SUPPLEMENTAL MATERIAL

Chang et al., https://doi.org/10.1084/jem.20160999

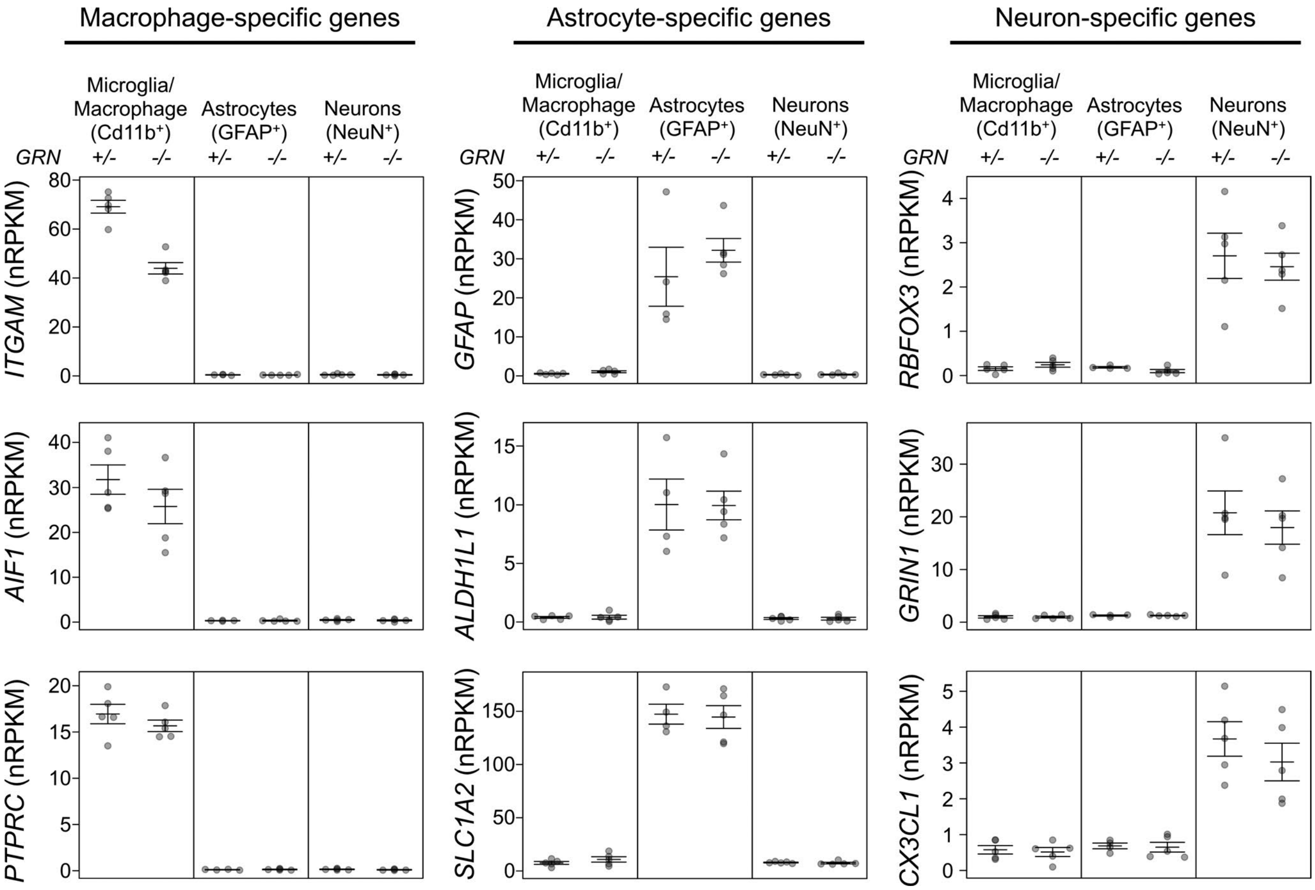

Figure S1. **Expression of representative cell-type–specific genes.** Normalized reads per kilobase of transcript per million mapped reads (nRPKM) of representative macrophage-specific (left), astrocyte-specific (middle), and neuron-specific (right) genes in sorted cells from *GRN*$^{+/-}$ and *GRN*$^{-/-}$ cortex. *n* = 5 mice from one experiment for all groups except *GRN*$^{+/-}$ astrocytes (*n* = 4 mice). Error bars represent mean ± SEM.

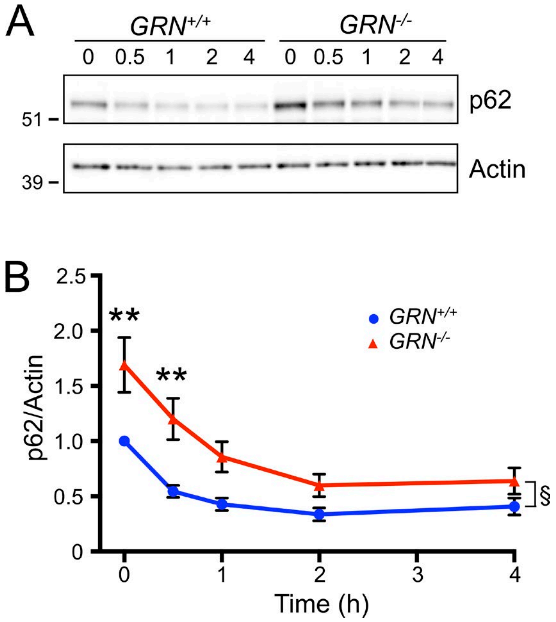

Figure S2. **Accumulation of p62 in *GRN*$^{-/-}$ BMDMs.** (A) Representative Western blot from *n* = 4 independent experiments of cell lysates from *GRN*$^{+/+}$ and *GRN*$^{-/-}$ BMDMs starved for the indicated time and probed for p62 and actin. The actin (loading control) immunoblots shown in Figs. 3 D and S2 A are identical; this actin immunoblot, as well as LC3 (Fig. 3 D) and p62 (Fig. S2 A), were obtained by reprobing of the same Western blot. Molecular mass is indicated in kilodaltons. (B) Quantification of p62 levels from experiments as in A. *n* = 4 independent experiments. §, P = 0.0018 for *GRN*$^{-/-}$ versus *GRN*$^{+/+}$ using two-way ANOVA and Sidak's multiple comparisons test (0 h = **, P < 0.01; 0.5 h = **, P < 0.01). Error bars represent mean ± SEM.

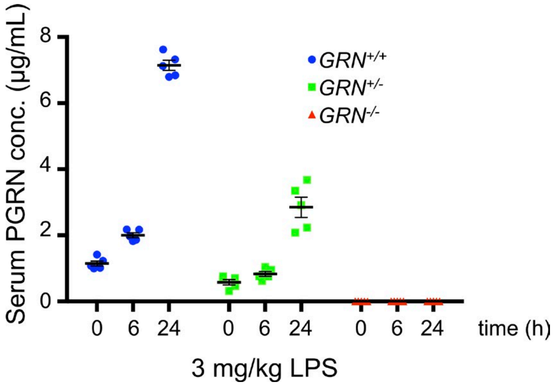

Figure S3. **Serum PGRN concentrations in *GRN*$^{+/+}$ (circles) and *GRN*$^{-/-}$ (triangles) mice in response to LPS.** *n* = 5 mice per group from one experiment. Error bars represent mean ± SEM.

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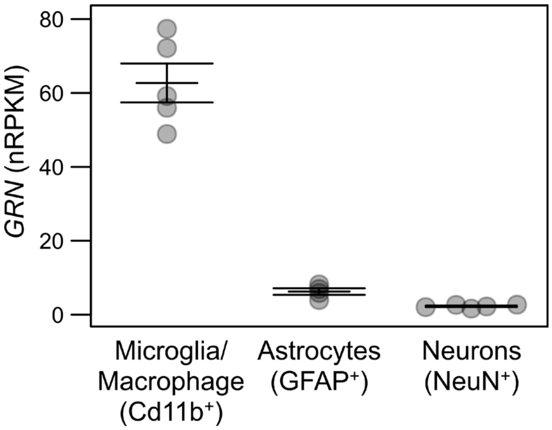

Figure S4. **Cell-type–specific expression of *GRN*.** Counts of sorted microglia/macrophages, astrocytes, and neurons from *GRN*$^{+/+}$ cortex expressed as normalized reads per kilobase of transcript per million mapped reads (nRPKM). *n* = 5 mice per group from five experiments. Error bars represent mean ± SEM.

Table S1. **Gene expression changes in *GRN*$^{+/-}$**

	Gene symbol	Gene name	$\log_2$ (fold change)	Adjusted p-value
1	*GRN*	Granulin	−1	5.96E-08
2	*NDN*	Necdin	−0.918	0.0000129
3	*UCP2*	Uncoupling protein 2 (mitochondrial, proton carrier)	−0.668	0.00027
4	*KRT12*	Keratin 12	−0.938	0.00432
5	*NNT*	Nicotinamide nucleotide transhydrogenase	−0.657	0.0265
6	*TEAD1*	TEA domain family member 1	−0.38	0.0441
7	*EPN3*	Epsin 3	−0.885	0.0456
8	*DAB2*	Disabled homolog 2	−0.505	0.0456
9	*ARHGAP27*	Rho GTPase activating protein 27	−0.295	0.0456
10	*FAM171A2*	Family with sequence similarity 171, member A2	−0.218	0.0456

List of genes down-regulated in *GRN*$^{+/-}$ brains relative to *GRN*$^{+/+}$ brains, listed by rank in increasing p-value. *n* = 5 mice per group from one experiment.

Table S2. **Gene expression enrichment in *GRN*$^{-/-}$ cortex**

	GO cellular component complete	No. of genes in cellular component group	No. of genes from the experimental dataset	Expected no. of genes	Fold enrichment	P-value
1	Vacuole (GO: 0005773)	500	54	10.15	>5	5.86E-20
2	Lytic vacuole (GO: 0000323)	429	50	8.71	>5	1.07E-19
3	Lysosome (GO: 0005764)	429	50	8.71	>5	1.07E-19
4	Proton-transporting two-sector ATPase complex (GO: 0016469)	43	8	0.87	>5	4.25E-03
5	Blood microparticle (GO: 0072562)	103	11	2.09	>5	1.33E-02
6	NADPH oxidase complex (GO :0043020)	9	4	0.18	>5	4.58E-02

GO cellular component enrichment analysis of genes up-regulated more than fivefold in *GRN*$^{-/-}$ brains relative to *GRN*$^{+/+}$ brains, ranked by p-value. *n* = 5 mice per group from one experiment.