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Supplemental Data

Mutations in the *SPTLC2* Subunit

of Serine Palmitoyltransferase Cause

Hereditary Sensory and Autonomic Neuropathy Type I

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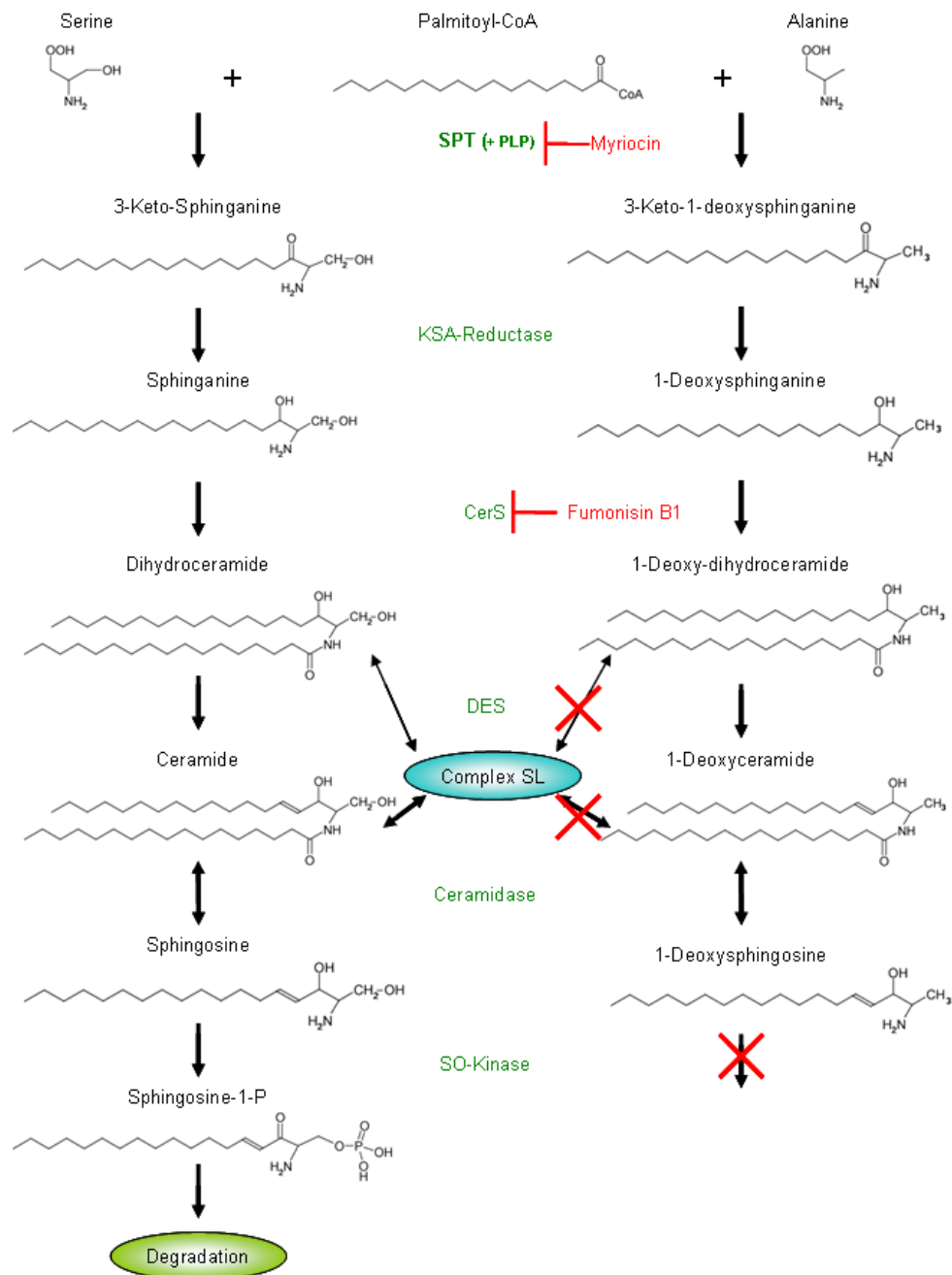


Figure S1. De Novo Sphingolipid Biosynthesis Pathway

Left: the canonical pathway with L-serine; right the alternative, disease-related pathway with L-alanine. Condensation with L-alanine instead of L-Serine gives rise to a metabolite lacking the C₁ hydroxyl group, obstructing conversion to complex SLs and degradation. The enzymes of the pathway are denoted in green. Myriocin and Fumonisin B1 are mycotoxins inhibiting the enzymes SPT and CerS respectively. SPT: serine palmitoyltransferase; PLP: pyridoxal-5'-phosphate; KSA: 3-keto-sphinganine; CerS: Ceramide synthase; DES: dihydroceramide desaturase; SO: sphingosine; SL: sphingolipids.

Table S1. Exon Primers Used for PCR and Direct Sequencing of *SPTLC2*

	Forward primer (5'-3')	Reverse primer (5'-3')
Exon 1	gcagccatttccggtttc	ggattgccagcggatgg
Exon 2	ttacaggtgtgagccagtgc	tgtcaaaaataactaagatttc
Exon 3	cacaatcttgacgtaatgaaa	cctcagctgctactcctatttg
Exon 4	tctgcttcttttgtgtcacc	tcagaaaaacaaagcattctca
Exon 5	agtctgaaaaggacacaacaca	gctcactctgactgcttttcaa
Exon 6	tgatcactgtgctgttgtgc	aagactggaccggaagaacat
Exon 7	tgaggcatggtttctgaatg	tgctgactctgtttccaggt
Exon 8	acttcagcctggacaatgga	gagcctaaaccagaggcaaa
Exon 9	gaccatgttggtgacctgt	gtccatggaaccacacacc
Exon 10	aaatattttatggtgaaatggaaaa	tgcatatgtaccaaataagagg
Exon 11	gcctgcacaccaaagagtt	cactgtcaccctctgtct
<i>Exon 12</i>	<i>cctgccgaaggataatcttg</i>	<i>gcaaaggaaggattagaagca</i>

Table S2. Exon Primers Used for PCR and Direct Sequencing of *SPTLC3*

	Forward primer (5'-3')	Reverse primer (5'-3')
Exon 1	caaacgggtgcagagacc	aaccctcataagatgaactcta
Exon 2	taacaggagaatgctaacctt	cacttagagaggagtaggc
Exon 3	agataaccttctacctctgttctaa	ttgtcatctagtggccat
Exon 4	gaatcgtgcataatcctgg	agagacagacacaaggaat
Exon 5	aatcttggccttgttga	tctaacaaggacctactcaga
Exon 6	ctgtccccacaagttgttt	gtcacctgaagagcagaa
Exon 7	ttaggtctgagtgtgaacata	tctgttagctaggaaagggtga
Exon 8	ggagggtattgttagtta	ggtgtggtgaactgaattg
Exon 9	agggatgggactagatgta	gggagattaatgaggcagaa
Exon 10	atgcttccaagttgac	cataatctaacgcctgtgc
Exon 11	catattcctttttgtcag	taaataaccaagagaaac
<i>Exon 12</i>	<i>gctattaatctgggctctg</i>	<i>ggagaaatccatttatattccttg</i>

Table S3. Sequences of Primers Used for Cloning and Site-Directed Mutagenesis

	Primer sequence (5'-3')
SPTLC2_attb1	gggacaagtttgtaaaaaagcaggctatgcggccggagcccggaggetgct
SPTLC2_attb2	ggggaccactttgtacaagaaagctgggtccgtcttctgtttcttcatacgtc
SPTLC2_V359M_fw	ccacaggccggggtatggtggagtac
SPTLC2_V359M_rv	gtactccaccataccccggcctgtgg
SPTLC2_G382V_fw	gaacgttcacaaagagttttgttctctggaggatattgg
SPTLC2_G382V_rv	ccaatatacctccagaagcaaaaaactctttgtgaacgttc
SPTLC2_I504F_fw	ttctgccacccaattttgagtccagagcc
SPTLC2_I504F_rv	ggctctggactcaaaaattggggtggcaggaa
LCB2_HA_fw	gccactacctgagcccgtgtcagcgtagtctgggacgtcgtatgggtaagcgtagtctg ggacgtcgtatgggtaagcgtagtctgggacgtcgtatgggtagacaccctccttatta catttc
LCB2_HA_rv	gaaatgtaataaggaggggtgtctaccatacgcgtcccagactacgcttaccatacgc acgtcccagactacgcttaccatacgcgtcccagactacgctgacaacgggctcagg tagtggc
LCB2_V346M_fw	gcccactggtcgcggtatgtgtgaaatatttggcg
LCB2_V346M_rv	cgccaaatatttcacacataccgcgaccagtgggc
LCB2_G369V_fw	gtactttcactaagtcgtttgttctgctggtggttacattg
LCB2_G369V_rv	caatgtaaccaccagcagcaacaacgacttagtgaaagtac
LCB2_I491F_fw	cttactctgctactccgctgtttgaatcaagagtaagattctg
LCB2_I491F_rv	cagaatcttactcttgattcaaacagcggagtagcaggataag
LCB2_K366T_fw	ctaagggtactttcactacttcgtttggctgctgctggtg
<i>LCB2_K366T_rv</i>	caccagcagcaccaaacgaagtagtgaaagtaccattag