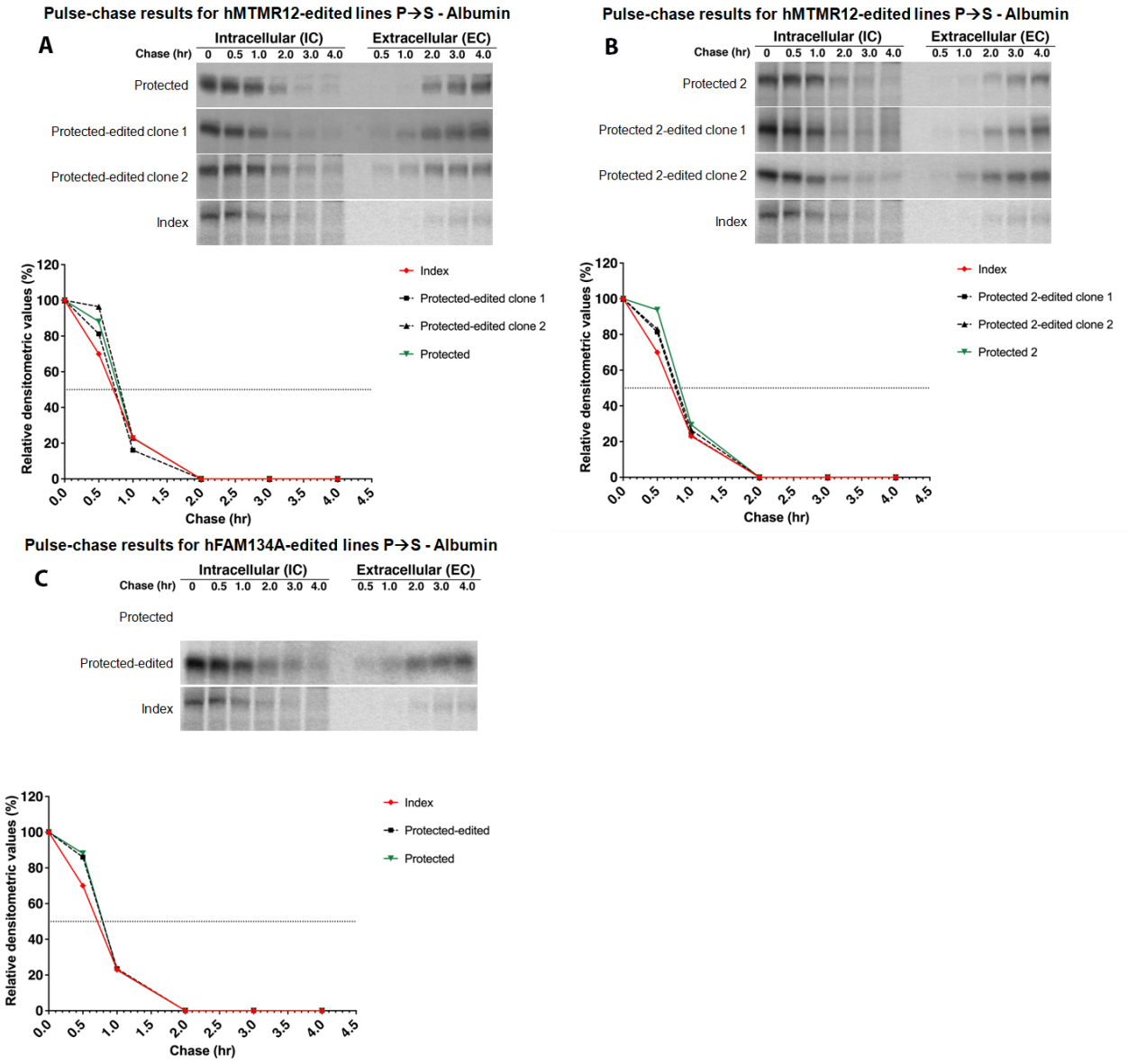


Fig. S5. Effect of introducing MTMR12 (**A**,**B**) and FAM134A (**C**) variants into iHeps from protected subjects on kinetics of albumin fate.

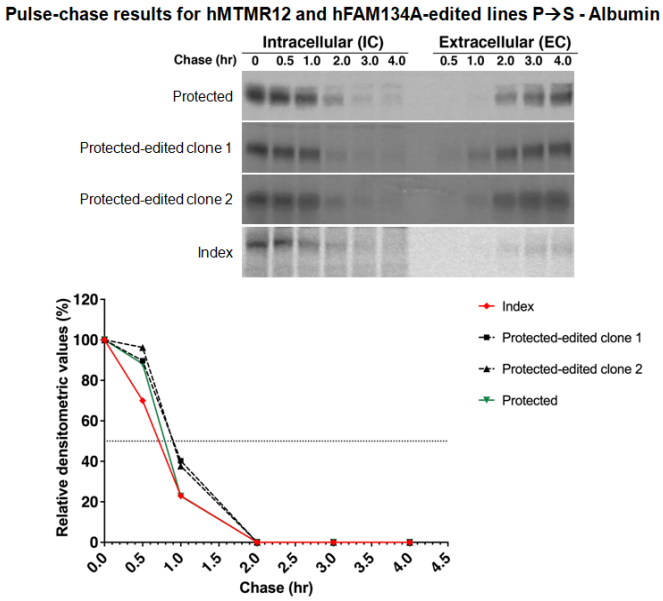
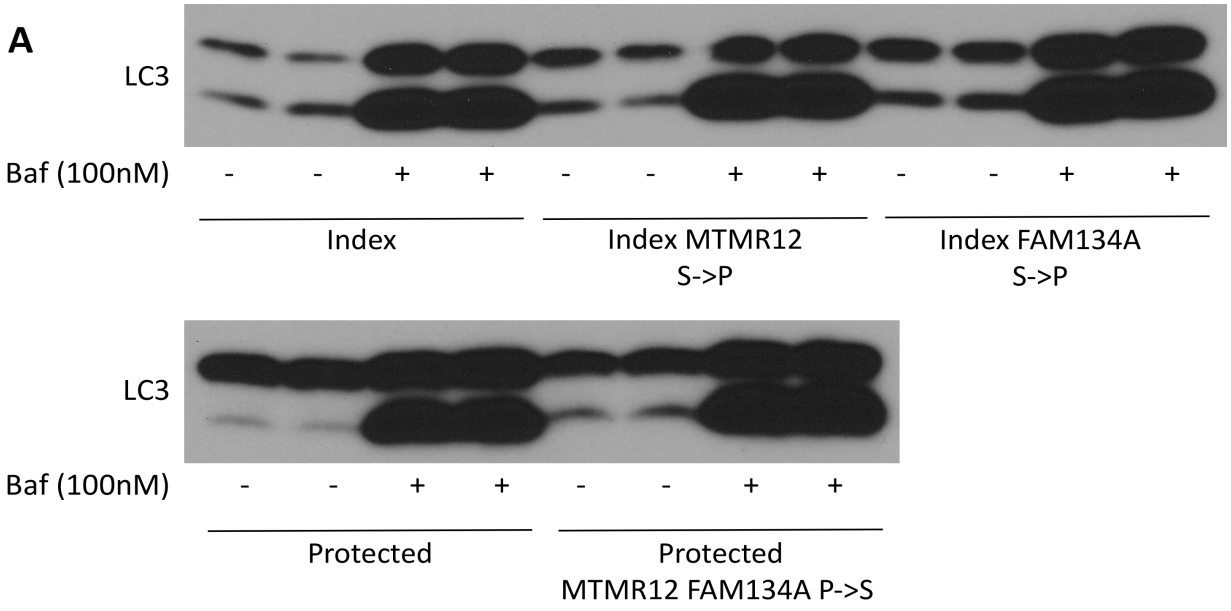


Fig. S6. Effect of introducing both MTMR12 and FAM134A variants into iHeps from protected subject on kinetics of albumin fate.



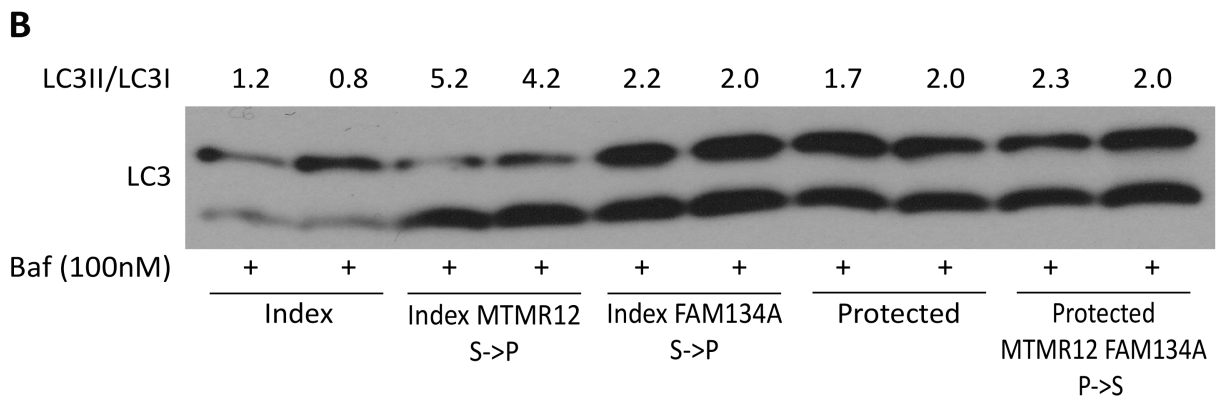


Fig S7

Effect of MTMR12 and FAM134A variants on autophagy flux in iHeps from index and protected subjects. In **A** the results are shown for duplicate samples after 24 hours in the absence or presence of bafilomycin (100 nM). In **B** the samples treated with bafilomycin are compared to each other with densitometric analysis of LC3II to LC3I ratio shown at the top.

ID	Chr	Pos(hg38)	REF	ALT	Gene	AA change	SIFT pred	Polyphen 2 HDIV pred	ExAc overall
H_UY-F3-F3	2	219182235	A	A	FAM134A	.	.	.	.
H_UY-F4-F4	2	219182235	A	A	FAM134A	.	.	.	.
H_UY-F5-F5	2	219182235	A	G	FAM134A	FAM134A:NM_001321110:exon8:c.A617G:p.N206S,RETREG2:NM_001321109:exon9:c.A617G:p.N206S,RETREG2:NM_024293:exon9:c.A1238G:p.N413S	D	D	0.0015
H_UY-F3-F3	5	32229921	G	G	MTMR12	.	.	.	.
H_UY-F4-F4	5	32229921	G	G	MTMR12	.	.	.	.
H_UY-F5-F5	5	32229921	G	A	MTMR12	MTMR12:NM_001294344:exon14:c.C1771T:p.R591C,MTMR12:NM_001294343:exon15:c.C1939T:p.R647C,MTMR12:NM_001040446:exon16:c.C2101T:p.R701C	D	D	0.0016

Table S1

ID	Chr	Pos(hg38)	REF	ALT	Gene	AA change	SIFT pred	Poly phen2	ExAC overall	gnomeAD _exome	gnomeAD _genome	CADD_ phred	MetaSVM _pred
H_UY-F5-F5	2	219182235	A	G	FAM134A	FAM134A:NM_001321110:exon8:c.A617G:p.N206S,RETREG2:NM_001321109:exon9:c.A617G:p.N206S,RETREG2:NM_024293:exon9:c.A1238G:p.N413S	D	D	0.0015	0.0018	0.0021	23.7	T
H_UY-F5-F5	5	32229921	G	A	MTMR12	MTMR12:NM_001294344:exon14:c.C1771T:p.R591C,MTMR12:NM_001294343:exon15:c.C1939T:p.R647C,MTMR12:NM_001040446:exon16:c.C2101T:p.R701C	D	D	0.0016	0.0018	0.0017	29.7	D

Table S2. Comprehensive annotations of the MTMR12 and FAM134A variants.
Chr=chromosome,
Pos=position,
REF=reference allele,
ALT=alternative allele,
AA change=amino acid change,
Polyphen2=polyphen2 HDIV prediction identifying human damaging mutations by assuming differences between human proteins and their closely related mammalian homologs as non-damaging
ExAc overall=ExAC allele frequency
gnomAD_exome=gnomAD minor allele frequency data based on whole-exome sequencing
gnomAD_genome=gnomAD minor allele frequency data based on whole-genome sequencing
CADD_phred= CADD (Combined Annotation Dependent Depletion scores, version 1.6) phred-like rank score based on whole genom CADD raw scores
MetaSVM_pred=MetaSVM predictions
D=damaging
T=tolerated

Category	3 siblings (IDT; N-3)	30 additional ATD patients (IDT;N=30)	50 Controls (IDT; N=50)
Read length (bp)	151	151	151
# of reads per sample (M)	870.7	53.5	42.4
Median coverage at each targeted base (X)	230	51.1	38.6
Mean coverage at each targeted base (X)	259.5	51.1	49.8
% of all reads that map to target	25.37%	62.06%	55.1%
% of all bases that map to target	30.81%	52.89%	46.76%
% of targeted bases read at least 8x	98.80%	95.33%	95.02%
% of targeted bases read at least 10x	98.70%	94.06%	93.35%
% of targeted bases read at least 815	98.57%	83.89%	79.32%
% Mean error rate	0.73%	0.39%	0.92%

Table S3. Summary sequencing statistics for index and protected subjects, cohort of 30 ATC patients with liver transplants and cohort of 50 control ATD patients.