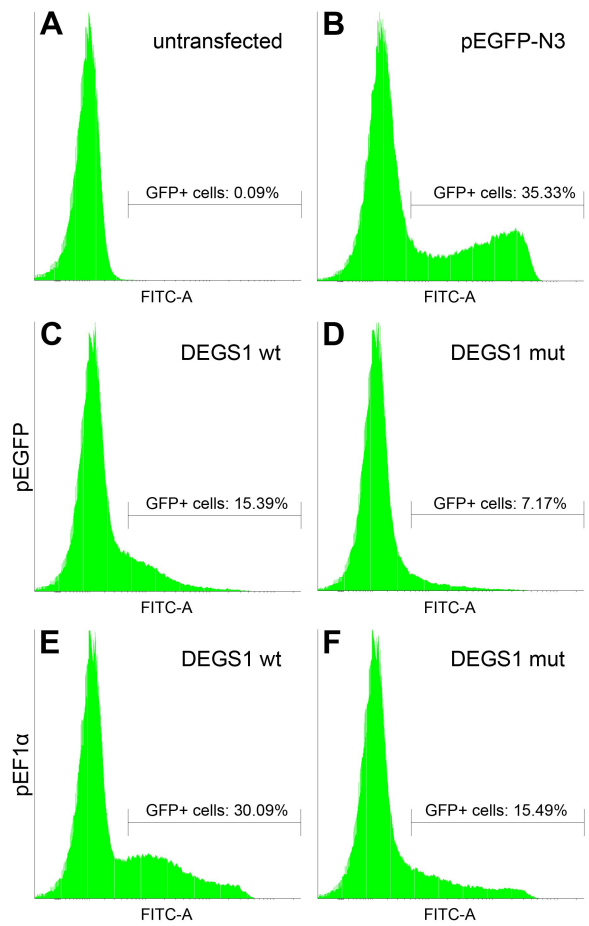


Supplemental data

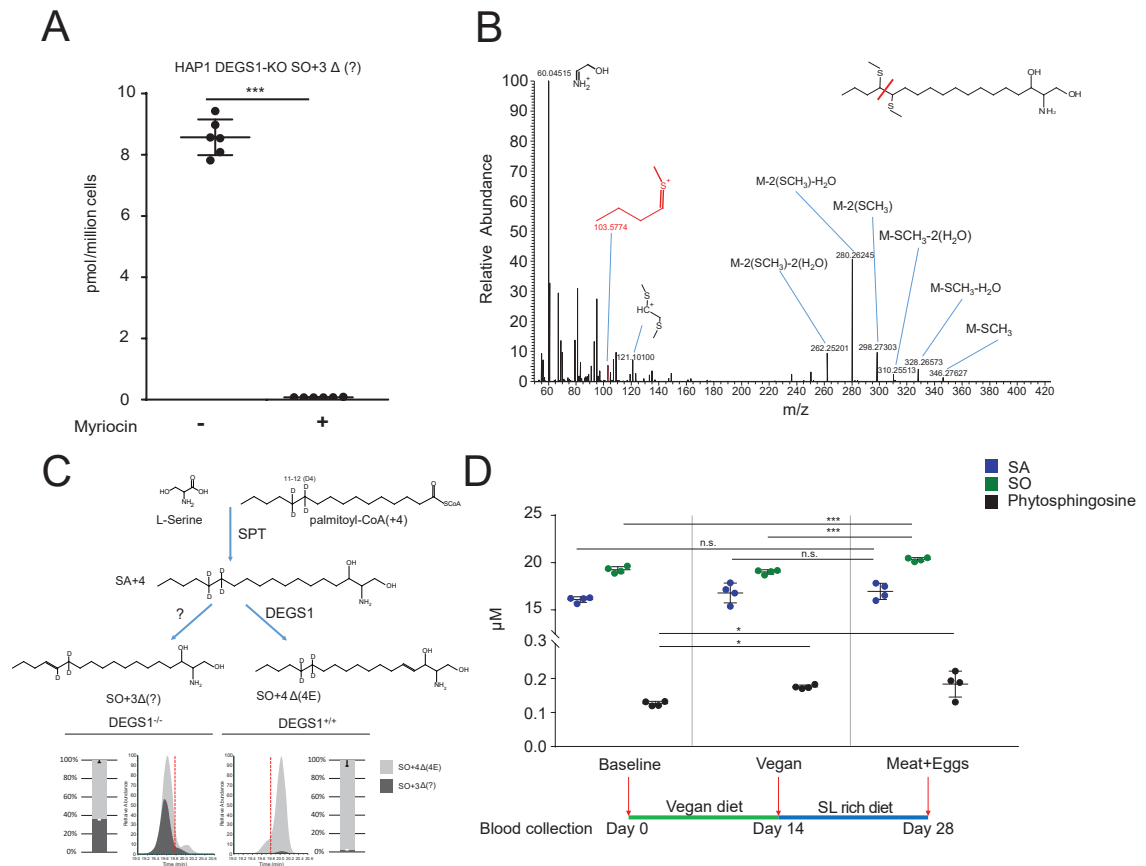
Aberrant DEGS1 sphingolipid metabolism impairs nervous system function in humans

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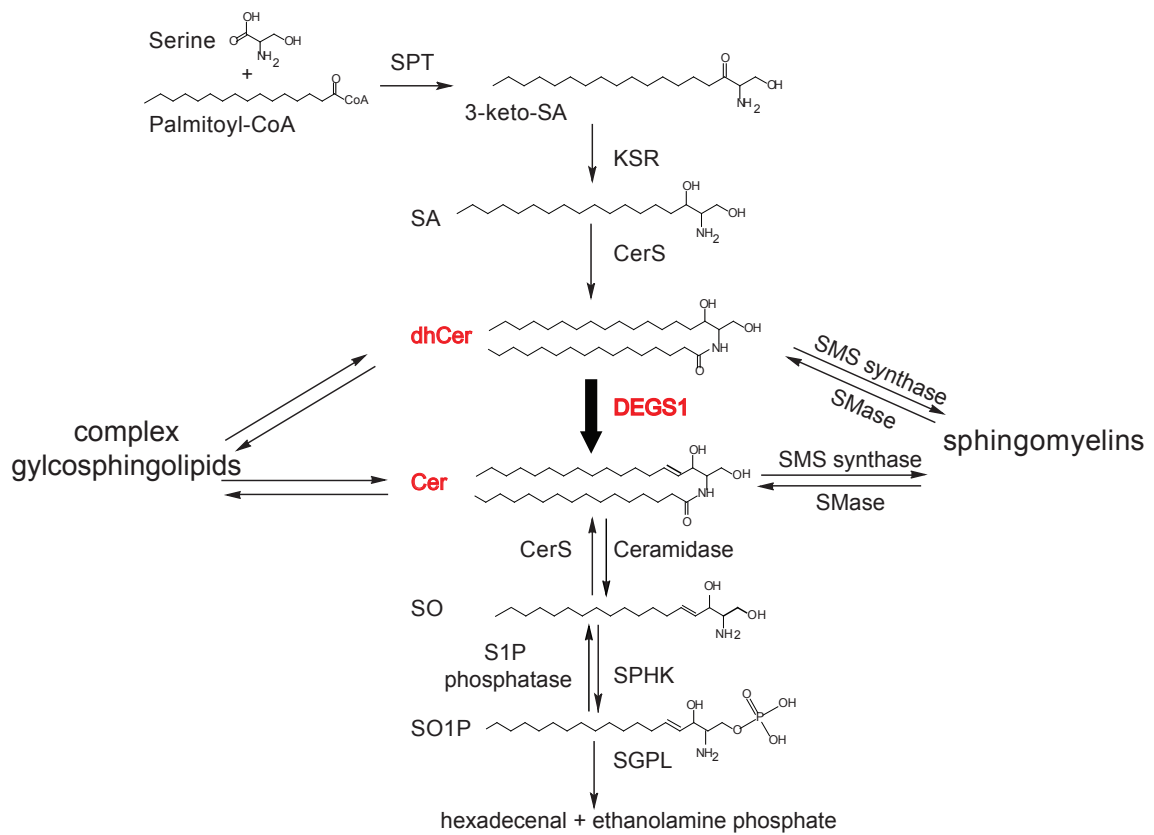
*,# These authors contributed equally to this work.



Supplemental Figure 1: FACS analysis of HAP1 cells (untransfected cells in **(A)** transfected with either, **(B)** pEGFP-N3, **(C)** wt DEGS1-pEGFP, **(D)** mut DEGS1-pEGFP and **(E)** pEF1 α - wt DEGS1-EGFP or **(F)** pEF1 α - mut DEGS1-EGFP.



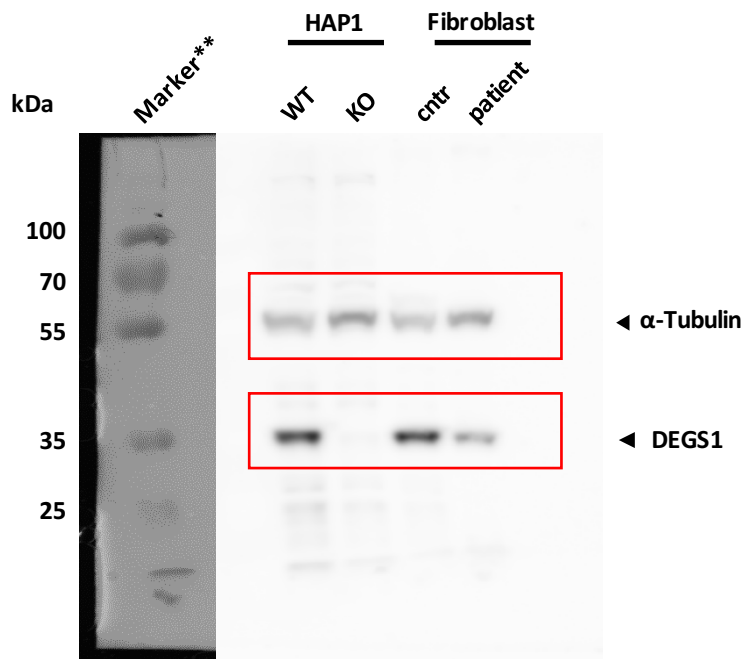
Supplemental Figure 2: (A) Quantification of the SO+3 Δ (?) peak in HAP1 DEGS1^{-/-} cells cultured in presence or absence of Myriocin. Error bars indicate mean \pm SD. **(B)** Structural analysis of native, unlabeled SO Δ (?) after chemical derivatization with dimethyl disulfide followed by collision induced HCD fragmentation. The fragment (m/z 103.5774) confirmed a Δ 14 DB position of the SO isomer. **(C)** Supplementation of HAP1 WT^{+/+} and DEGS1^{-/-} cells with d4 (C₁₁-C₁₂) labelled palmitate. HAP1 WT cells produce exclusively the canonical SO+4 while the isomeric SO Δ 14Z was found to be SO+3 labelled. Error bars indicate SD. **(D)** Change in total plasma SA, SO and phytosphingosines (phytoSO) levels after the supplementation with either a vegan (green) or a SL rich diet (blue). Error bars indicate the mean \pm SD. *P < 0.05, **P < 0.01, and ***P < 0.001 (one way ANOVA and Tukey's correction for multiple testing).



Supplemental Figure 3: Overview of the sphingolipid de-novo synthesis pathway. DEGS1 catalyzes the conversion of dhCer to Cer by the introduction of a Δ^4E double bond. Complex sphingolipids (e.g sphingomyelins) can be formed from dhCer and Cer.

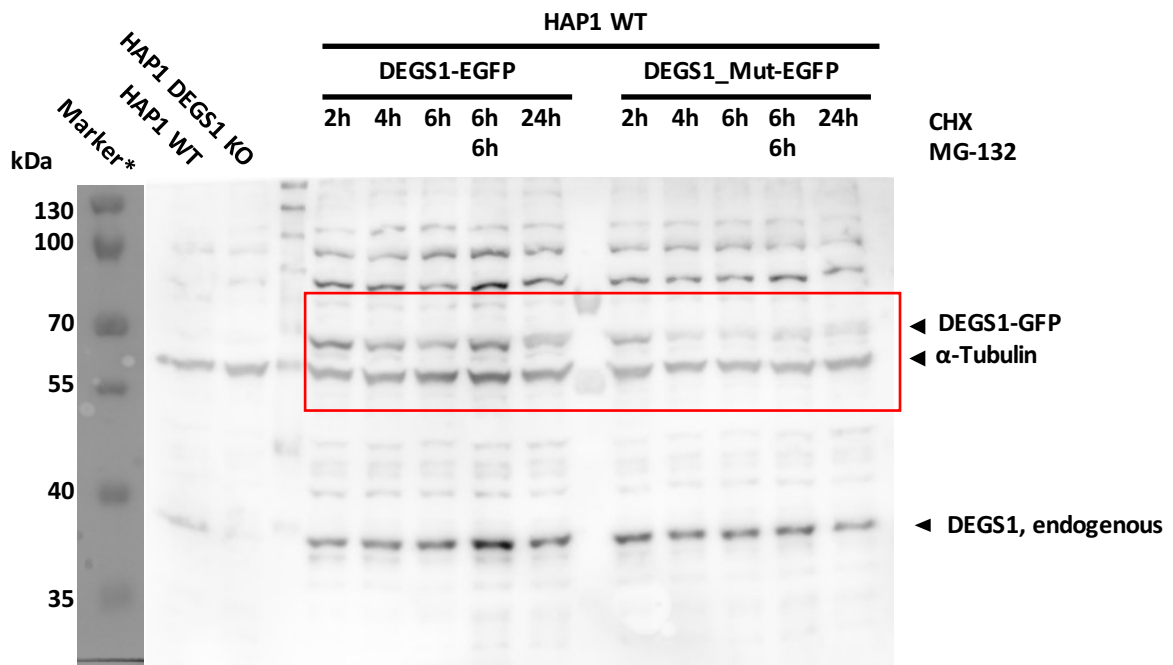
Supplemental Table 1: Whole exome sequencing data from five family members.

Supplemental Video: Index patient at age 22.



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Full unedited gel for Figure 2F



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