**Fig. S1. Reciprocal co-immunoprecipitation of STAT3-GRN complex in TNBC cells.**

STAT3-GRN interaction in MDA-MB-468 and SUM159PT cells expressing HIS-tagged GRN were analyzed by immunoprecipitation using antibodies for GRN, STAT3, or a non-specific immunoglobulin G (IgG), followed by immunoblots with the indicated antibodies. Input indicates 5% of pre-immunoprecipitated samples.
Fig. S2. Immunofluorescent staining showing the colocalization of STAT3 and GRN in TNBC cell lines MDA-MB-468 and SUM159PT. Nuclei were counterstained with DAPI (blue).
Fig. S3. SUM159PT cells cotransfected with siRNA targeting GRN and a turboGFP (tGFP)-tagged expression construct for mouse GRN (mGRN) were analyzed by (A) immunoblot (GRN antibody recognizes both human and mouse GRN protein) and by (B) STAT3-dependent luciferase reporter assay (N = 3). siCon, non-targeting control siRNA. mGRN has a larger molecular weight on immunoblot due to addition of tGFP tag, 26 kDa.
Fig. S4. Validation of STAT3-bound genes in TNBC cells. Chromatin immunoprecipitation with an antibody to STAT3 in (A) MDA-MB-468 cells and (B) SUM159PT cells transfected with siRNA targeting STAT3 or a non-targeting control. Data expressed as % input.
Fig. S5. (A) SK-BR-3 cells stimulated with LIF, oncostatin M (OSM), or interleukin-6 (IL-6) were analyzed by immunoblot for levels of tyrosine-phosphorylated (PY-STAT3), serine-phosphorylated (PS-STAT3), and total STAT3. (B) SKBR3 cells transfected with siRNA targeting GRN then stimulated with LIF, OSM, or IL-6 were analyzed by luciferase reporter assay for STAT3-driven transcriptional activity.
Fig. S6. (A) SK-BR-3 cells stimulated with LIF, prolactin (PRL), or interferon γ (IFNγ) were analyzed by immunoblot for levels of tyrosine-phosphorylated (PY) and total STAT proteins. SK-BR-3 cells transfected with siRNA targeting GRN (pool siGRN and individual constructs siGRN-B and siGRN-C) then stimulated with IFN γ were analyzed by (B) immunoblot, (C) luciferase reporter assay for STAT1-dependent transcriptional activity (N = 3) and (D) qRT-PCR for expression of endogenous STAT1 target genes (normalized to HPRT; representative of N = 3).
Fig. S7. Extracellular granulin does not activate STAT3 tyrosine phosphorylation or transcriptional activity in breast cancer cells.

SK-BR-3 cells stimulated with LIF or recombinant human progranulin (PGRN) were analyzed by (A) immunoblot and (B) STAT3-specific luciferase reporter assay. (C) STAT3 luciferase reporter cells transfected with siRNA targeting GRN for 48 hours were stimulated with IL-6 for STAT3-specific activation then analyzed by Bright-Glo Luciferase Assay (Promega) on a Luminoskan Ascent luminometer (N = 4). Immunoblot verifies depletion of GRN protein levels. (D) STAT3 luciferase reporter cells stimulated with IL-6 and PGRN, alone and in combination, were analyzed by Bright-Glo for luciferase production (N = 3).
**Fig. S8.** (A) MDA-MB-468 cells stimulated with PGRN were analyzed by immunoblot for levels of tyrosine-phosphorylated (PY-STAT3) and total STAT3. LIF serves as a positive control for induction of STAT3 activity. (B) MDA-MB-468 cells stimulated with PGRN were analyzed by qRT-PCR for mRNA levels of the indicated STAT3 target genes.
Fig. S9. Silencing GRN reduces cytokine-stimulated nuclear accumulation of STAT3.

(A) SK-BR-3 cells were transfected with siRNA targeting GRN or a non-targeting control for 48 hours, then stimulated with LIF for the indicated times. Cells were harvested and analyzed by immunoblot for levels of tyrosine-phosphorylated (PY-STAT3) and total STAT3 in nuclear fractions. PARP serves as a nuclear fraction loading control. (B) Immunoblot band intensities plotted as ratios of PY-STAT3 to PARP.
Fig. S10. SUM159PT cells transfected with siRNA targeting GRN and a FLAG-tagged expression construct for constitutively active STAT3 (S3C) were analyzed by (A) immunoblot, (B) qRT-PCR for expression of the indicated STAT3 target genes normalized to HPRT (N = 2), and (C) wound healing assay.
**Fig. S11.** GRN expression is positively correlated with (A) tumor grade but not with (B) tyrosine-phosphorylated STAT3 (PY-STAT3) histologic staining (scores of 0 to 3+) in breast tumors. 200678, 211284, and 216041 denote three different microarray probes to the GRN transcript.
Supplemental Table 1. Primer sequences used for quantitative real-time PCR analysis (hqRT) of mRNA expression and chromatin immunoprecipitation (hChIP) of STAT3 DNA binding.