

Supplementary Materials: Mutational Landscape of the BAP1 Locus Reveals an Intrinsic Control to Regulate the miRNA Network and the Binding of Protein Complexes in Uveal Melanoma

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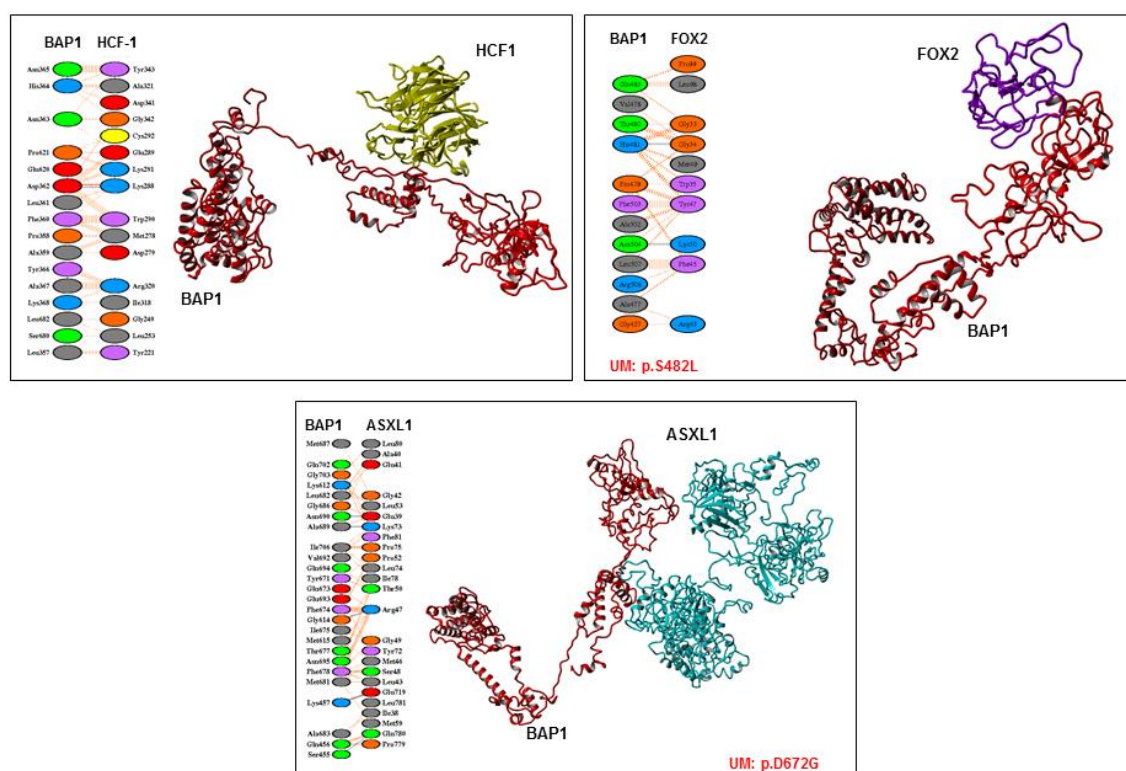


Figure S1. BAP1 variants and stability of multiprotein complexes. Simultaneous view of residue interaction network (left) and 3D structure (*in silico analysis*) of BAP1-associated protein complexes such as BAP1-HCF1, BAP1-FOXK2 and BAP1-ASXL1 (right) is shown. UM associated mutations are marked (red) for each protein complex.

BAP1 Protein Sequence

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MNKGWLELESDPGLFTLLVEDFGVKGVQVEEIYDLQSKCQGPVYGFIFLF 050
KWIEERRSRKVSSTLVDDTSVIDDDIVNNMFFAHQLIPNSCATHALLSVL 100
LNCSSVDLGPTLSRMKDFTKGFSPEKGYAIGNAPELAKAHNSHARPEPR 150
HLPEKQNGLSAVRTMEAFHFVSYVPI TGRLFELDGLKVYPIDHGPWGEDE 200
EWTDKARRVIMERIGLATAGEPYHDIRFNLMAVVPDRRIKYEALHVLKV 250
NRQTVLEALQQLIRVTQPELIQTHKSQESQLPEESKSA$NKSPLVLEANR 300
APAA$EGNHTDGAEAAAGSCAQAPSH$PPNPKPLVVKPPGS$SLNGVHPNP 350
TPIVQRLPAFLDNHNYAKSPMQEEEDLAAGVGRSRVPVRPPQY$DDEDD 400
YEDDEEDDVQNTNSALRYKKGKTGKPGALSG$ADQLSVLQPNNTINVLAE 450
KLKESQKDL$SIPL$IKTSSGAGSPAVAVPTH$QPSPTPSNE$STD$ASEIG 500
SAFNSPLRSPIRSANPTRPSSPVTSHISKVLFGEDD$LLRVDCIRYNRAV 550
RDLGPVISTGLHLAEDGVL$PLALTEGGKGS$PSIRPIQGSQGS$SPVE 600
KEVVEATDSREKTGMVRPGEPLSGEKY$PKELLALLKCVEAEIANYEACL 650
KEEVEKRKKFKIDDQRTHNYDEFICTFISMLAQEGMLANLVEQNI$SVRR 700
RQGV$IGRLHKQRPDRRKR$RPYKAKRQ 750

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Figure S2. Phosphorylation residues in BAP1 protein are marked (red).**Table S1.** List of phosphorylation and kinases in BAP1 protein.

# Sequence	#	x	Context	Score	Kinase	Answer
# Sequence	33	Y	VEEIYDLQS	0.645	unsp	YES
# Sequence	37	S	YDLQSKCQG	0.673	unsp	YES
# Sequence	37	S	YDLQSKCQG	0.662	PKC	YES
# Sequence	58	S	EERRSRKRV	0.996	unsp	YES
# Sequence	58	S	EERRSRKRV	0.569	PKC	YES
# Sequence	63	S	RRKVSTLVD	0.982	unsp	YES
# Sequence	63	S	RRKVSTLVD	0.834	PKA	YES
# Sequence	63	S	RRKVSTLVD	0.571	PKG	YES
# Sequence	63	S	RRKVSTLVD	0.53	cdc2	YES
# Sequence	63	S	RRKVSTLVD	0.521	RSK	YES
# Sequence	64	T	RKVSTLVDD	0.841	unsp	YES
# Sequence	64	T	RKVSTLVDD	0.518	PKC	YES
# Sequence	69	T	LVDDTSVID	0.532	CKII	YES
# Sequence	70	S	VDDTSVIDD	0.995	unsp	YES
# Sequence	70	S	VDDTSVIDD	0.554	CKI	YES
# Sequence	70	S	VDDTSVIDD	0.526	CKII	YES
# Sequence	98	S	HALLSVLLN	0.854	PKC	YES
# Sequence	105	S	LNCSSVDLG	0.538	cdc2	YES
# Sequence	119	T	MKDFTKGFS	0.743	PKC	YES
# Sequence	119	T	MKDFTKGFS	0.501	CKI	YES
# Sequence	123	S	TKGFSPESK	0.993	unsp	YES
# Sequence	123	S	TKGFSPESK	0.521	p38MAPK	YES
# Sequence	123	S	TKGFSPESK	0.505	GSK3	YES
# Sequence	126	S	FSPESKGYA	0.557	CKI	YES
# Sequence	126	S	FSPESKGYA	0.535	unsp	YES
# Sequence	129	Y	ESKGYAIGN	0.857	unsp	YES
# Sequence	129	Y	ESKGYAIGN	0.52	INSR	YES
# Sequence	143	S	KAHNSHARP	0.559	unsp	YES
# Sequence	160	S	QNGLSAVRT	0.814	unsp	YES
# Sequence	160	S	QNGLSAVRT	0.526	cdc2	YES
# Sequence	164	T	SAVRTMEAF	0.508	PKC	YES
# Sequence	177	T	YVPITGRLF	0.592	unsp	YES
# Sequence	177	T	YVPITGRLF	0.521	PKC	YES
# Sequence	203	T	DEEWTDKAR	0.699	unsp	YES
# Sequence	223	Y	AGEPYHDIR	0.937	unsp	YES
# Sequence	254	T	VNRQTVLEA	0.941	unsp	YES
# Sequence	254	T	VNRQTVLEA	0.617	PKA	YES
# Sequence	266	T	LIRVTQPEL	0.562	DNAPK	YES
# Sequence	266	T	LIRVTQPEL	0.562	PKA	YES
# Sequence	266	T	LIRVTQPEL	0.505	PKG	YES
# Sequence	273	T	ELIQTHKSQ	0.672	unsp	YES
# Sequence	273	T	ELIQTHKSQ	0.619	PKC	YES
# Sequence	276	S	QTHKSQESQ	0.991	unsp	YES
# Sequence	276	S	QTHKSQESQ	0.619	ATM	YES
# Sequence	276	S	QTHKSQESQ	0.516	DNAPK	YES

# Sequence	279	S	KSQESQLPE	0.545	DNAPK	YES
# Sequence	279	S	KSQESQLPE	0.531	unsp	YES
# Sequence	279	S	KSQESQLPE	0.522	CKII	YES
# Sequence	287	S	EESKSASNK	0.939	unsp	YES
# Sequence	287	S	EESKSASNK	0.552	cdc2	YES
# Sequence	289	S	SKSASNKSP	0.987	unsp	YES
# Sequence	289	S	SKSASNKSP	0.783	PKC	YES
# Sequence	289	S	SKSASNKSP	0.524	cdc2	YES
# Sequence	292	S	ASNKSPLVL	0.908	unsp	YES
# Sequence	292	S	ASNKSPLVL	0.519	p38MAPK	YES
# Sequence	305	S	APAASEGNH	0.969	unsp	YES
# Sequence	310	T	EGNHTDGAE	0.645	CKII	YES
# Sequence	319	S	EAAGSCAQA	0.563	PKC	YES
# Sequence	327	S	APSHSPPNK	0.867	unsp	YES
# Sequence	327	S	APSHSPPNK	0.521	GSK3	YES
# Sequence	342	S	PPGSSLNGV	0.503	PKA	YES
# Sequence	351	T	HPNPTPIVQ	0.639	cdk5	YES
# Sequence	366	Y	DNHNYAKSP	0.871	unsp	YES
# Sequence	369	S	NYAKSPMQE	0.617	unsp	YES
# Sequence	369	S	NYAKSPMQE	0.539	CKII	YES
# Sequence	395	S	PQQYSDDDED	0.954	unsp	YES
# Sequence	395	S	PQQYSDDDED	0.716	CKII	YES
# Sequence	401	Y	DEDDYEDDE	0.993	unsp	YES
# Sequence	401	Y	DEDDYEDDE	0.569	SRC	YES
# Sequence	401	Y	DEDDYEDDE	0.536	INSR	YES
# Sequence	418	Y	SALRYKGKG	0.599	unsp	YES
# Sequence	423	T	KGKGTGKPG	0.761	unsp	YES
# Sequence	423	T	KGKGTGKPG	0.551	PKC	YES
# Sequence	423	T	KGKGTGKPG	0.528	PKG	YES
# Sequence	430	S	PGALSGSAD	0.835	unsp	YES
# Sequence	430	S	PGALSGSAD	0.538	PKC	YES
# Sequence	432	S	ALSGSADGQ	0.541	cdc2	YES
# Sequence	455	S	KLKESQKDL	0.998	unsp	YES
# Sequence	455	S	KLKESQKDL	0.625	ATM	YES
# Sequence	460	S	QKDLSIPLS	0.553	unsp	YES
# Sequence	464	S	SIPLSIKTS	0.889	unsp	YES
# Sequence	464	S	SIPLSIKTS	0.761	PKC	YES
# Sequence	469	S	IKTSSGAGS	0.807	unsp	YES
# Sequence	469	S	IKTSSGAGS	0.716	PKC	YES
# Sequence	473	S	SGAGSPAVA	0.909	unsp	YES
# Sequence	473	S	SGAGSPAVA	0.567	cdk5	YES
# Sequence	473	S	SGAGSPAVA	0.519	GSK3	YES
# Sequence	480	T	VAVPTHSQP	0.651	PKC	YES
# Sequence	482	S	VPTHSQPSP	0.645	DNAPK	YES
# Sequence	482	S	VPTHSQPSP	0.553	ATM	YES
# Sequence	485	S	HSQPSPTPS	0.985	unsp	YES
# Sequence	485	S	HSQPSPTPS	0.546	p38MAPK	YES
# Sequence	485	S	HSQPSPTPS	0.538	cdk5	YES
# Sequence	485	S	HSQPSPTPS	0.503	GSK3	YES
# Sequence	487	T	QPSPTPSNE	0.526	cdk5	YES
# Sequence	489	S	SPTPSNEST	0.987	unsp	YES
# Sequence	492	S	PSNESTDTA	0.863	unsp	YES
# Sequence	492	S	PSNESTDTA	0.539	CKII	YES
# Sequence	493	T	SNESTDTAS	0.547	CKII	YES
# Sequence	493	T	SNESTDTAS	0.514	CKI	YES
# Sequence	495	T	ESTDTASEI	0.567	unsp	YES
# Sequence	497	S	TDTASEIGS	0.878	unsp	YES
# Sequence	497	S	TDTASEIGS	0.528	cdc2	YES
# Sequence	505	S	SAFNSPLRS	0.833	unsp	YES
# Sequence	505	S	SAFNSPLRS	0.7	cdk5	YES
# Sequence	505	S	SAFNSPLRS	0.517	GSK3	YES
# Sequence	509	S	SPLRSPIRS	0.972	unsp	YES
# Sequence	509	S	SPLRSPIRS	0.707	cdk5	YES
# Sequence	509	S	SPLRSPIRS	0.531	p38MAPK	YES
# Sequence	509	S	SPLRSPIRS	0.528	GSK3	YES
# Sequence	513	S	SPIRSANPT	0.722	unsp	YES
# Sequence	513	S	SPIRSANPT	0.592	PKG	YES
# Sequence	517	T	SANPTRPSS	0.743	PKC	YES
# Sequence	517	T	SANPTRPSS	0.504	GSK3	YES
# Sequence	520	S	PTRPSSPVT	0.678	unsp	YES

# Sequence	520	S	PTRPSSPVT	0.585	PKC	YES
# Sequence	520	S	PTRPSSPVT	0.533	cdc2	YES
# Sequence	521	S	TRPSSPVT	0.994	unsp	YES
# Sequence	521	S	TRPSSPVT	0.656	cdk5	YES
# Sequence	521	S	TRPSSPVT	0.538	GSK3	YES
# Sequence	521	S	TRPSSPVT	0.507	p38MAPK	YES
# Sequence	524	T	SSPVTSHIS	0.529	PKC	YES
# Sequence	525	S	SPVTSHISK	0.866	unsp	YES
# Sequence	537	S	GEDDSLLRV	0.511	cdc2	YES
# Sequence	558	S	GPVISTGLL	0.524	PKA	YES
# Sequence	559	T	PVISTGLLH	0.529	cdc2	YES
# Sequence	571	S	DGVLSPAL	0.584	p38MAPK	YES
# Sequence	583	S	GKGSSPSIR	0.713	unsp	YES
# Sequence	583	S	GKGSSPSIR	0.562	cdk5	YES
# Sequence	585	S	GSSPSIRPI	0.819	unsp	YES
# Sequence	585	S	GSSPSIRPI	0.664	PKC	YES
# Sequence	592	S	PIQGSQGSS	0.663	unsp	YES
# Sequence	592	S	PIQGSQGSS	0.63	DNAPK	YES
# Sequence	592	S	PIQGSQGSS	0.623	PKC	YES
# Sequence	592	S	PIQGSQGSS	0.612	ATM	YES
# Sequence	596	S	SQGSSSPVE	0.613	PKC	YES
# Sequence	596	S	SQGSSSPVE	0.535	CKII	YES
# Sequence	597	S	QGSSSPVEK	0.997	unsp	YES
# Sequence	597	S	QGSSSPVEK	0.506	cdc2	YES
# Sequence	607	T	VVEATDSRE	0.541	CKII	YES
# Sequence	609	S	EATDSREKT	0.956	unsp	YES
# Sequence	613	T	SREKTGMVR	0.896	unsp	YES
# Sequence	623	S	GEPLSGEY	0.956	unsp	YES
# Sequence	623	S	GEPLSGEY	0.533	ATM	YES
# Sequence	627	Y	SGEKYSPKE	0.886	unsp	YES
# Sequence	628	S	GEKYSPKEL	0.997	unsp	YES
# Sequence	677	T	EFICTISM	0.519	PKC	YES
# Sequence	680	S	CTFISMLAQ	0.504	cdc2	YES
# Sequence	697	S	EQNISVRRR	0.804	PKC	YES
# Sequence	705	S	RQGVSIGRL	0.869	unsp	YES
# Sequence	721	S	RRKRSRPYK	0.877	unsp	YES
# Sequence	721	S	RRKRSRPYK	0.693	PKA	YES
# Sequence	721	S	RRKRSRPYK	0.682	PKG	YES
# Sequence	721	S	RRKRSRPYK	0.561	RSK	YES

Table S2. Binding minimum free energy of BAP1 variants with miRNAs.

Heading title	mi-RNA-31	mi-RNA-125a	mi-RNA-125b	mi-RNA-200b	mi-RNA-423	mi-RNA-505	mi-RNA-140
BAP1-WT	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
M1T	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
M1I	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
G45R	-59.5	-81.3	-74.7	-85.1	-79.5	-74.4	-82.0
S63C	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
Q85P	-62.0	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
C91G	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
L97Q	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
S98R	-65.2	-83.7	-76.3	-91.8	-82.9	-83.2	-91.8
L100P	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
L112R	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
M115V	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
G128R	-64.8	-80.7	-83.2	-100.4	-79.5	-75.5	-87.8
H141R	-64.5	-81.3	-75.0	-91.0	-79.5	-83.2	-86.0
R146K	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
H169P	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
S172R	-64.4	-87.7	-80.2	-90.4	-79.9	-82.2	-90.4
Y173C	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
P175R	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
T177R	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
L180P	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
E182D	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8

E182G	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
G185R	-62.4	-82.5	-81.1	-97.4	-78.5	-80.2	-89.7
E212D	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
N229D	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
S278L	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
S280T	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
D400Y	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
N443T	-65.2	-88.7	-75.6	-100.4	-82.9	-83.2	-91.8
S482L	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
L570V	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
E577N	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
E577Q	-68.4	-88.7	-83.2	-100.4	-82.9	-83.2	-91.8
E602D	-27.4	-81.3	-75.6	-91.8	-82.9	-75.5	-87.8
D672G	-26.3	-80.6	-75.6	-89.9	-79.4	-74.7	-83.1



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