proplatelet formation causing thrombocytopenia

Sphingolipid dysregulation due to lack of functional KDSR impairs proplatelet formation causing thrombocytopenia


Disclosures: Funding - T.K.B is supported by the British Society of Haematology and NHS Blood and Transplant. K.F and C.V.G. are supported by the Fund for Scientific Research-Flanders (FWO Vlaanderen, Belgium; G.0B17.13N) and by the Research Council of the University of Leuven (BOF KU Leuven, Belgium; OT/14/098). C.V.G is holder of the Bayer and Norbert Heimburger (CSL Behring) Chairs. The structured illumination microscope was acquired through a CLME grant from Minister Lieten to the VIB BiolImaging Core, Leuven. J.H is supported by the Fund for Scientific Research-Flanders (FWO Vlaanderen, Belgium) grant no.1S00816N. A.K and B.J are funded by the National Institute for Health Research (NIHR) Biomedical Research Centre (RG64245). M.F. is supported by the British Heart Foundation (BHF) Cambridge Centre of Excellence (RE/13/6/30180). The Ouwehand laboratory receives support from the BHF, Bristol-Myers Squibb, European Commission, MRC, NHS Blood and Transplant, Rosetrees Trust, the NIHR Biomedical Research Centre based at Cambridge University Hospitals NHS Foundation Trust, and the University of Cambridge. The Tg(cd41:EGF)11 line was a gift from Professor Leonard Zon (Hematology Division, Brigham and Women’s Hospital, Boston, MA).

Contributions: T.K.B analysed the results, performed the iPSC and iMK experiments, and wrote the manuscript. E.T and D.G performed statistical analyses and E.T edited the manuscript. C.T. performed stem cell differentiations. J.H. performed granule immunostainings and quantifications. M.D.R. performed zebrafish experiments. F.B assisted with cDNA library synthesis. L.G and D.S performed RNA-seq analysis. B.J performed mass spectrometry of sphingolipids. M.F and A.K analysed results and edited the paper. D.W provided sample logistics, QC and whole genome sequencing oversight. O.S analysed the sequencing results. C.G and K.G edited the paper. V.L and C.V.G are clinicians following up this pedigree. W.H.O leads the NIHR BioResource- Rare Diseases and co-wrote the paper. K.F. designed the study and analysis plan, and co-wrote the paper.