

Table S1. List of forward and reverse primers and respective PCR conditions used to make FISH probes, to perform 5' RACE-PCR and RT-PCR investigations, and for *BRAF*, *NRAS*, *HRAS*, and *KRAS* genes sequencing.

Primers names	Primers sequence
<i>BRAF</i> i3 ⁽¹⁾	5' TTCTCCCGCTATGTTAGGGCCA 3'
<i>BRAF</i> e7 ⁽¹⁾	5' TCCTGTGGTATTGGGTGGTGTCA 3'
<i>BRAF</i> e11 ⁽²⁾	5' TGATTGGGAGATTCTGATGGCA 3'
<i>BRAF</i> i13 ⁽²⁾	5' TCCAAGCAGGCTCTAACTGGAA 3'
<i>BRAF</i> SP4 ⁽³⁾	5' CATGAAGAGTAGGATATTACA 3'
<i>BRAF</i> SP5 ⁽³⁾	5' GTAAGTGCTGAGGTGTAGGTGCTGT 3'
<i>BRAF</i> SP6 ⁽³⁾	5' CACATTCAACATTTCACTGCCACAT 3'
forward fusion FCHSD1a ⁽⁴⁾	5' GTACTGCAACGACTGGAGCA 3'
reverse fusion <i>BRAF</i> ⁽⁴⁾	5' CTCGAGTCCCCTACCAAG 3'
forward fusion FCHSD1b ⁽⁵⁾	5' GCTGTCCCAGAGGGACCTCT 3'
reverse SP8 ⁽⁵⁾	5' GTTCTGATGCCTGCGGTGA 3'
FBRAFe10 ⁽⁶⁾	5' TCATTACCTGGCTCACTAACTAA 3'
BRAFe15 ⁽⁶⁾	5' TGGATCCAGACAACGTGTTCA 3'
BRAFe14 ⁽⁷⁾	5' CTTACACGCCAAGTCAATCATC 3'
SP9 ⁽⁷⁾	5' TGGCAATGAGCGGGCCA 3'
NRASF1 ⁽⁸⁾	5' AATCTGTCCAAAGCAGAGGCAGTG 3'
NRASR1 ⁽⁸⁾	5' TGGCAATCCCATAACAACCCTGAGT 3'
NRASF4 ⁽⁹⁾	5' ACCAGACAGGGTGTGAAGATGCT 3'
NRASR4 ⁽⁹⁾	5' GCAGATGCCAGTTAGAGAACAGGCC 3'
KRASF1 ⁽¹⁰⁾	5' ATTCGGACTGGAGCGAGC 3'
KRASR1 ⁽¹⁰⁾	5' CTTCTTGCTAAGTCCTGAGCCTGT 3'
HRASF1 ⁽¹¹⁾	5' AGGAGACCCCTGTAGGAGGACC 3'
HRASR1 ⁽¹¹⁾	5' TCTTGGCCGAGGTCTCGATGTA 3'

⁽¹⁾ & ⁽²⁾ primer sets used to make FISH probes targeting regions covering intron 3 to exon 7, and exon 11 to intron 13 of *BRAF* gene, respectively. PCR were performed using the Expand Long Template PCR System (Roche, Basel, Switzerland) in a final volume of 50 µl, including buffer 3, 300 nM of primers, 400 µM of dNTP mix, and 3.75 U of DNA Polymerase. The amplification protocol was performed following manufacturer's instructions, except for the annealing temperature (58°C). Five hundreds ng of these PCR products were labeled using the Vysis Nick Translation Kit and Vysis SpectrumOrange-dUTP (Downers Grove, IL, USA).

⁽³⁾ Poly(A)⁺ RNA were reverse transcribed with a *BRAF*-specific primer SP4. For 5' RACE – PCR assay (Rapid Amplification of cDNA Ends, Version 2.0, Invitrogen, Carlsbad, CA,

USA), first and second PCR rounds were performed according to the manufacturer's instructions, and with the use of specific *BRAF* reverse primers SP5 and SP6.

⁽⁴⁾ primer set used to detect the *FCHSD1 – BRAF* hybrid transcript. Thirty ng of cDNA were subjected to amplification in a final volume of 50 µl, with 200 nM of primers, 200 µM of dNTP mix, 2 mM of MgCl₂, and 2.5 U of Taq DNA Polymerase in Invitrogen buffer (Invitrogen, Carlsbad, CA, USA). Amplification conditions were 94°C (3 minutes), followed by 35 cycles of 94°C (30 seconds), 55°C (30 seconds), and 72°C (1 minute 30 seconds), and a final elongation of 7 minutes at 72°C.

⁽⁵⁾ primer set used to confirm the presence of the whole *BRAF* PKD in the fusion transcript. PCR were performed using the Expand Long Template PCR System (Roche, Basel, Switzerland) in a final volume of 50 µl, including buffer 2, 300 nM of primers, 400 µM of dNTP mix, and 3.75 U of DNA Polymerase. The amplification protocol was performed following manufacturer's instructions, except for the annealing temperature (60°C).

^{(6), (7), (8),(9),(10)} & ⁽¹¹⁾ primer sets used to screen for *BRAF*, *NRAS*, *KRAS* and *HRAS* point mutations. Thirty ng of cDNA were subjected to amplification in a final volume of 50 µl, with 200 nM of primers, 200 µM of dNTP mix, MgCl₂ (2.5 mM for primers ⁽⁶⁾, primers ⁽¹⁰⁾ and primers ⁽¹¹⁾, 1.5 mM for primers ⁽⁷⁾ and primers ⁽⁸⁾, and 2 mM for primers ⁽⁹⁾), and 2.5 U of Taq DNA Polymerase (Invitrogen, Carlsbad, CA, USA). The amplification conditions were 94°C (3 minutes), followed by 35 cycles of 94°C (30 seconds), 57°C, 54°C, 59°C, 58°C, 56°C and 56°C respectively (30 seconds), 72°C (1 minute 30 seconds), and a final elongation of 7 minutes at 72°C.

Figure S1. *FCHSD1-BRAF* fusion cDNA sequence and predicted amino acid sequence for patient 1. *Vertical red arrow* points the breakpoint location, *italic boldface* the PKD of the *BRAF* gene.

	M	Q	P
1	GGCTTCCTCCAGTCCGGAGTCCAGTGGCTGACCGCCTGCTGGAGCGGAGATGCAGCCG		
4	P P R K V K P A Q E V K L R F L E Q L S		
61	CCGCCCGAAAAGTGAAGCCGGCCAGGAGGTGAAGCTCGCTCTGGAACAGCTGAGC		
24	I L Q T W Q Q R E A D L L E D I R S Y S		
121	ATCCTTCAGACCTGGCAGCAGAGGGAGGCGATCTGCTGGAGGACATCAGATCCTACAGC		
44	K Q R A A I E R E Y G Q A L Q K L A G P		
181	AAGCAGAGGGCAGCCATTGAACGGGAGTATGGGCAGGCACCTCAGAAACTGGCTGGCCA		
64	F L K R E G H R S G E M D S R G R T V F		
241	TTCCTGAAGAGGGAAGGGCACCGGAGCGGTGAGATGGACAGCAGGGCAGGACAGTGGTC		
84	G A W R C L L D A T V A G G Q T R L Q A		
301	GGTGCCTGGCCTGCCTGGATGCCACCGTGGCTGGCTGGGGCCAAACCCGACTCCAGGGC		
104	S D R Y R D L A G G T G R S A K E Q V L		
361	TCTGACCGATAACCGTGACCTAGCAGGGGGTACAGGGCGGAGCGCCAAGGAGCAGGTGCTT		
124	R K G T E N L Q R A Q A E V L Q S V R E		
421	AGGAAGGAAACAGAGAACCTCCAGAGGGCGCAGGCTGAGGTGCTGCAGTCTGTCCGGAG		
144	L S R S R K L Y G Q R E R V W A L A Q E		
481	CTGAGCCGAAGTCGGAAGCTGTATGGCAGCGGGAACGTGTGTTGGCCTTGGCACAGGAG		
164	K A A D V Q A R L N R S D H G I F H S R		
541	AAGGCAGCTGATGTCCAGGCCAGGCTAAACCGAAGTGCACATGGATCTTCACTCTCGG		
184	T S L Q K L S T K L S A Q S A Q Y S Q Q		
601	ACCAGTCTCCAGAAACTGAGCACCAAGCTGTCCGCCAGTCAGCCCAGTACTCCCAGCAG		
204	L Q A A R N E Y L L N L V A T N A H L D		
661	CTGCAAGCAGCCCGCAATGAGTACCTGCTTAACCTGGTGGCTACCAATGCCACCTCGAC		
224	H Y Y Q E E L P A L L K A L V S E L S E		
721	CATTACTACCAGGAGGAACCTGCAAGCTCTGCTCAAGGCCCTGGTCAGTGAGCTGTCAAGAG		
244	H L R D P L T S L S H T E L E A A E V I		
781	CACTTGAGGGACCCCTGACCTCCCTGAGGCCACACTGAGCTGGAAGCCGCAGAGGTCACTC		
264	L E H A H R G E Q T T S Q V S W E Q D L		
841	CTGGAGCATGCCACCAGCGGGGAGCAGACAACCTCCAGGTAAGCTGGAGCAAGACCTG		
284	K L F L Q E P G V F S P T P P Q Q F Q P		
901	AAGCTGTTCTTCAGGAGCCTGGTGTATTTCACCCACCCACTCAGCAGTTCAAGCCA		
304	A G T D Q V C V L E W G A E G V A G K S		
961	GCAGGGACTGATCAGGTGTGTCCTGGAGTGGGGAGCAGAAGCGTGGCTGGCAAGAGT		
324	G L E K E V Q R L T S R A A R D Y K I Q		
1021	GGCCTGGAGAAAGAGGTTCAGCGCTTGACCGCAGCTGCCCCTGACTACAAGATCCAG		
344	N H G H R V L Q R L E Q R R Q Q A S E R		
1081	AACCATGGCATGGGTACTGCAACGACTGGAGCAGAGGCAGCAGGCTTCAGACGG		
364	E A P S I E Q R L Q E V R E S I R R A Q		
1141	GAGGCTCCAAGCATAGAACAGAGGTTACAGGAAGTGCAGAGAGACATCCGCCGGCACAG		
384	V S Q V K G A A R L A L L Q G A G L D V		
1201	GTGAGCCAGGTGAAGGGGCTGCCGGCTGGCCCTGCTGCAGGGGGCTGGCTAGATGTG		
404	E R W L K P A M T Q A Q D E V E Q E R R		
1261	GAGCGCTGGCTGAAGCCAGCCATGACCCAGGCCAGGATGAGGTGGAGCAGGAGCGCCGG		
424	L S E A R L S Q R D L S P T D L I R D Q		
1321	CTCAGTGAGGCTCGGCTGTCCCAGAGGGACCTCTCTCCAAACCGACTTGATTAGAGACAA		
444	G F R G D G G S T T G L S A T P P A S L		
1381	GGATTTCTGGTGTAGGGAGGATCAACCAACAGGTTGCTGCTACCCCCCTGCCCTATTA		
464	P G S L T N V K A L Q K S P G P Q R E R		
1441	CCTGGCTCACTAACGTGAAAGCCTTACAGAAATCTCCAGGACCTCAGCGAGAAAGG		
484	K S S S S S E D R N R M K T L G R R D S		
1501	AAGTCATCTCATCCTCAGAACAGGAATCGAATGAAAACACTGGTAGACGGGACTCG		
504	S D D W E I P D G Q I T V G Q R I G S G		
1561	AGTGTGATTGGGAGATTCCCTGATGGCAGATTACAGTGGGACAAAGAATTGGATCTGGA		

524 **S F G T V Y K G K W H G D V A V K M L N**
1621 TCATTTGGAACAGTCTACAAGGAAAGTGCATGGTATGTGGCAGTGAAAATGTTGAAT
544 **V T A P T P Q Q L Q A F K N E V G V L R**
1681 GTGACAGCACCTACACCTCAGCAGTTACAAGCCTTCAAAAATGAAGTAGGAGTACTCAGG
564 **K T R H V N I L L F M G Y S T K P Q L A**
1741 AAAACACGACATGTGAATATCCTACTCTTCATGGGCTATTCCACAAAGCCACAACGGCT
584 **I V T Q W C E G S S L Y H H L H I I E T**
1801 ATTGTTACCCAGTGGTGTGAGGGCTCCAGCTGTATCACCATCTCCATATCATTGAGACC
604 **K F E M I K L I D I A R Q T A Q G M D Y**
1861 AAATTGAGATGATCAAACCTTATAGATATTGCACGACAGACTGCACAGGGCATGGATTAC
624 **L H A K S I I H R D L K S N N I F L H E**
1921 TTACACGCCAAGTCAATCATCCACAGAGACCTCAAGAGTAATAATATTTCTTCATGAA
644 **D L T V K I G D F G L A T V K S R W S G**
1981 GACCTCACAGTAAAAATAGGTGATTTGGCTAGCTACAGTGAAATCTCGATGGAGTGGG
664 **S H Q F E Q L S G S I L W M A P E V I R**
2041 TCCCACAGTTGAACAGTTGCTGGATCCATTGGATGGCACCAGAACAGTCAAG
684 **M Q D K N P Y S F Q S D V Y A F G I V L**
2101 ATGCAAGATAAAAATCCATACAGCTTCAAGTCTGATATGCATTGGAATTGTTCTG
704 **Y E L M T G Q L P Y S N I N N R D Q I I**
2161 TATGAATTGATGACTGGACAGTTACCTTATTCAAACATCAACACAGGGACCAGATAATT
724 **F M V G R G Y L S P D L S K V R S N C P**
2221 TTTATGGGGACGAGGATACCTGTCTCCAGATCTCAGTAAGGTACGGAGTAACGTCCA
744 **K A M K R L M A E C L K K K R D E R P L**
2281 AAAGCCATGAAGAGATTAAATGGCAGAGTGCCCTAAAAAGAAAAGAGATGAGAGACCAC
764 **F P Q I L A S I E L L A R S L P K I H R**
2341 TTTCCCCAAATTCTGGCCTCTATTGAGCTGGCTGGCCCGCTATTGCCAAAAATTCAACCGC
784 **S A S E P S L N R A G F Q T E D F S L Y**
2401 AGTGCATCAGAACCCCTCTGAATGGGCTGGTTCAAACAGAGGATTTAGTCTATAT
804 **A C A S P K T P I Q A G G Y G A F P V H**
2461 GCTTGTGCTTCTCCAAAACACCCATCCAGGCAGGGGATATGGTGCCTGTCCAC
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2521 TGAAACAAATGAGTGAGAGAGTTCAAGGAGAGTAGCAACAAAGAAAATAATGAACATA
2581 TGTTTGCTTATATGTTAAATTGAATAAAACTCTTTTTTAAGGTGAACCAAAGA
2641 AAAAAAAAAAAAAAAAAAAAAACCC