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Supplemental Data

A Specific *IFIH1* Gain-of-Function Mutation Causes Singleton-Merten Syndrome

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Table S1. Whole exome sequencing: filtering criteria and output.

Family	Filter criteria	Variants/Genes
1+2+3	Basic filtering for all families: coverage>6; phred scaled variant quality score>10; allele read frequency>30%; VQSLOD score>2; minor allele frequency (EVP+1000genomes) <0.25%; minor allele frequency (in-house,N=511)<2%; variants on enrichment target+100bp; protein coding genes; RVIS score<95%; predicted change in protein sequence or major effects on core splice sites	Not documented
1	shared by affected patients (2)	*ADAM33, APOA5, ARHGAP39, ATL2, ATR, AXDND1, BOK, BSN, C16orf74, C3orf23, C3orf62, CAPN3, CCDC83, CEACAM4, CFI, CILP, CLK4, COL1A1, COL23A1, CSNK1A1L, CYP2E1, CYR61, DAPK2, DEPDC5, DHX29, DHX34, DLC1, DNAH2, DUSP15, EFR3B, ENKUR, EPC2, FAM178B, FBXO16, FCHO2, FREM2, HELB,* ***IFIH1:p.R822Q****, IL6ST, INSR, IP6K1, IRAK4, ITGA1, ITGA9, ITPKB, JARID2, KBTBD12, KCNK1, LONP1, LRRFIP2, MMAB, NAT6, NBAS, NEB, OBSCN, P2RY11, PFAS, PHTF2, PKHD1, PLEC, PLEKHG3, PPAN, PPAN-P2RY11, RASA2, SDSL, SEMA5A, SLC35D1, SLC43A2, SLC6A16, SLCO1B1, SLCO3A1, SPHKAP, SPTBN2, TAF6, TET3, TMEM41B, TRAPPC6A, TXNDC16, WARS, WARS2, WDR12, WNK1, ZFHX4, ZNF485, ZNF497, ZNF696*
2	shared by affected patients (2) while absent in unaffected family members (2)	*A2M, ABCA7, ANO2, ASB10, CPE, DTNA,* ***IFIH1:p.R822Q****, KARS, KCNH8, KIAA0947, LARP4B, MTRR, NUMB, PRB4, RPE65, SH3TC2, SLC4A3, TRAF3IP1, TTLL5, ZNF749*
3	*de novo* mutations in the affected patient	c.308-1G>A in *SPECC1L* c.2465G>A (p.R822Q) in ***IFIH1***

Table S2. Primer sets used in this study

	Forward primer (5′ to 3′)	Reverse primer (5′ to 3′)
*IFN	ATTGCTCTCCTGTTGTGCTT	TCTCCTCAGGGATGTCAAAGT
*MDA5	GGGGCATGGAGAATAACTCA	TGCCCATGTTGCTGTTATGT
*IFI27	ACTCCTCCAATCACAACTGTAG	CCTCTGCTCTCACCTCATCA
*IFI44L	TCGTATTTGTTGAACCAGGGA	GCGAAGATTCACTGGATGAAAG
*IFIT1	GCTCCAGACTATCCTTGACCT	CCACAAGACAGAATAGCCAGAT
*ISG15	GCCTTCAGCTCTGACACC	CGAACTCATCTTTGCCAGTACA
*RSAD2	GFCACAGGAGATAGCGAGAATG	CGTGAGCATCGTGAGCAAT
*IGLEC1	TGTCACTGCCTGTCCTTC	CAAGTGCTCAGCCACCAA
*GAPDH	AGGTCGGAGTCAACGGATTTG	TGTAAACCATGTAGTTGAGGTCA
@human-MDA5	AAAGGATCCATGTCGAATGGGTATTCCACAGAC	GATCTCGAGCTAATCCTCATCACTAAATAAACAGCA
#human-MDA5- MUT	ATGGTCCAGGCCCGTGGTCAA	GCTCTCATCAGCTCTGGCTTG
	GCCAGAGCTGATGAGAGC	ACCACGGGCCTGGACCAT

Note: *primer sets were designed to quantitatively amplify the indicated genes; @ primer sets were used to clone the indicated genes; #primer sets were used to generate single nucleotide mutation. Restriction enzyme sites in primers were underlined.