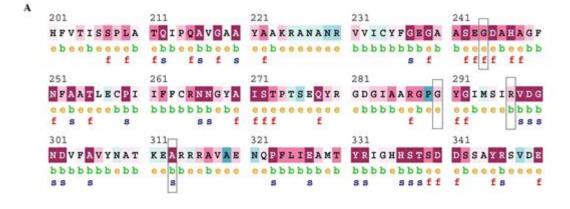
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A Danio rerio	ANRVVICYFGEGAASEGDAHAGENESATLECPLIFFCRNNGYAISTPTNEQYRGDGIAAR	288
Xenopus tropicalis	ADRAVICYFGEGAASEGDAHAAFNFSATLECPVLFFCRNNGYAISTPTSEQYRGDGIAAR	275
Gallus gallus	ASRAVICYFGEGAASEGDAHAGENEAATLECPIVEECRNNGYAISTPTSEQYRGDGIAAR	273
Rattus norvegicus	ANQIVICYFGEGAASEGDAHAGENEAATLECPIIFECRNNGYAISTPTSEQYRGDGIAAR	288
Mus musculus	ANRIVICYFGEGAASEGDAHAGENFAATLECPIIFFCRNNGYAISTPTSEQYRGDGIAAR	288
Bos taurus	ANRVVICYFGEGAASEGDAHAGFNFAATLECPIIFFCRNNGYAISTPTSEQYRGDGIAAR	297
Canis lupus familiaris	ANRVVICYFGEGAASEGDAHAGFNFAATLECPIIFFCRNNGYAISTPTSEQYRGDGIAAR	288
Macaca fascicularis Homo sapiens	ANRVVICYFGEGAASEGDAHAGFNFAATLECPIIFFCRNNGYAISTPTSEQYRGDGIAAR ANRVVICYFGEGAASEGDAHAGFNFAATLECPIIFFCRNNGYAISTPTSEQYRGDGIAAR	287
Pan troglodytes	ANRVVICYFGEGAASEGDAHAGFNFAATLECPIIFFCRNNGYAISTPTSEQYRGDGIAAR	287
	*	02020
	290 297 313	
Danio rerio	GPGYGLMSIRVDGNDVFAVYNATKEARRRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS	348
Xenopus tropicalis	GPGYGIMSIRVDGNDVFAVYNATKEARRRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS	335
Gallus gallus	GPGYGLMSIRVDGNDVFAVYNATKEARRRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS	333
Rattus norvegicus Mus musculus	GPGYGIMSIRVDGNDVFAVYNATKEARRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS	348
Bos taurus	GPGYGIMSIRVDGNDVFAVYNATKEARRRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS GPGYGILSIRVDGNDVFAVYNATKEARRRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS	348 357
Canis lupus familiaris	GPGYGINSIRVDGNDVFAVYNATKEARRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS	348
Macaca fascicularis	GPGYGIMSIRVDGNDVFAVYNATKEARRRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS	347
Homo sapiens	GPGYGIMSI VDGNDVFAVYNATKEARRRAVAENOPFLIEAMTYRIGHHSTSDDSSAYRS	347
Pan troglodytes	GPGYGIMSIRVDGNDVFAVYNATKEARRRAVAENQPFLIEAMTYRIGHHSTSDDSSAYRS	347
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В	107 1/0 1/6 170	
NAME OF A DESCRIPTION OF A	137 162 166 170	122101
Danio rerio	KDRVFNTPLCEQGIVGFGIGAAAAGATAIAEIQFADYIFPAFDQIVNEAAKYRYRSGNMY	174
Xenopus tropicalis	KDRVFNTPLCEQGIVGFGIGVAVAGATSIAEIQFADYIFPAFDQIVNEAAKYRYRSGDLF	158
Gallus gallus	KDRVFNTPLCEQGIVGFGIGVAVAGATAIAEIQFADYIFPAFDQIVNEAAKYRYRSGDLF	162
Rattus norvegicus	KDRVFNTPLCEQGIVGFGIGIAVTGATAIAEIQFADYIFPAFDQIVNEAAKYRYRSGDLF	173
Mus musculus	KDRVFNTPLCEQGIVGFGIGIAVTGATAIAEIQFADYIFPAFDQIVNEAAKYRYRSGDLF	173
Homo sapiens	KDRVFNTPLCEQGIVGFGIGIAVTGATAIAEIQFADYIFPAFDQIVNEAAKYRYFSGDLF	175 175
Pan troglodytes Macaca fascicularis	KDRVFNTPLCEQGIVGFGIGIAVTGATAIAEIQFADYIFPAFDQIVNEAAKYRYFSGDLF	175
Bos taurus	KDRVFNTPLCEQGIVGFGIGIAVTGATAIAEIQFADYIFPAFDQIVNEAAKYRYRSGDLF KDRVFNTPLCEQGIVGFGIGIAVTGATAIAEIQFADYIFPAFDQIVNEAAKYRYRSGDLF	175
Canis lupus familiaris	KDRVFNTPLCEQGIVGFGIGIAVTGATATAEIQFADYIFPAPDQIVIEAAKTRTSGDLF KDRVFNTPLCEQGIVGFGIGIAVTGATAIAEIQFADYIFPAPDQIVIEAAKTRTSGDLF	170
Call's Topus Familiaris		110
	218	
Danio rerio	DCGKLTIRSPWGCVGHGSLYHSQSPEAFFAHCPGLKVVVPRGPVQAKGLLLSCIEDKNPC	234
Xenopus tropicalis	NCGSLTIRAPWGCVGHGALYHSQSPEAFFAHAPGIKVVIPRSPIQAKGLLLSCIEDKNPC	218
Gallus gallus	NCGNLTIRAPWGCVGHGALYHSOSPEAFFAHCPGIKIVIPRSPLOAKGLLLSCIEDKNPC	222
Rattus norvegicus	NCGSLTIRAPWGCVGHGALYHSQSPEAFFAHCPGIKVVIPRSPFQAKGLLLSCIEDKNPC	233
Mus musculus	NCGSLTIRAPWGCVGHGALYHSQSPEAFFAHCPGIKVVIPRSPFQAKGLLLSCIEDKNPC	233
Homo sapiens	NCGSLTIRSPWGCVGHGALYHSQSPEAFFAHCPGIKVVIPRSPFQAKGLLLSCIEDKNPC	235
Pan troglodytes	NCGSLTIRSPWGCVGHGALYHSQSPEAFFAHCPGIKVVIPRSPFQAKGLLLSCIEDKNPC	235
Macaca fascicularis	NCGSLTIRSPWGCVGHGALYHSQSPEAFFAHCPGIKVVIPRSPFQAKGLLLSCIEDKNPC	235
Bos taurus	NCGSLTIRSPWGCVGHGALYHSØSPEAFFAHCPGIKVVVPRSPFØAKGLLLSCIEDKNPC	235
Canis lupus familiaris	NCGSLTIRAPWGCVGHGALYHSQSPEAFFAHCPGIKVVVPRSPFQAKGLLLSCIEDRNPC	230
	;**,****;********;********************	
	330	351
Danio rerio	GVSCELIDLQTILPWDKETVCKSVMKTGRLLISHEAPVTGGFAAEISSAVQEECFLNLEA	
Xenopus tropicalis	GLSCEVIDLRTILPWDVETVCKSVSKTGRLLISHEAPVTGGFASEISATVQEECFLNLEA	
Gallus gallus	GVSCEVIDLRTILPWDTETICKSVVKTGRLLISHEAPLTGGFASEISSTVQEECFLNLEA	
Rattus norvegicus	GVSCEVIDLRTIVPWDVDTVCKSVIKTGRLLISHEAPLTGGFASEISSTVQEECFLNLEA	
Mus musculus	GVSCEVIDLRTIVPWDVDTVCKSVIKTGRLLISHEAPLTGGFASEISSTVQEECFLNLEA	
Homo sapiens	GVSCEVIDLRTIIPWDVDTICKSVIKTGRLLISHEAPLTGGFASEISSTVQEECFLNLEA	
Pan troglodytes Macaca fascicularis	GVSCEVIDLRTIIPWDVDTICKSVIKTGRLLISHEAPLTGGFASEISSTVQEECFLNLEA	
	GVSCEVIDLRTIIPWDVDTVCKSVIKTGRLLISHEAPLTGGFASEISSTVQEECFLNLEA	
Bos taurus	GVSCEVIDLRTILPWDVDTVCKSVIKTGRLLVSHEAPLTGGFASEISSTVQEECFLNLEA	
Canis lupus familiaris	GVSCEVIDLRTILPWDVDTVCKSVIKTGRLLISHEAPLTGGFASEISSTVQEECFLNLEA	350

Figure S1: Amino acid conservational study of BCKDHA(A) and BCKDHB(B) proteins sequence using Clustal Omega across 10 different species. High-risk variants are marked in red.





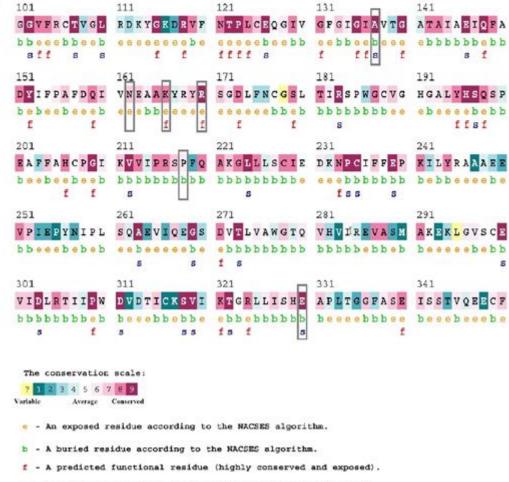


Figure S2: Evolutionary conservation profile of BCKDHA(A) and BCKDHB(B) proteins according to Consurf web server, showing by sequence. The gray boxes indicate the high-risk variants.

s - A predicted structural residue (highly conserved and buried).

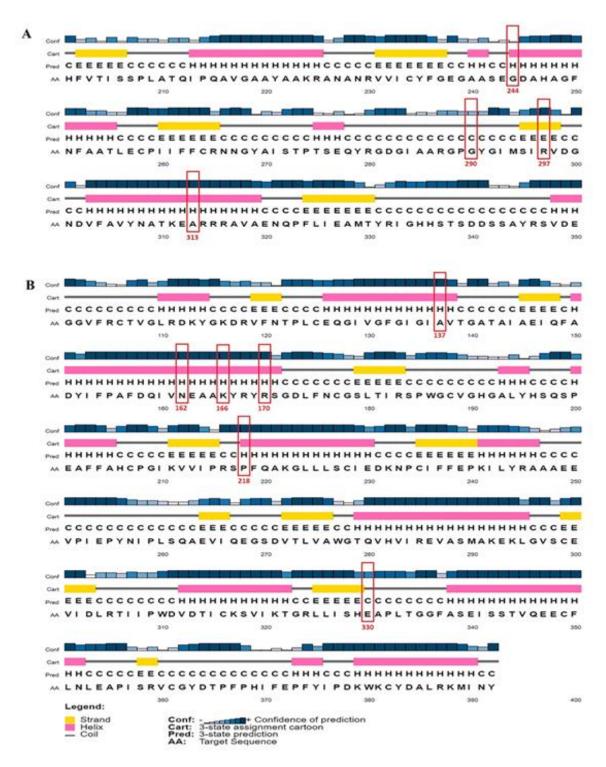


Figure S3: Secondary structure of BCKDHA(A) and BCKDHB(B) proteins created by PSIPRED web server.Red rectangles shows the exact location of deemed pathogenic missense variants in our cohort.

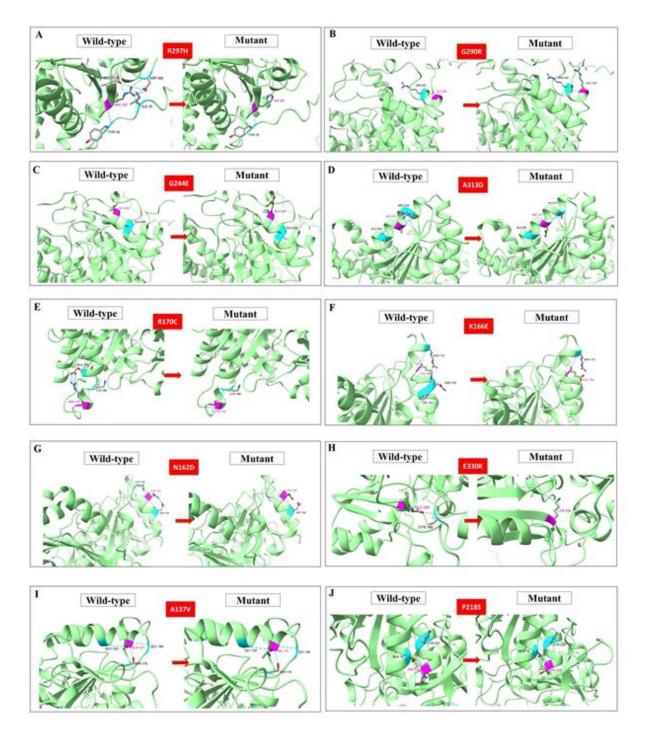


Figure S4: Effect of the high-risk variants in our cohort on 3D structure of BCKDHA(A-D) and BCKDHB(E-I) proteins.