Identifying Novel Genes and Variants in Immune and Coagulation Pathways Associated with Macular Degeneration

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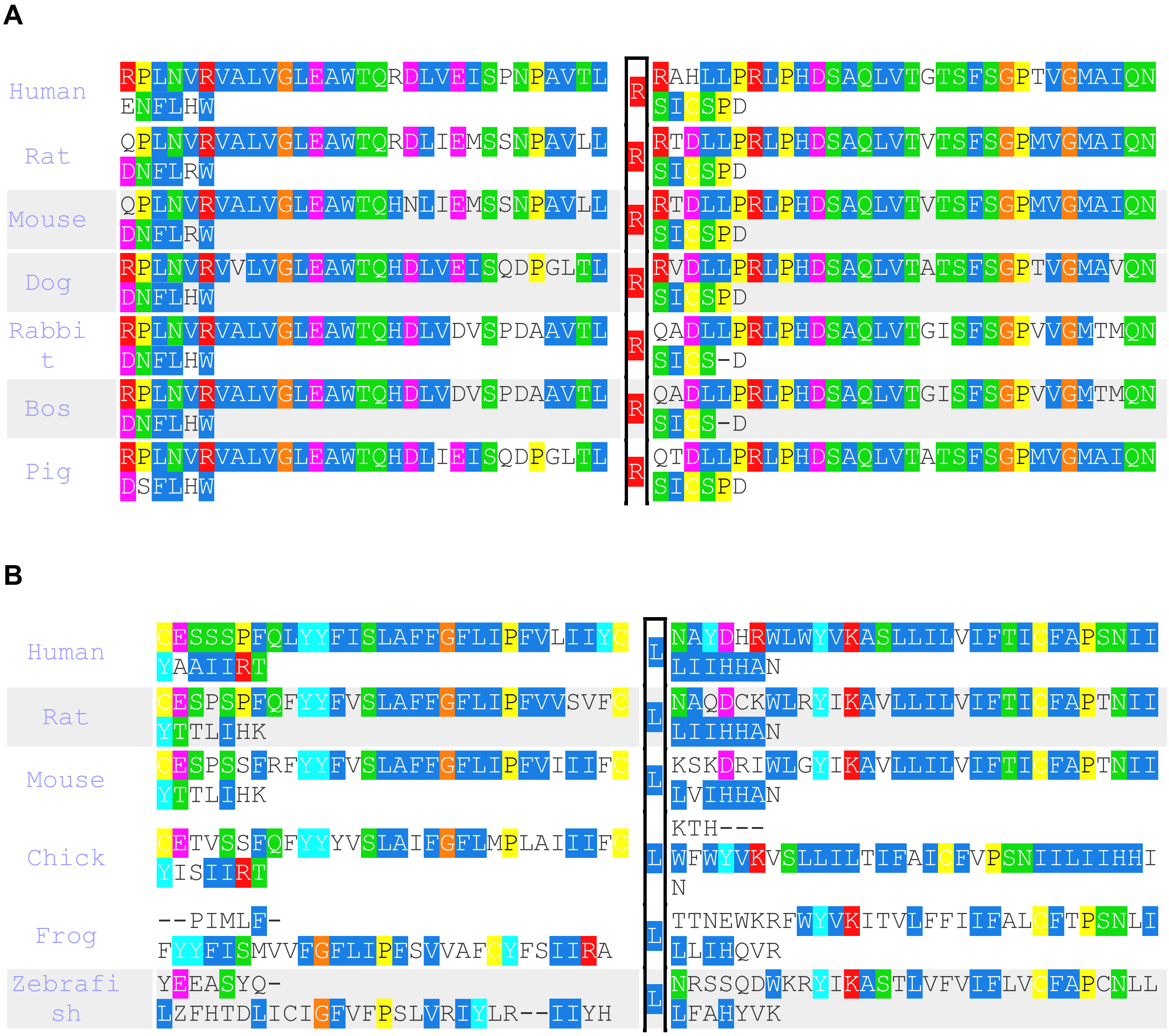
Supplementary Figure 1: Multiple sequence alignment and conservation of protein-coding variants in ADAM15 and F2RL2. Rectangles show the location of rs757672473 [Arg288Cys] in *ADAM15* (A) and rs147969213 [Leu289Arg] in *F2RL2* (B).



A

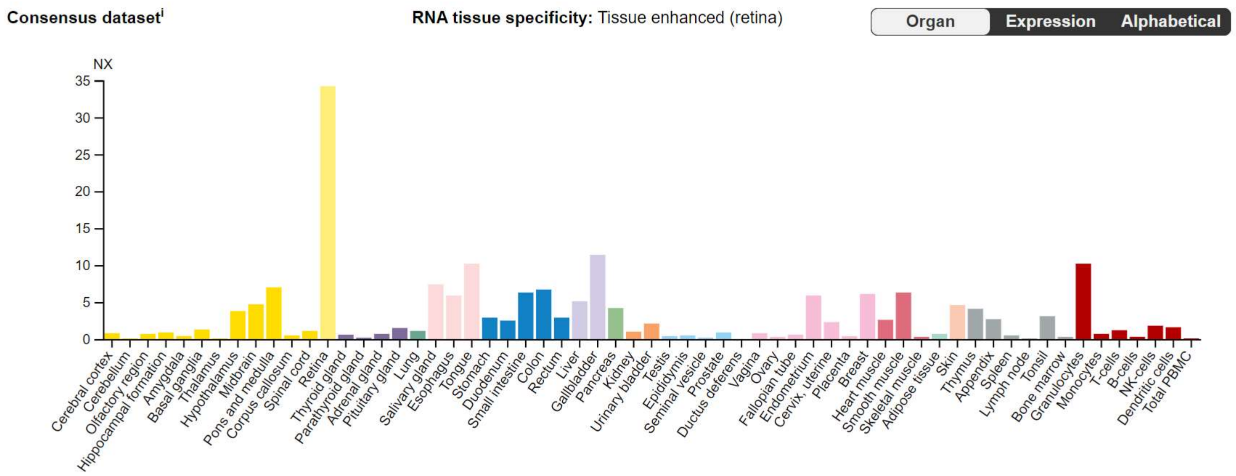
Human	RPLNVRVALVGLEAWTQRDLVEISPNPAVTLENFLHW	R	RAHLLPRLPHDSAQLVTGTSFSGPTVGMAIQNSICSPD
Rat	QPLNVRVALVGLEAWTQRDLIEMSSNPAVLLDNFLRW	R	RTDLLPRLPHDSAQLVTVTSFSGPMVGMAIQNSICSPD
Mouse	QPLNVRVALVGLEAWTQHNLIEMSSNPAVLLDNFLRW	R	RTDLLPRLPHDSAQLVTVTSFSGPMVGMAIQNSICSPD
Dog	RPLNVRVVLVGLEAWTQHDLVEISQDPGLTLDNFLHW	R	RVDLLPRLPHDSAQLVTATSFSGPTVGMAVQNSICSPD
Rabbit	RPLNVRVALVGLEAWTQHDLVDVSPDAAVTLDNFLHW	R	QADLLPRLPHDSAQLVTGISFSGPVVGMTMQNSICS-D
Bos	RPLNVRVALVGLEAWTQHDLVDVSPDAAVTLDNFLHW	R	QADLLPRLPHDSAQLVTGISFSGPVVGMTMQNSICS-D
Pig	RPLNVRVALVGLEAWTQHDLIEISQDPGLTLDSFLHW	R	QTDLLPRLPHDSAQLVTATSFSGPMVGMAIQNSICSPD

B

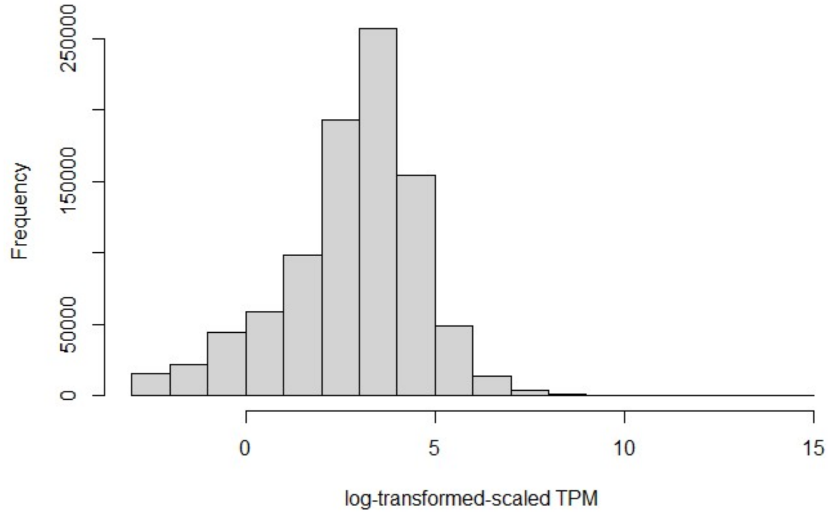
Human	CESSSPFQLYYFISLAFFGFLIPFVLIIYCYAAIIRT	L	NAYDHRWLWYVKASLLILVIFTICFAPSNIILIIHHAN
Rat	CESPSPFQFYYFVSLAFFGFLIPFVVSVFCYTTLIHK	L	NAQDCKWLRYIKAVLLILVIFTICFAPTNIILIIHHAN
Mouse	CESPSSFRFYYFVSLAFFGFLIPFVIIIFCYTTLIHK	L	KSKDRIWLGYIKAVLLILVIFTICFAPTNIILVIHHAN
Chick	CETVSSFQFYYYVSLAIFGFLMPLAIIIFCYISIIRT	L	KTH---WFWYVKVSLLILTIFAICFVPSNIILIIHHIN
Frog	--PIMLF-FYYFISMVVFGFLIPFSVVAFCYFSIIRA	L	TTNEWKRFWYVKITVLFFIIFALCFTPSNLILLIHQVR
Zebrafish	YEEASYQ-LZFHTDLICIGFVFPSLVRIYLR--IIYH	L	NRSSQDWKRYIKASTLVFVIFLVCFAPCNLLLFAHYVK

Supplementary Figure 2: F2RL2 expression levels measured in RNA-seq and single-cell RNA-seq. The figures are generated by the human protein atlas (more information are provided by https://www.proteinatlas.org/). (A) F2RL2 RNA expression in different tissues. Consensus Normalized expression (NX) levels for 55 tissue types and 6 blood cell types, created by combining the data from the three transcriptomics datasets (HPA, GTEx and FANTOM5) using the internal normalization pipeline. Color-coding is based on tissue groups, each consisting of tissues with functional features in common. (B) The distribution of log transformed TPM values for 18,156 genes in 60 tissues from FANTOM5. (C) Single-cell RNA-seq of F2RL2 expression in human retinas. The single-cell RNA-seq data are from Menon M et al. (Reference 28). pTPM: protein-transcripts per million.

A



B



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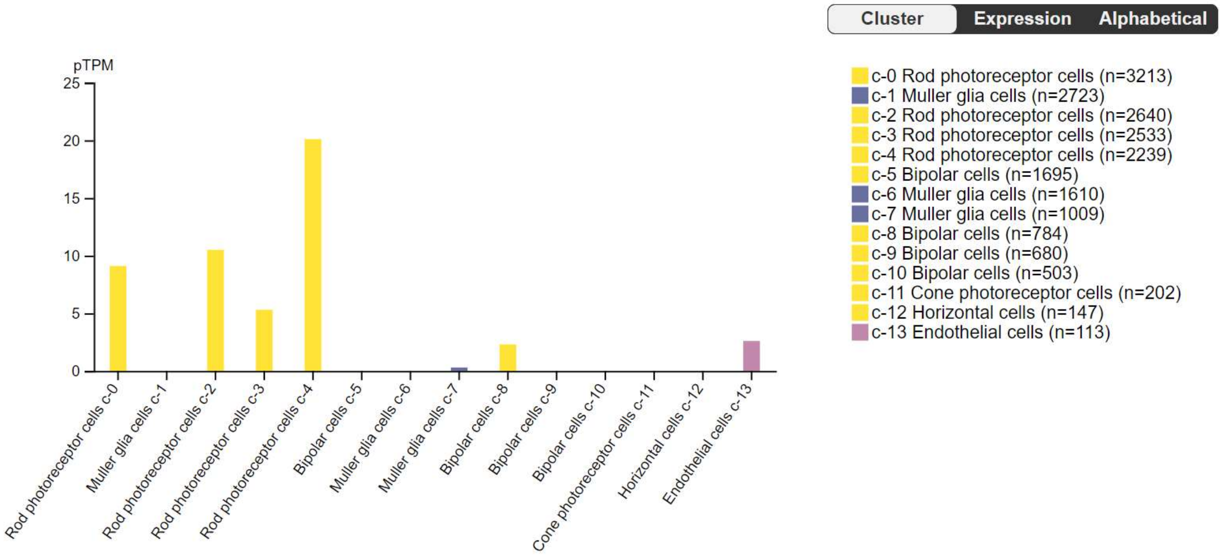
Cluster
Expression
Alphabetical
pTPM
25
20
15
10
5
0
Rod photoreceptor cells c-0
Muller glia cells c-1
Rod photoreceptor cells c-2
Rod photoreceptor cells c-3
Rod photoreceptor cells c-4
Bipolar cells c-5
Muller glia cells c-6
Muller glia cells c-7
Bipolar cells c-8
Bipolar cells c-9
Bipolar cells c-10
Cone photoreceptor cells c-11
Horizontal cells c-12
Endothelial cells c-13
c-0 Rod photoreceptor cells (n=3213)
c-1 Muller glia cells (n=2723)
c-2 Rod photoreceptor cells (n=2640)
c-3 Rod photoreceptor cells (n=2533)
c-4 Rod photoreceptor cells (n=2239)
c-5 Bipolar cells (n=1695)
c-6 Muller glia cells (n=1610)
c-7 Muller glia cells (n=1009)
c-8 Bipolar cells (n=784)
c-9 Bipolar cells (n=680)
c-10 Bipolar cells (n=503)
c-11 Cone photoreceptor cells (n=202)
c-12 Horizontal cells (n=147)
c-13 Endothelial cells (n=113)

Supplementary Figure 3: Plots of functional domains and mutations of proteins. (A) rs757672473 [Arg288Cys] in *ADAM15*; **(B)** rs147969213 [Leu289Arg] in *F2RL2*.