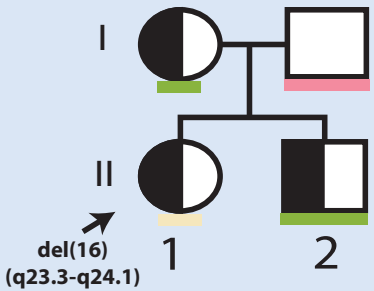
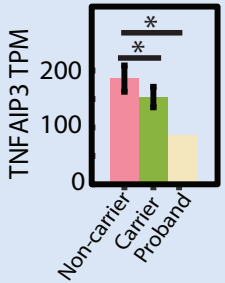
Evan's Syndrome Driven by a Familial Novel TNFAIP3 Splice Variant and De-Novo MBTPS1 Deletion

Genotype

c. -15.-2A A>G, heterozygous

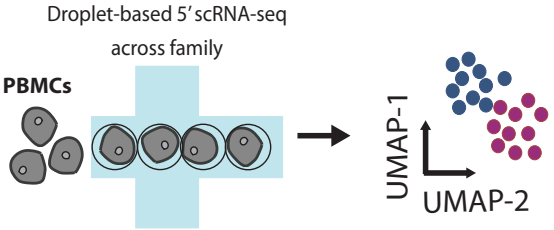




Reduced A20 expression in splice variant carriers & more significant in proband

Single-Cell RNA-seq Reveals Skewed Cytotoxic Immune Skewing and Activation in Proband

Phenotype



Enrichment of cytotoxic CD8+ T cells, Natural Killer cells, and non-classical monocytes

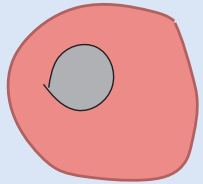
Flow Cytometry and scRNA-seq suggests lineage specific NF-kB Dysegulation

Mechanism

TFNAIP3 (A20) ⬇
Impaired NF-κB negative feedback

MBTPS1 (S1P) ⬇
Reduced ATF6 UPR buffering
Altered SREBP processing

Monocyte
NF-κB ⬆
UPR ⬆
Inflammation ⬆



CD8 T-cell
NF-κB ⬇
Exhaustion ⬆
Cytotoxic IFN ⬆

Chronic Inflamatory Loop = ***Evan's Syndrome (AIHA and ITP)***