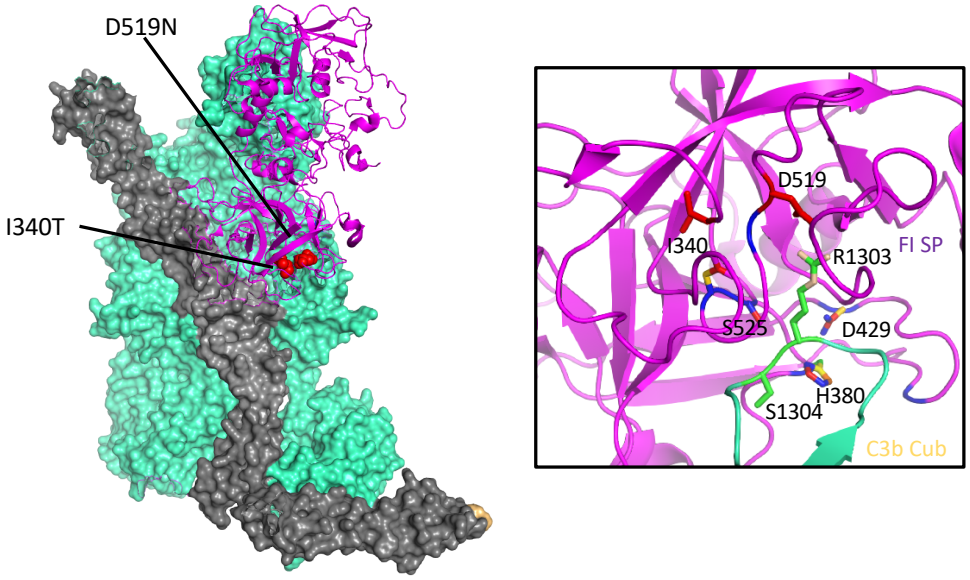
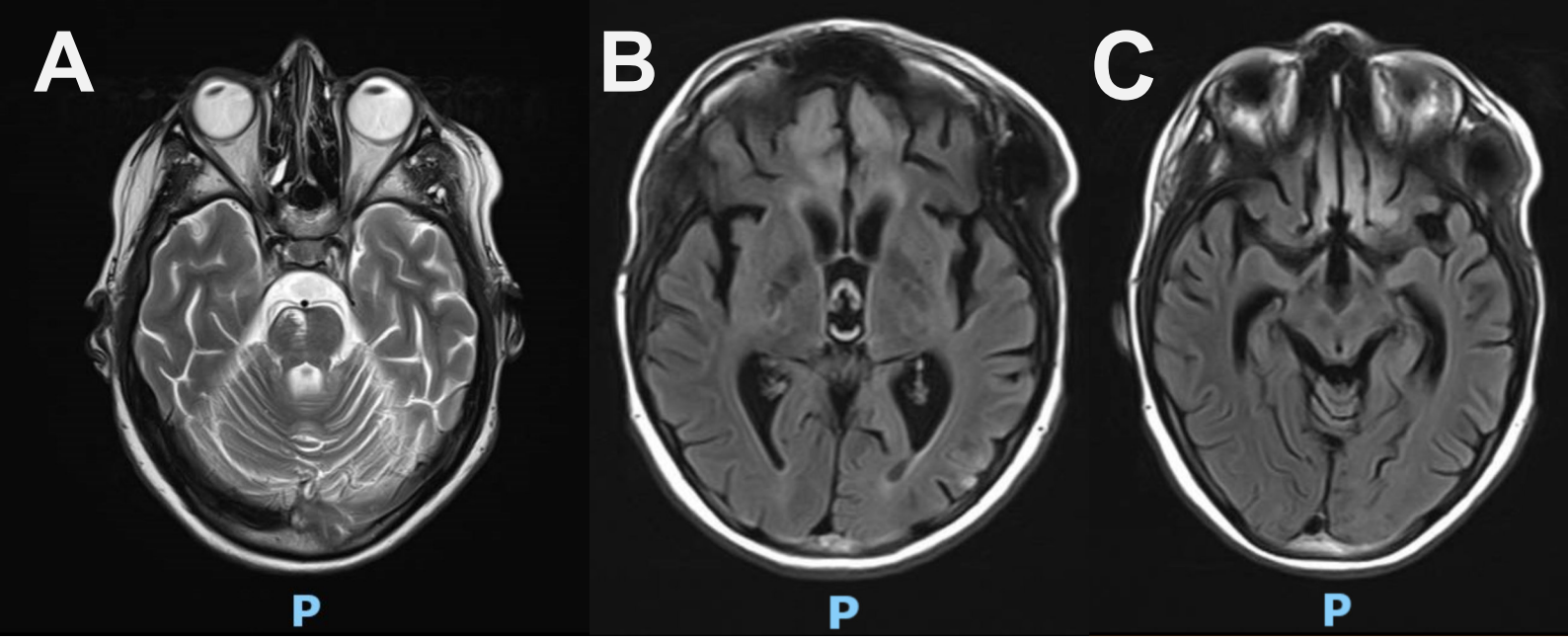
Supplementary Figure 1- Functional consequences of CFI I I340T and D519N mutations are explained by their location on the C3b/CFH/FI tri-molecular complex



An x-ray–derived co-crystal structure of Factor H CCP1-4_19-20/C3b/Factor I was used to model the rare genetic variants and displayed with Pymol (Delano Scientific). The location of the Factor I I340T and D519N variants (red spheres) are shown within a co-crystal structure of Factor I (blue), Factor H (dark gray) and C3b (wheat). Insert, The SP domain of factor I (blue) binds the first scissile loop in C3b CUB domain (wheat) in its active site (catalytic triad H380, D429 and S525). Factor I first cleaves C3b between R1303–S1304. The rare genetic variants identified are important in the interaction of factor I with C3b. The terminal NH^2 group of I340 of of the SP domain of FI stabilize the oxyanion hole while D519 of the SP domain binds to R1303 of the C3b CUB domain. (Protein Database ID code **5O32**). [Xue]

Kavanagh D, Richards A, Noris M, Hauhart R, Liszewski MK, Karpman D, et al. Characterization of mutations in complement factor I (CFI) associated with hemolytic uremic syndrome. Mol Immunol. 2008;45(1):95-105.

Xue X, Wu J, Ricklin D, Forneris F, Di Crescenzio P, Schmidt CQ, et al. Regulator-dependent mechanisms of C3b processing by factor I allow differentiation of immune responses. Nature Structural &Amp; Molecular Biology. 2017;24:643.



Supplementary Figure 2. Representative MRI at six months post-presentation.

Imaging shows multifocal encephalomalacia and gliosis especially bi-frontally, in the left parietal lobe, post-central gyrus and right mid-brain and pons; with several small areas of cortical gliosis. There is marked generalised volume loss especially of white matter and some volume loss in deep grey nuclei (A= T2 weighted; B, C = FLAIR sequence).