

### A. Conservation of *AKT1* mutation in different

species	match	gene	aa	alignment
Human			189	S R E R V F S E D R A R F Y G A E I V S A L D Y
mutated	not conserved		189	R V F S E D R A C F Y G A E I V S A L D
Ptrogodytes	all identical	<a href="#">ENSPTRG00000006775</a>	251	R V F S E D R A R F Y G A E I V S A L D
Mmulatta	all identical	<a href="#">ENSMMUG00000001044</a>	251	R V F S E D R A R F Y G A E I V S A L D
Fcatus	all identical	<a href="#">ENSFCAG00000004957</a>	235	S R E R V F P E D R A R F Y G A E I V S A L D
Mmusculus	all identical	<a href="#">ENSMUSG00000001729</a>	251	R V F S E D R A R F Y G A E I V S A L D
Ggallus	all identical	<a href="#">ENSGALG000000011620</a>	251	R V F S E D R A R F Y G A E I V S A L D
Trubripes	all identical	<a href="#">ENSTRUG000000013476</a>	244	R V F S E E R A R F Y G A E I V S A L D
Drerio	no homologue			
Dmelanogaster	all identical	<a href="#">FBgn0010379</a>	367	S H E R I F T E D R T R F Y G A E I I S A L G
Celegans	all identical	<a href="#">C12D8.10</a>	294	N R E V Q M N K E G F S E P R A R F Y G S E I V L A L G
Xtropicalis	all identical	<a href="#">ENSXETG000000008603</a>	256	E R I F S E D R A R F Y G A E I V S A L D

### B. Conservation of *MLH3* mutation in different species

species	match	gene	aa	alignment
Human			608	S Y G R V K L C S T G F I T H V V Q N E K T K S
mutated	not conserved		608	V K L C S T G I I T H V V Q N E K T K
Ptrogodytes	all identical	<a href="#">ENSPTRG000000006548</a>	608	V K L C S T G F I T H V V Q N E K T K
Mmulatta	all identical	<a href="#">ENSMMUG000000002911</a>	611	Y G R V K L C S T G F I T H I V Q N E K T K
Fcatus	no homologue			
Mmusculus	all identical	<a href="#">ENSMUSG000000021245</a>	612	S Y G Q V K L C S T G F I T H V V Q S E H A K
Ggallus	no homologue			
Trubripes	no homologue			
Drerio	no alignment	<a href="#">ENSARG000000056334</a>	n/a	
Dmelanogaster	no homologue			
Celegans	no homologue			
Xtropicalis	no homologue			

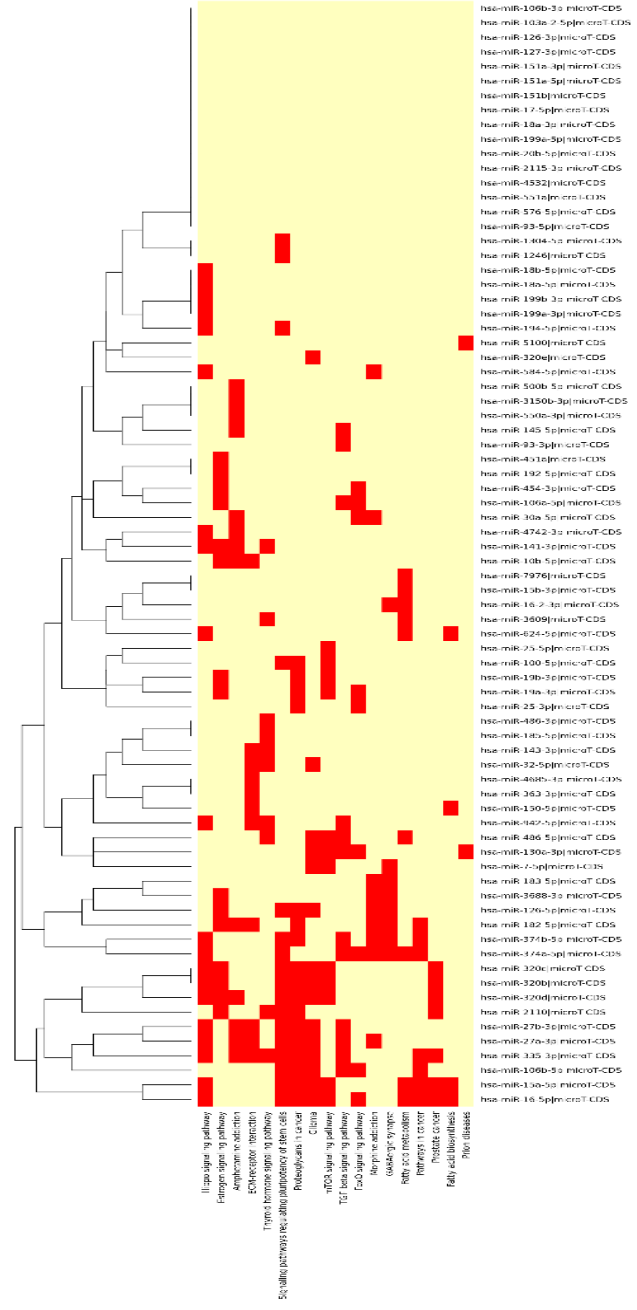
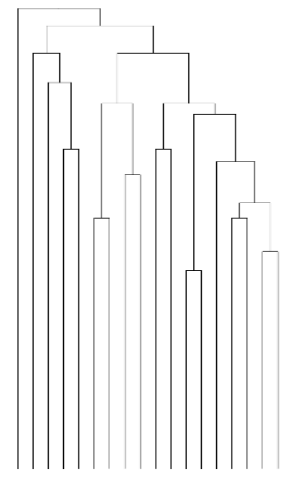
### C. Conservation of *MYH9* mutation in different species

species	match	gene	aa	alignment
Human			1477	R A E A E A R E K E T K A L S L A R A L E E A M
mutated	not conserved		1477	R A E A E A R E K E T <b>N</b> A L S L A R A L E E A
Ptrogodytes	no homologue			
Mmulatta	all identical	<a href="#">ENSMUG00000006101</a>	1374	E A R E K E T K A L S L A R A L E E A
Fcatus	all identical	<a href="#">ENSFCAG00000001124</a>	1416	R A E A E A R E K E T K A L S L A R A L E E A
Mmusculus	all identical	<a href="#">ENSMUSG000000022443</a>	1477	R A E A E A R E K E T K A L S L A R A L E E A
Ggallus	all identical	<a href="#">ENSGALG000000012533</a>	852	R A E A E A R E K E T K A L S L A R A L E E A
Trubripes	no homologue			
Drerio	no homologue			
Dmelanogaster	all identical	<a href="#">FBgn0005634</a>	1567	T A E R E A R E K E T K V L S V S R E L D E A
Celegans	all conserved	<a href="#">F52B10.1</a>	1481	A M S Q E L R D R E T R V L S L L N E V D I M
Xtropicalis	all identical	<a href="#">ENSXETG00000000233</a>	1473	R A E A E A R E K E T K A L A L A R S L E E A

### D. Conservation of *PTPN11* mutation in different species

species	match	gene	aa	alignment
Human			61	A V T H I K I Q N T G D Y Y D L Y G G E K F A T
mutated	not conserved		61	Y Y Y D L Y G G E K F A
Ptrogodytes	all identical	<a href="#">ENSPTRG000000042397</a>	61	D Y Y D L Y G G E K F A
Mmulatta	all identical	<a href="#">ENSMUG000000013253</a>	61	D Y Y D L Y G G E K F A
Fcatus	no homologue			
Mmusculus	all identical	<a href="#">ENSMUSG000000043733</a>	61	D Y Y D L Y G G E K F A
Ggallus	all identical	<a href="#">ENSGALG000000004821</a>	62	G D Y Y D L Y G G E K F A
Trubripes	all identical	<a href="#">ENSTRUG000000018529</a>	61	D Y Y D L Y G G E K F A
Drerio	all identical	<a href="#">ENSDARG000000020334</a>	61	D Y Y D L Y G G E K F A
Dmelanogaster	no alignment	<a href="#">FBgn0000382</a>	n/a	
Celegans	no homologue			
Xtropicalis	all identical	<a href="#">ENSXETG000000004305</a>	61	A V T H I K I Q N T G D Y Y D

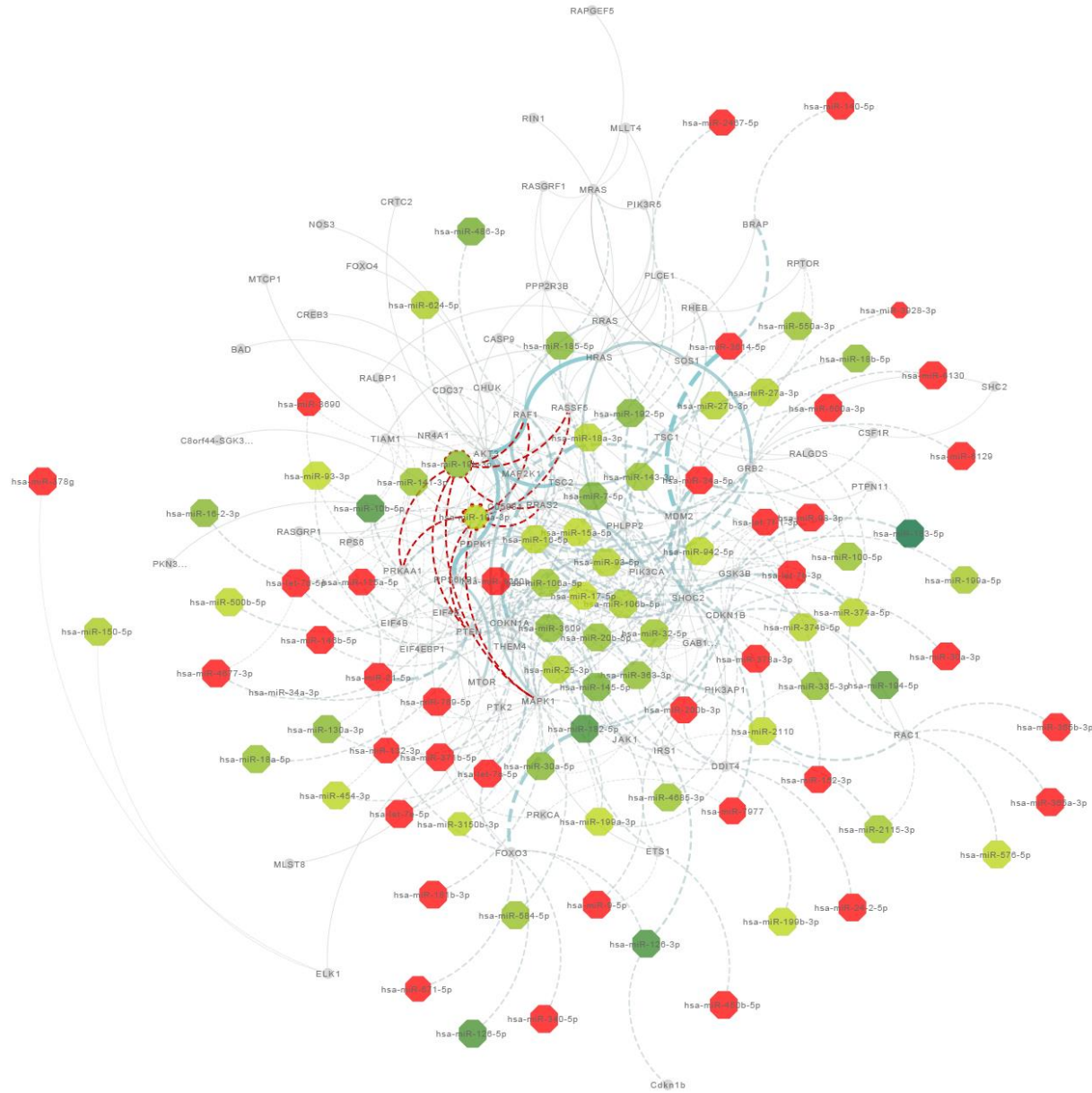
**Figure S1. Conservation of protein sequence of the four important mutations identified in this study.** The residue at which the point mutation is seen is shown in bold. The mutated row sequence in the Species column belongs to JMML patient. Most mutations identified tend to occur in highly conserved regions. The results of conservation were obtained from MutationTaster (Schwarz, J. M. *et al.* 2010). (A) *AKT1* mutation site conservation across various species. (B) *MLH3* mutation site conservation across various species. (C) *MYH9* mutation site conservation across various species. (D) *PTPN11* mutation site conservation across various species.



**Figure S2. The enrichment heat map for all upregulated microRNAs.** All upregulated microRNAs were used for generating heatmap of pathway enrichment from miRPath (Vlachos, I. S. *et al.* 2015). Many important pathways which play an important role in cancer or have crosstalk with AKT pathway are shown enriched in the heatmap (e.g., mTOR pathway, Prostate Cancer pathway and other pathways in Cancer).







**Figure S5. MicroRNA and cross-talk.** The network below shows cross-talk genes and the microRNAs which are experimentally validated to target these genes. Only the microRNAs which were two fold upregulated or downregulated were taken for this study. The node size of microRNAs (shown as hexagon) varies with the significance of corrected p-values. The colour of microRNA nodes varies with respect to fold-change with red being downregulated and green nodes being upregulated. MicroRNA edges are shown as dotted lines while gene connections are shown as solid lines. A family of oncomiRs (mir-19) is shown in dotted circles and its edges are shown in dotted red lines. These oncomiRs target some important genes in the AKT and RAS-pathway namely PTEN, MAPK1, RAF1, RRAS2 (visualize Cytoscape sessions file in Cytoscape 3.2.1 for more details).