

Multiple sequence alignments of BTB domains from BTB-ZF, BBK, Skp1, T1-Kv, MATH-BTB and BTB-NPH3 proteins.

These alignments include selected BTB domains from the major LSE's of BTB genes. LSE's were defined as expansions of more than 20 BTB genes from a specific domain architecture class in a specific phylogenetic taxa. The organism abbreviation (Hs = *Homo sapiens*, Mm = *Mus musculus*, Rn = *Rattus norvegicus*, Fr = *Fugu rubripes*, Dr = *Danio rerio*, Dm = *Drosophila melanogaster*, Ag = *Anopheles gambiae*, Ce = *Caenorhabditis elegans*, At = *Arabidopsis thaliana*, Sc = *Saccharomyces cerevisiae*, Sp = *Schizosaccharomyces pombe*), common protein name and Uniprot identifiers for each protein are indicated. The BTB domain region (with or without N- or C-terminal extensions) of the full-length protein is boxed. Black shading indicates residues that are 90% identical; grey shading with white text indicates 75% identity; light grey shading with black text indicates 50% identity. Residues that are known (in the BTB-ZF, Skp1, T1 families) or predicted (in the BBK, MATH-BTB, BTB-NPH3 families) to be buried in each structure are indicated by black circles: a filled black circle indicates 100% similarity and a half-filled black circle indicates 75% similarity across the family. The grid below each alignment shows the known or putative involvement of each residue in protein-protein interactions: known dimerization contacts from BTB-ZF structures (blue); known tetramerization contacts from the T1 structure from Kv1.1 (red); cullin-contacting residues inferred by analogy from the Skp1-Cul1 structures (dark green); F-box-

contacting residues in Skp1 (light green). Consensus secondary structure predictions by PHD are shown below the alignments.

A: Multiple sequence alignment of BTB domains from BTB-ZF proteins. The N-terminal methionine is indicated in bold.

B: Multiple sequence alignment of BTB domains from BBK proteins. The N-terminal methionine is indicated in bold, and BACK domain residues are shaded green.

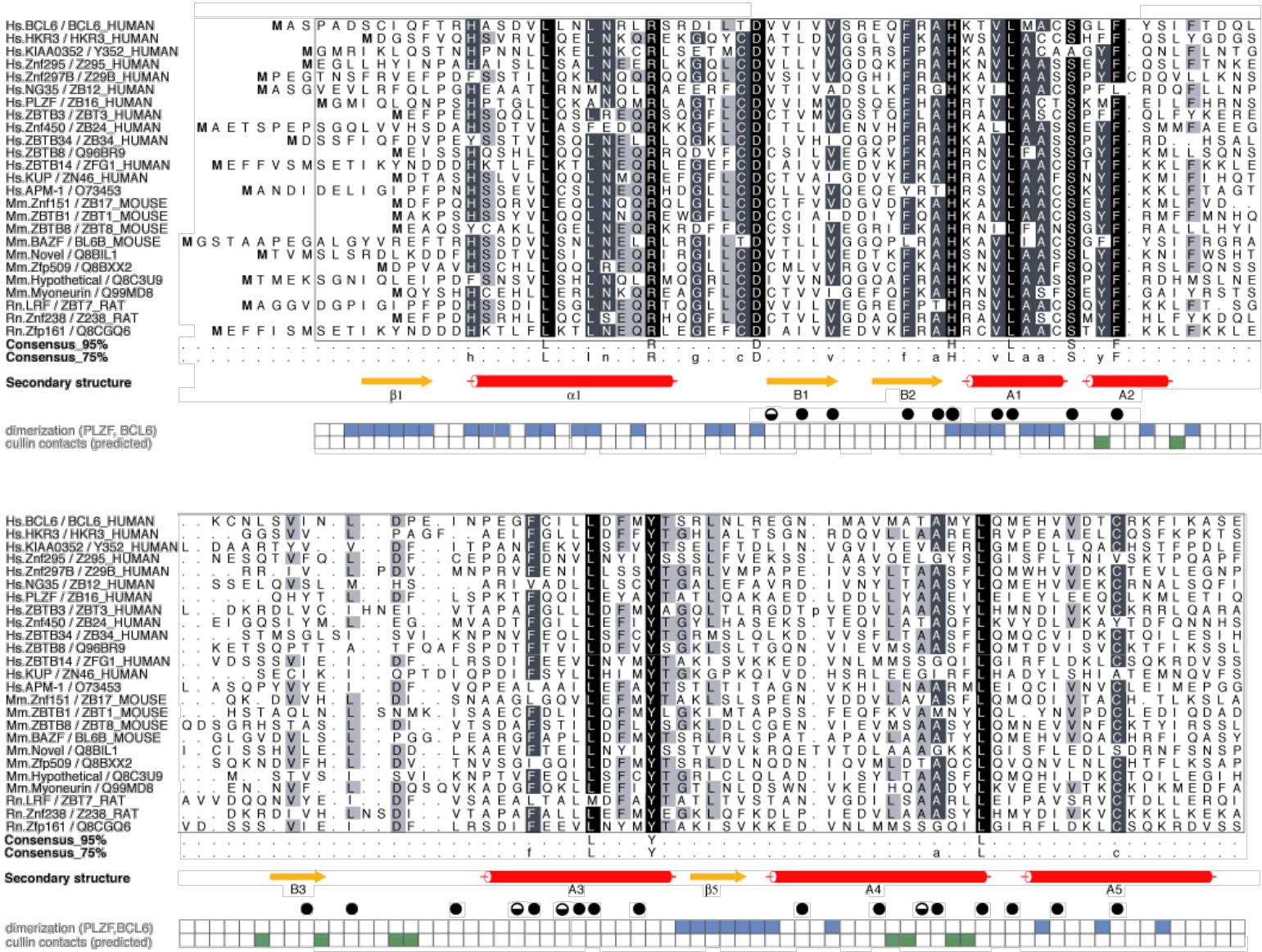
C: Multiple sequence alignment of Skp1 proteins. The N-terminal methionine is bold type, the C-terminal residue is italicized. Note that the secondary structure naming differs from other BTB domains because Skp1 lacks the N-terminal extension to the core BTB fold. Triangles indicate insertions of 27 and 30 residues in CB34_YEAST and O77430, respectively.

D: Multiple sequence alignment of T1 domains. The N-terminal methionine is bold type, and the region immediately trailing the BTB domain and the transmembrane (TM) domain (shaded purple) is indicated. Note that the secondary structure naming differs from other BTB domains as T1 lacks the N-terminal extension to the core BTB fold.

E: Multiple sequence alignment of BTB domains from MATH-BTB proteins. The MATH domain is shaded cyan, consensus predicted secondary structure C-terminal to the BTB domain is shown in pink, and C-terminal residues are italicized.

F: Multiple sequence alignment of BTB domains from BTB-NPH3 proteins. The N-terminal methionine is bold type, and the linker (with two predicted helices and a poorly conserved region) and NPH3 regions are shown.

A. BTB domains from BTB-ZF proteins

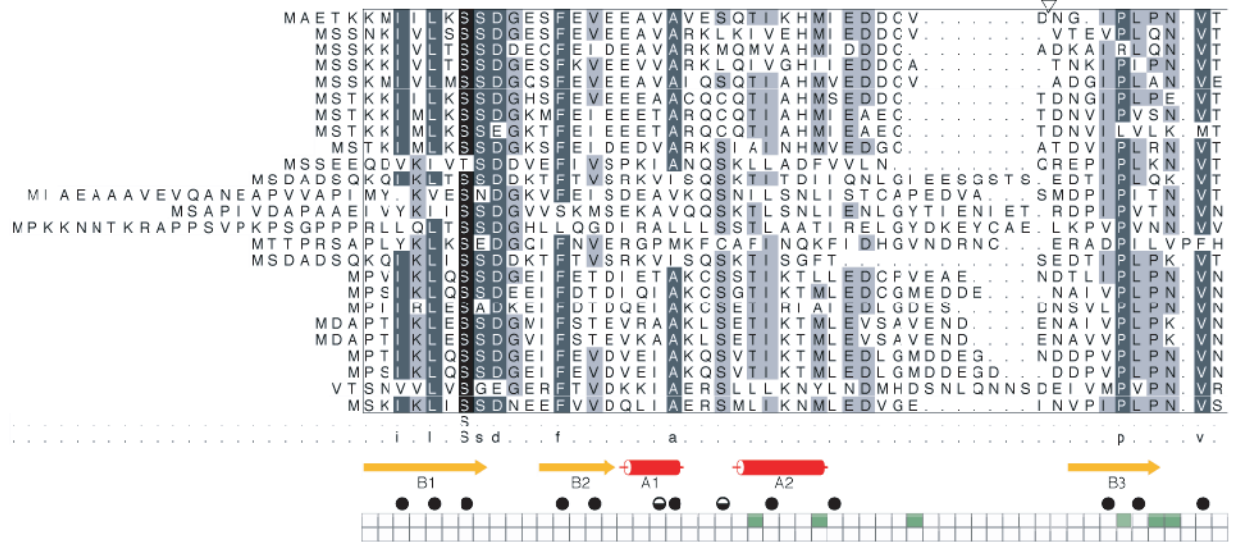


C. Skp1 proteins

At.A13_putative / Q9SL93
At.A14_putative / Q81057
At.A17_putative / Q9SL65
At.A19_putative / Q81058
At.Skp1-like / Q49484
At.Skp1-like / Q9LSX8
At.Skp1-like / Q9LSY0
At.Skp1-like / Q9LSY1
At.Skp1-like / Q9M1X4
Ce.F47H4.10 / Q9XU27
Ce.SKR-3 / Q45517
Ce.SKR-8 / Q966N8
Ce.SKR-12 / Q22871
Ce.SKR-17 / Q17696
Ce.SKR-20 / Q21969
Ce.Y60A3A.18 / Q9U1Y9
Dm.CG12227-PA / Q9W1Q0
Dm.SkpA / Q77430
Dm.SkpB / Q9V360
Dm.SkpC / Q9VWC4
Dm.SkpD / Q9VWC5
Mm.Skp1a / Q8C5H6
Hs.Skp1 / SKP1_HUMAN
Sc.Skp1 / CB34_YEAST
Sp.Skp1 / Q9Y709
Consensus_75%
Consensus_95%

Secondary structure

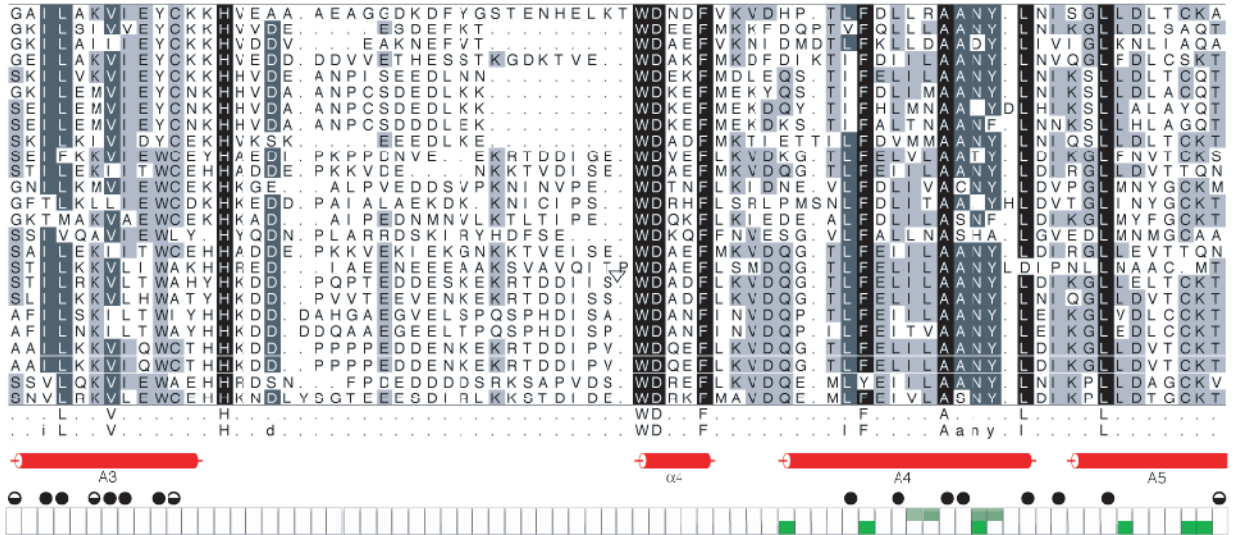
cullin contacts
f-box contacts



At.A13_putative / Q9SL93
At.A14_putative / Q81057
At.A17_putative / Q9SL65
At.A19_putative / Q81058
At.Skp1-like / Q49484
At.Skp1-like / Q9LSX8
At.Skp1-like / Q9LSY0
At.Skp1-like / Q9LSY1
At.Skp1-like / Q9M1X4
Ce.F47H4.10 / Q9XU27
Ce.SKR-3 / Q45517
Ce.SKR-8 / Q966N8
Ce.SKR-12 / Q22871
Ce.SKR-17 / Q17696
Ce.SKR-20 / Q21969
Ce.Y60A3A.18 / Q9U1Y9
Dm.CG12227-PA / Q9W1Q0
Dm.SkpA / Q77430
Dm.SkpB / Q9V360
Dm.SkpC / Q9VWC4
Dm.SkpD / Q9VWC5
Hs.Skp1 / SKP1_HUMAN
Mm.Skp1a / Q8C5H6
Sc.Skp1 / CB34_YEAST
Sp.Skp1 / Q9Y709
Consensus_75%
Consensus_95%

Secondary structure

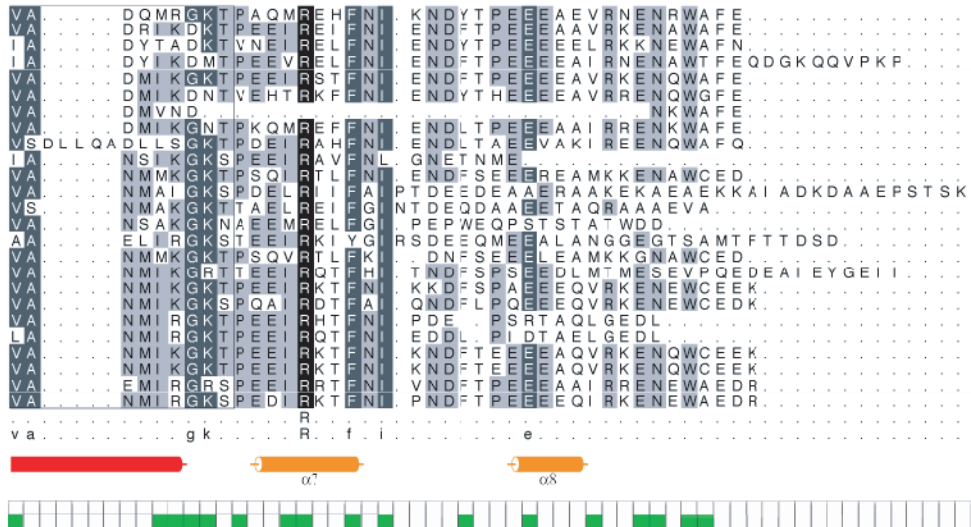
cullin contacts
f-box contacts



At.A13_putative / Q9SL93
At.A14_putative / Q81057
At.A17_putative / Q9SL65
At.A19_putative / Q81058
At.Skp1-like / Q49484
At.Skp1-like / Q9LSX8
At.Skp1-like / Q9LSY0
At.Skp1-like / Q9LSY1
At.Skp1-like / Q9M1X4
Ce.F47H4.10 / Q9XU27
Ce.SKR-3 / Q45517
Ce.SKR-8 / Q966N8
Ce.SKR-12 / Q22871
Ce.SKR-17 / Q17696
Ce.SKR-20 / Q21969
Ce.Y60A3A.18 / Q9U1Y9
Dm.CG12227-PA / Q9W1Q0
Dm.SkpA / Q77430
Dm.SkpB / Q9V360
Dm.SkpC / Q9VWC4
Dm.SkpD / Q9VWC5
Mm.Skp1a / Q8C5H6
Hs.Skp1 / SKP1_HUMAN
Sc.Skp1 / CB34_YEAST
Sp.Skp1 / Q9Y709
Consensus_75%
Consensus_95%

Secondary structure

cullin contacts
f-box contacts



D. T1 domains from T1-Kv proteins

HsKv1.3 / CIK3_HUMAN
HsKv2.1 / KCB1_HUMAN
HsKv2.2 / KCB2_HUMAN
HsKv6.1 / KCG1_HUMAN
HsKv6.2 / KCG2_HUMAN
HsKv9.1 / KCS_HUMAN
HsKv9.2 / KCS2_HUMAN
HsKv9.3 / KCS3_HUMAN
MmKv1.4 / CIK4_MOUSE
MmKv9.1 / KCS1_MOUSE
RnKv1.1 / CIK1_RAT
RnKv1.2 / CIK2_RAT
RnKv1.3 / CIK3_RAT
RnKv1.5 / CIK5_RAT
RnKv1.6 / CIK6_RAT
DmShaker / CIKS_DROME
DmShab / CIKB_DROME
DmShal / CIKL_DROME
DrLeftover / Q80A04
DrShal / Q7ZW36
AgAgCP13550 / Q7QFG9
AgEbiP7629 / Q7QIS7
CeT05E12.3 / Q8XUR6
CeY73B6BL19 / Q95XD1
AtT16O11.1 / Q9S7R7
Consensus 95%
Consensus 75%

Secondary structure

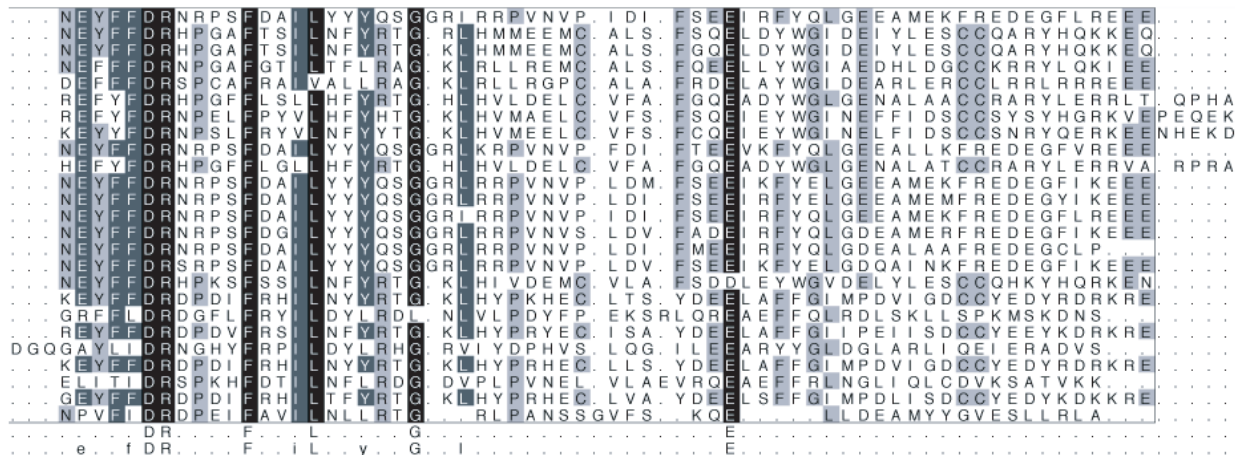
tetramerization contacts (Kv1.1)
cullin contacts (predicted)



HsKv1.3 / CIK3_HUMAN
HsKv2.1 / KCB1_HUMAN
HsKv2.2 / KCB2_HUMAN
HsKv6.1 / KCG1_HUMAN
HsKv6.2 / KCG2_HUMAN
HsKv9.1 / KCS_HUMAN
HsKv9.2 / KCS2_HUMAN
HsKv9.3 / KCS3_HUMAN
MmKv1.4 / CIK4_MOUSE
MmKv9.1 / KCS1_MOUSE
RnKv1.1 / CIK1_RAT
RnKv1.2 / CIK2_RAT
RnKv1.3 / CIK3_RAT
RnKv1.5 / CIK5_RAT
RnKv1.6 / CIK6_RAT
DmShaker / CIKS_DROME
DmShab / CIKB_DROME
DmShal / CIKL_DROME
DrLeftover / Q80A04
DrShal / Q7ZW36
AgAgCP13550 / Q7QFG9
AgEbiP7629 / Q7QIS7
CeT05E12.3 / Q8XUR6
CeY73B6BL19 / Q95XD1
AtT16O11.1 / Q9S7R7
Consensus 95%
Consensus 75%

Secondary structure

tetramerization contacts (Kv1.1)
cullin contacts (predicted)



HsKv1.3 / CIK3_HUMAN
HsKv2.1 / KCB1_HUMAN
HsKv2.2 / KCB2_HUMAN
HsKv6.1 / KCG1_HUMAN
HsKv6.2 / KCG2_HUMAN
HsKv9.1 / KCS_HUMAN
HsKv9.2 / KCS2_HUMAN
HsKv9.3 / KCS3_HUMAN
MmKv1.4 / CIK4_MOUSE
MmKv9.1 / KCS1_MOUSE
RnKv1.1 / CIK1_RAT
RnKv1.2 / CIK2_RAT
RnKv1.3 / CIK3_RAT
RnKv1.5 / CIK5_RAT
RnKv1.6 / CIK6_RAT
DmShaker / CIKS_DROME
DmShab / CIKB_DROME
DmShal / CIKL_DROME
DrLeftover / Q80A04
DrShal / Q7ZW36
AgAgCP13550 / Q7QFG9
AgEbiP7629 / Q7QIS7
CeT05E12.3 / Q8XUR6
CeY73B6BL19 / Q95XD1
AtT16O11.1 / Q9S7R7
Consensus 95%
Consensus 75%

Secondary structure



Transmembrane



F. BTB domains from BTB-NPH3 proteins

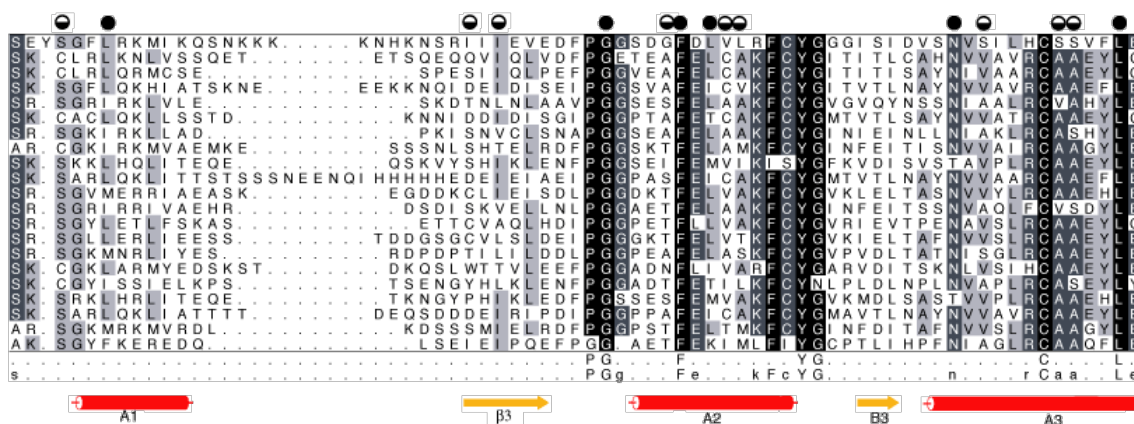
ALAAD50054.1 / Q9LT24
 ALAAF16571.1 / Q9LIM6
 ALA11g67900 / Q9C9V6
 ALA12g23050 / Q64814
 ALA12g47860 / Q82253
 ALA12g4820 / Q80970
 ALA1003.17 / Q9SA69
 ALA17014.4 / Q9C9Z7
 ALA18B3.120 / Q9SVL5
 ALA19F18.80 / Q9SZF2
 ALA26G16.2 / Q9S9C9
 ALNPH-like / Q9FKB6
 ALNPH-like / Q9FNB3
 ALNPH-like / Q9LYW0
 ALNPH3 / Q9FMF5
 ALNPH3-like / Q9FYC8
 ALNPH3-like / Q9LFU0
 ALPhotoreceptor-int. like / Q9FJY3
 ALPhotoreceptor-int. like / Q9FN09
 ALPutative_NPH / Q9C9Z0
 ALSim_to_bZip / Q9LUB9
 Consensus_95%
 Consensus_75%

Secondary structure (predicted)



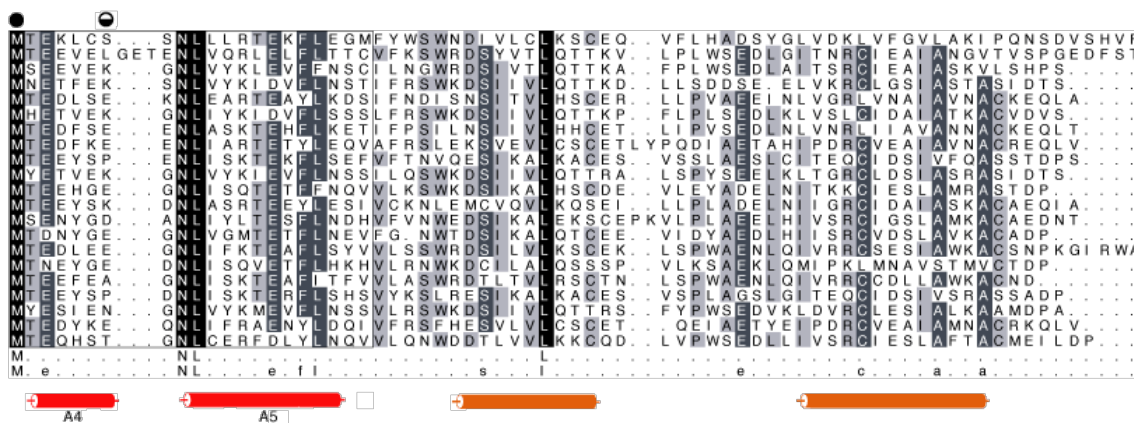
ALAAD50054.1 / Q9LT24
 ALAAF16571.1 / Q9LIM6
 ALA11g67900 / Q9C9V6
 ALA12g23050 / Q64814
 ALA12g47860 / Q82253
 ALA12g4820 / Q80970
 ALA1003.17 / Q9SA69
 ALA17014.4 / Q9C9Z7
 ALA18B3.120 / Q9SVL5
 ALA19F18.80 / Q9SZF2
 ALA26G16.2 / Q9S9C9
 ALNPH-like / Q9FKB6
 ALNPH-like / Q9FNB3
 ALNPH-like / Q9LYW0
 ALNPH3 / Q9FMF5
 ALNPH3-like / Q9FYC8
 ALNPH3-like / Q9LFU0
 ALPhotoreceptor-int. like / Q9FJY3
 ALPhotoreceptor-int. like / Q9FN09
 ALPutative_NPH / Q9C9Z0
 ALSim_to_bZip / Q9LUB9
 Consensus_95%
 Consensus_75%

Secondary structure (predicted)



ALAAD50054.1 / Q9LT24
 ALAAF16571.1 / Q9LIM6
 ALA11g67900 / Q9C9V6
 ALA12g23050 / Q64814
 ALA12g47860 / Q82253
 ALA12g4820 / Q80970
 ALA1003.17 / Q9SA69
 ALA17014.4 / Q9C9Z7
 ALA18B3.120 / Q9SVL5
 ALA19F18.80 / Q9SZF2
 ALA26G16.2 / Q9S9C9
 ALNPH-like / Q9FKB6
 ALNPH-like / Q9FNB3
 ALNPH-like / Q9LYW0
 ALNPH3 / Q9FMF5
 ALNPH3-like / Q9FYC8
 ALNPH3-like / Q9LFU0
 ALPhotoreceptor-int. like / Q9FJY3
 ALPhotoreceptor-int. like / Q9FN09
 ALPutative_NPH / Q9C9Z0
 ALSim_to_bZip / Q9LUB9
 Consensus_95%
 Consensus_75%

Secondary structure (predicted)



ALAAD50054.1 / Q9LT24
 ALAAF16571.1 / Q9LIM6
 ALA11g67900 / Q9C9V6
 ALA12g23050 / Q64814
 ALA12g47860 / Q82253
 ALA12g4820 / Q80970
 ALA1003.17 / Q9SA69
 ALA17014.4 / Q9C9Z7
 ALA18B3.120 / Q9SVL5
 ALA19F18.80 / Q9SZF2
 ALA26G16.2 / Q9S9C9
 ALNPH-like / Q9FKB6
 ALNPH-like / Q9FNB3
 ALNPH-like / Q9LYW0
 ALNPH3 / Q9FMF5
 ALNPH3-like / Q9FYC8
 ALNPH3-like / Q9LFU0
 ALPhotoreceptor-int. like / Q9FJY3
 ALPhotoreceptor-int. like / Q9FN09
 ALPutative_NPH / Q9C9Z0
 ALSim_to_bZip / Q9LUB9
 Consensus_95%
 Consensus_75%

Secondary structure (predicted)



NPH3 domain