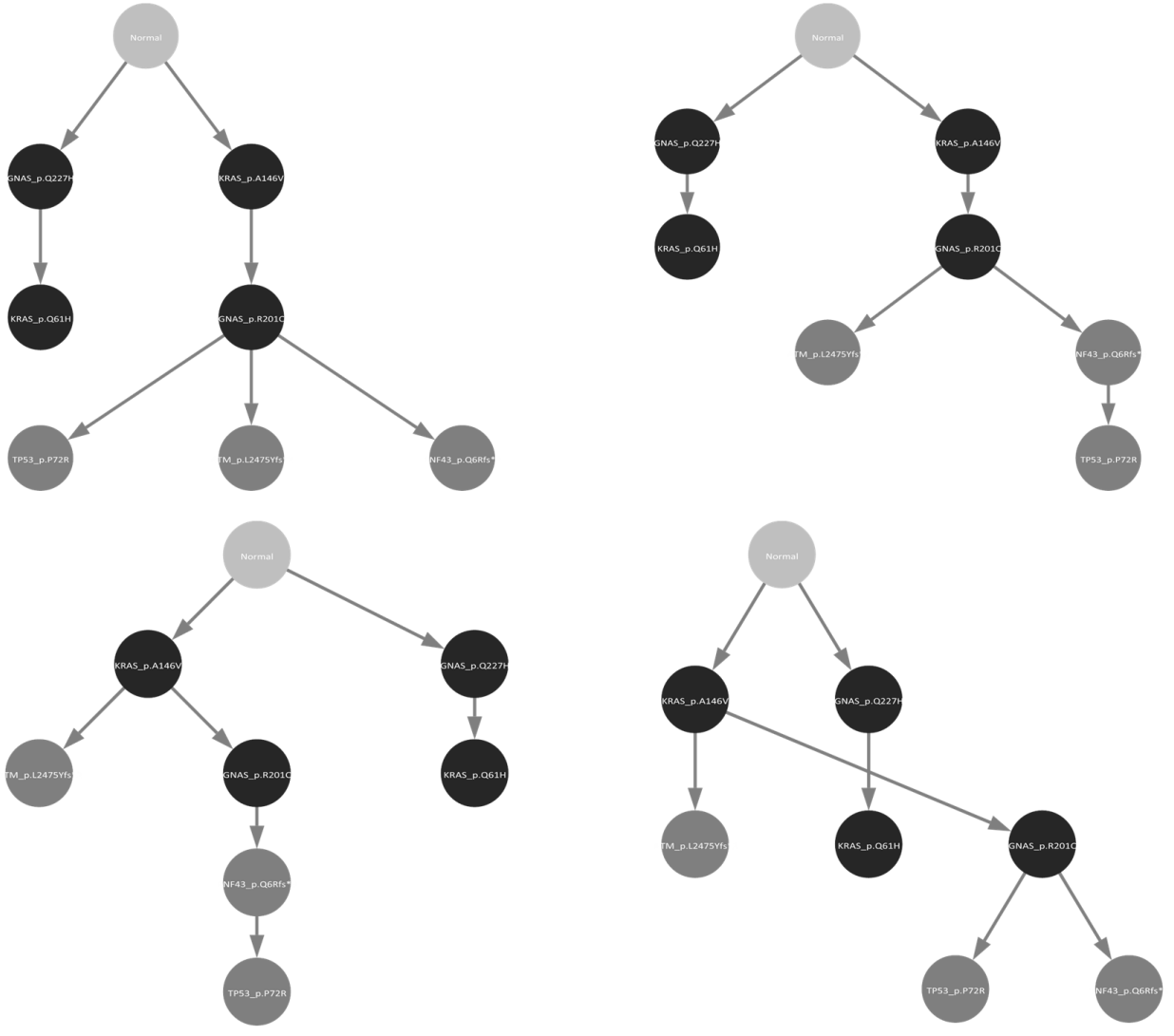
T06_IG_S19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TP53_p.P72R
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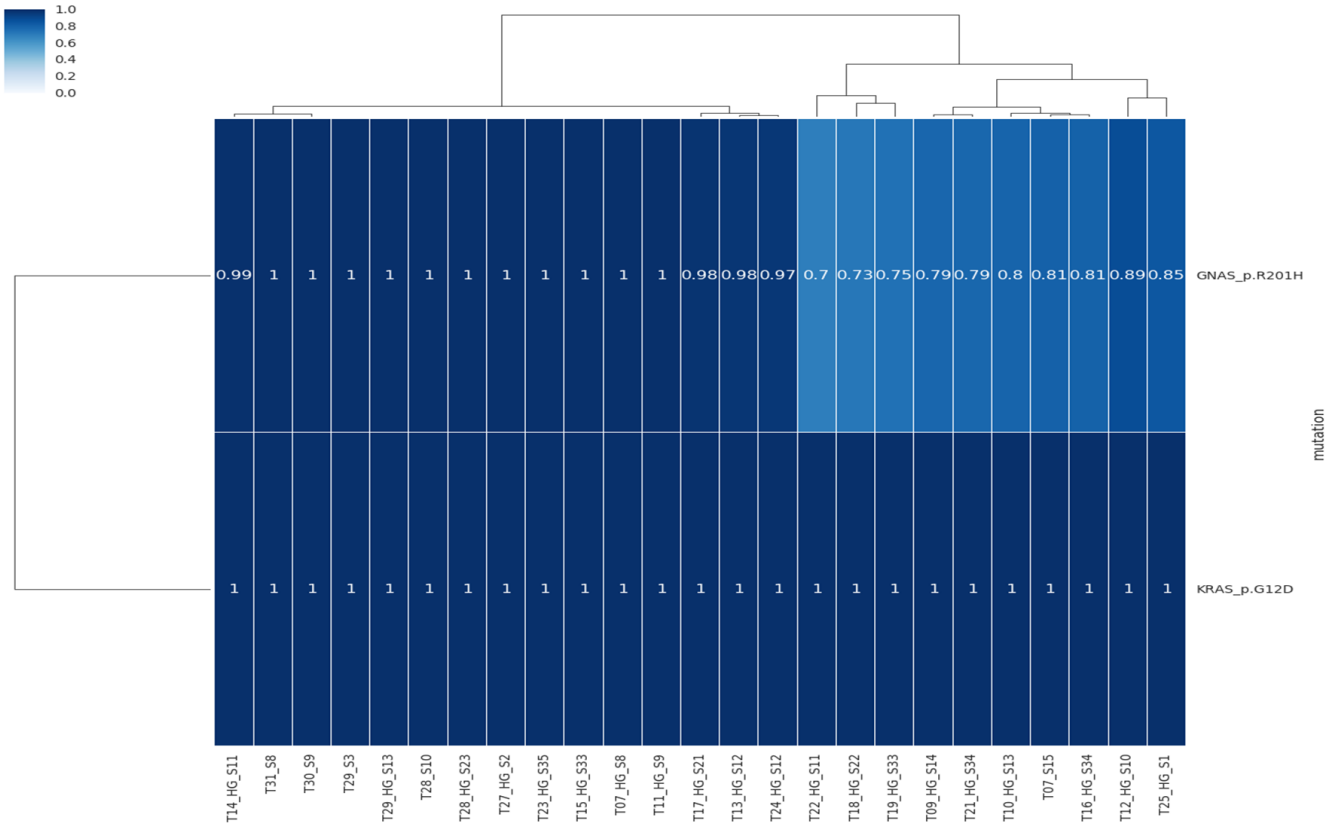
RNF43_p.Q6Rfs*

L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0.0
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GNAS_p.R201H
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
KRAS_p.G12D
mutation
T14_HG_S11
T31_S8
T30_S9
T29_S3
T29_HG_S13
T28_S10
T28_HG_S23
T27_HG_S2
T23_HG_S35
T15_HG_S33
T07_HG_S8
T11_HG_S9
T17_HG_S21
T13_HG_S12
T24_HG_S12
T22_HG_S11
T18_HG_S22
T19_HG_S33
T09_HG_S14
T21_HG_S34
T10_HG_S13
T07_S15
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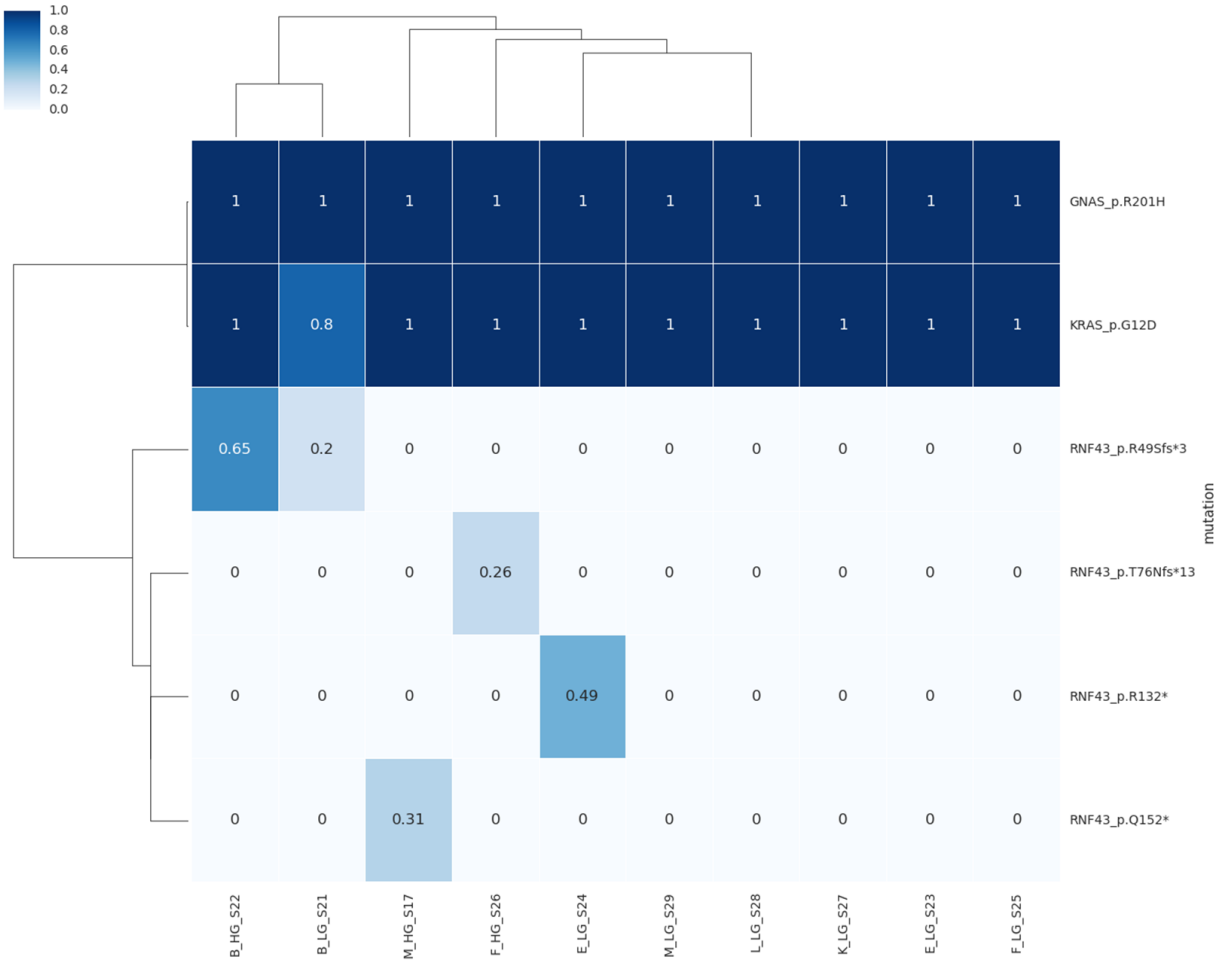
T12_HG_S10
T25_HG_S1

Normal
KRAS_p.G12D
GNAS_p.R201H

M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0.4
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0.0
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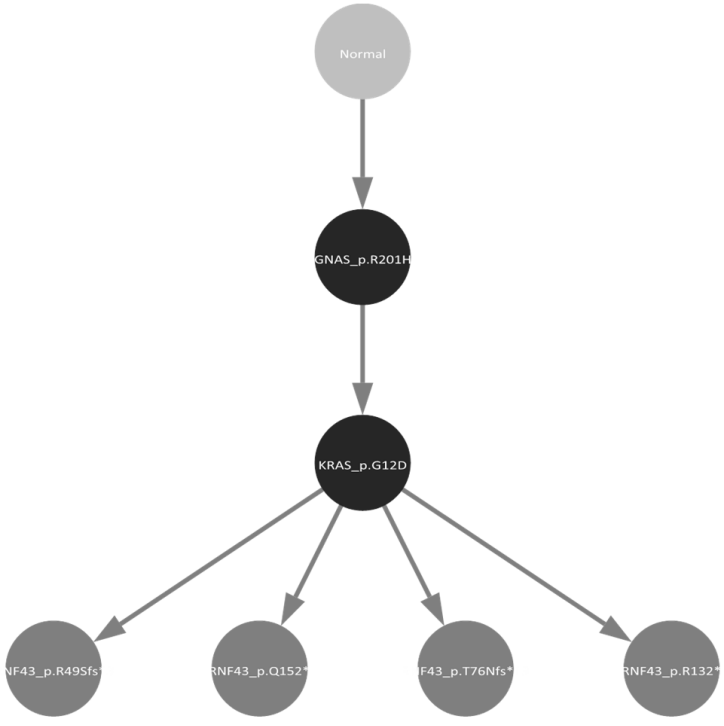
KRAS_p.G12D
RNF43_p.R49Sfs*3
RNF43_p.T76Nfs*13
RNF43_p.R132*
RNF43_p.Q152*
mutation
B_HG_S22
B_LG_S21
M_HG_S17
F_HG_S26
E_LG_S24
M_LG_S29
L_LG_S28
K_LG_S27
E_LG_S23
F_LG_S25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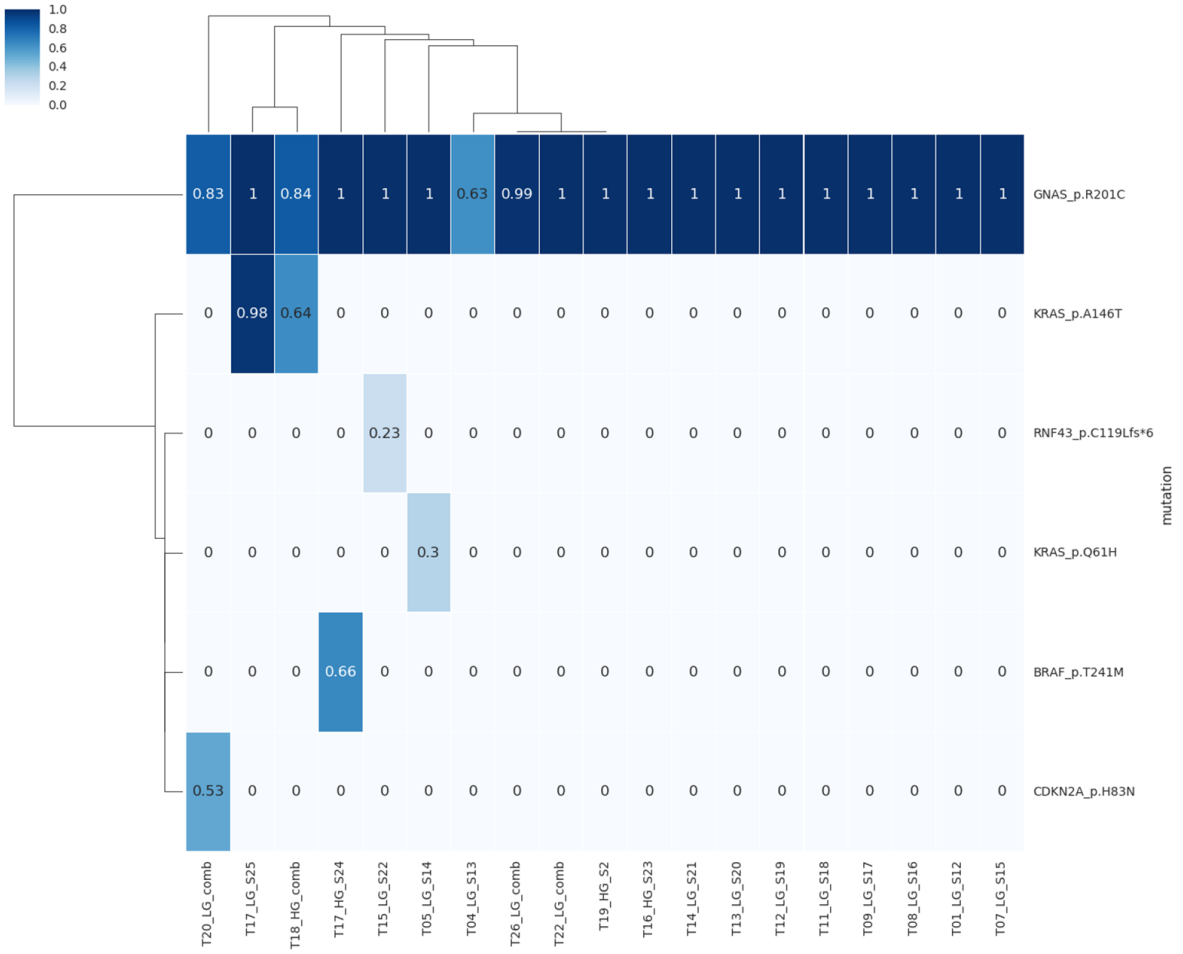
KRAS_p.G12D
NF43_p.R49Sfs*
RNF43_p.Q152*
F43_p.T76Nfs*
RNF43_p.R132*

N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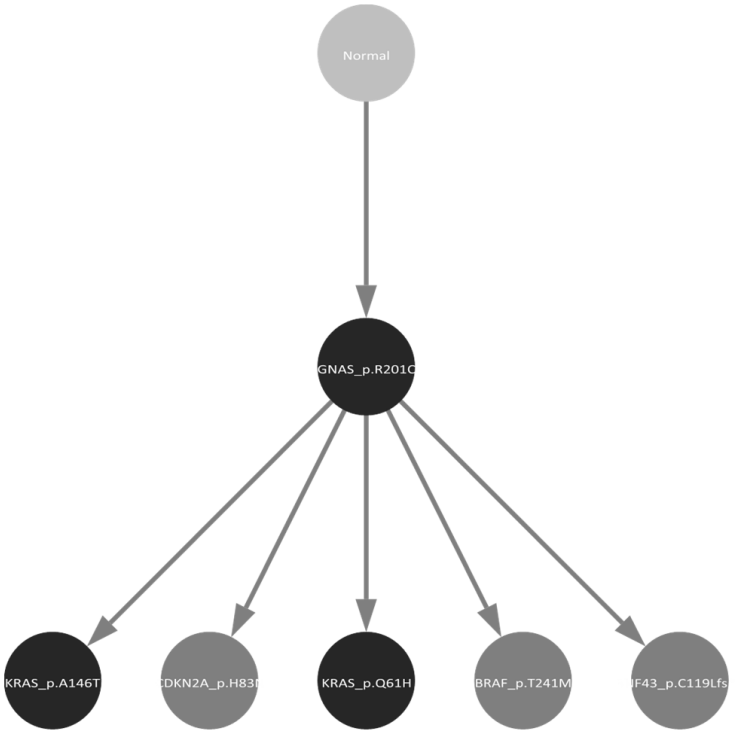
RNF43_p.C119Lfs*6
KRAS_p.Q61H
BRAF_p.T241M
CDKN2A_p.H83N
mutation
T20_LG_comb
T17_LG_S25
T18_HG_comb
T17_HG_S24
T15_LG_S22
T05_LG_S14
T04_LG_S13
T26_LG_comb
T22_LG_comb
T19_HG_S2
T16_HG_S23
T14_LG_S21
T13_LG_S20
T12_LG_S19
T11_LG_S18
T09_LG_S17
T08_LG_S16
T01_LG_S12
T07_LG_S15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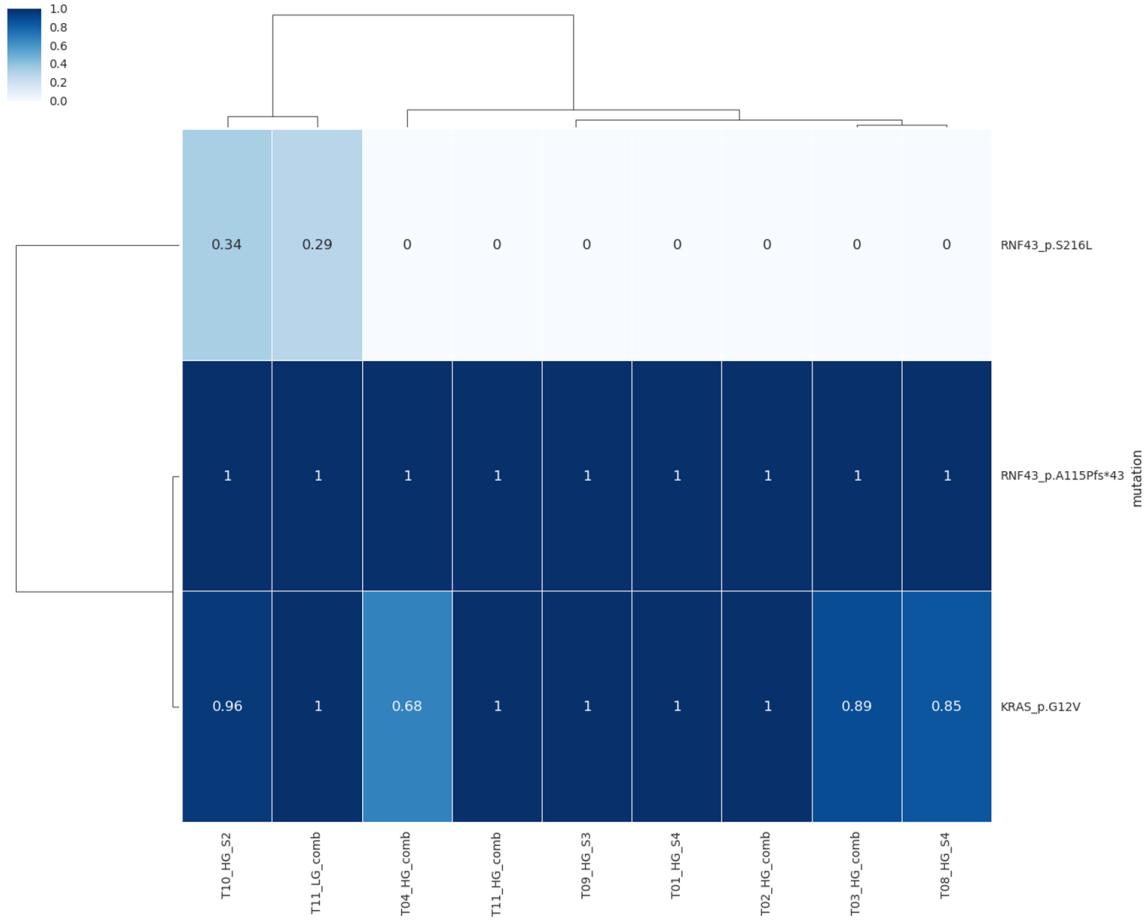
KRAS_p.A146T
KRAS_p.Q61H
BRAF_p.T241M

O



Supplementary Figure S1. Evolutionary tree reconstruction. **A-O**. Mutation neoplastic cell fractions (NCFs) are presented in heatmaps with each row representing a mutation and each column representing a sample. Each NCF heat map corresponds to a schematic of tumor evolution – SCHISM was used to reconstruct somatic mutation hierarchy trees. **A**. IPC01 **B**. IPC02 **C**. IPC04 **D**. IPC05 **E**. IPC06 **F**. IPC07 **G**. IPC08 **H**. IPC09 **I**. IPC10 **J**. IPC11 **K**. IPC12 **L**. IPC13 **M**. IPC16 **N**. IPC17 **O**. IPC18