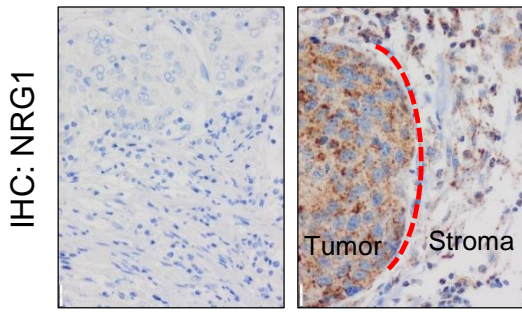
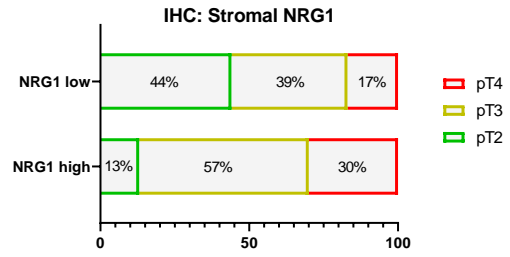
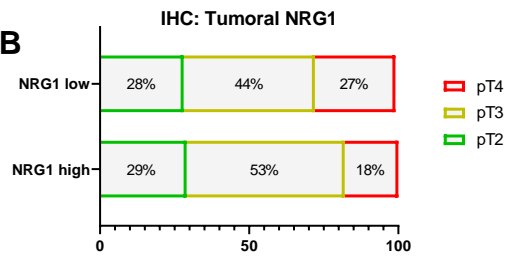


Supplementary Figure S6.

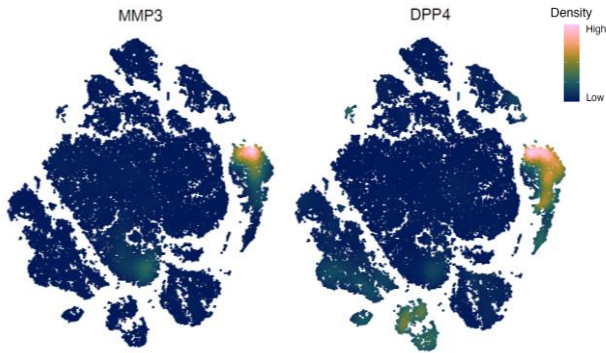
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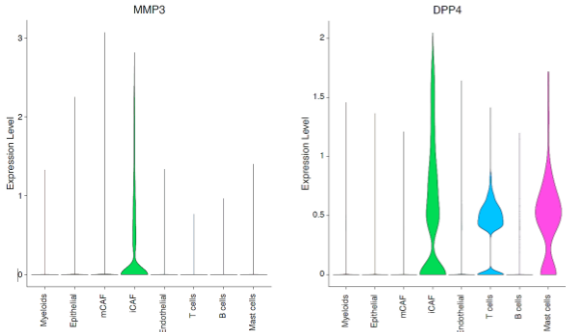
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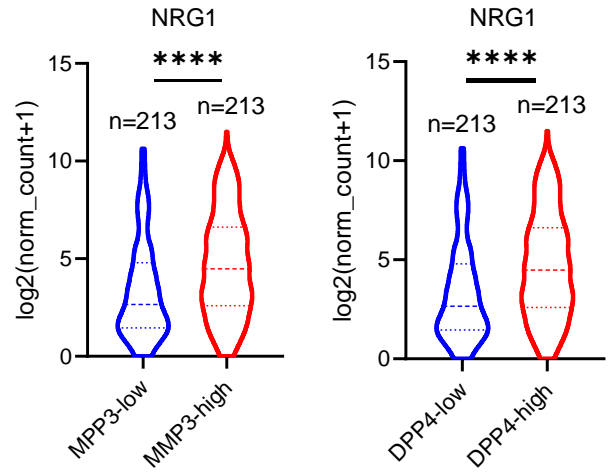
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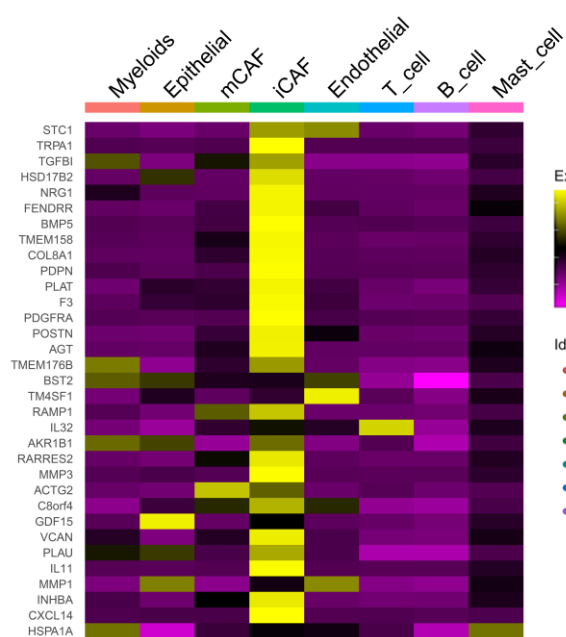
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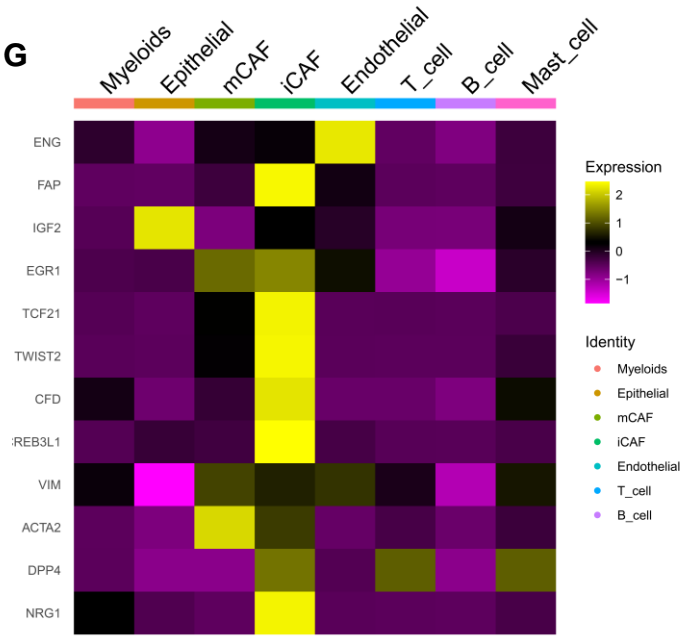
E



F



G



Supplementary Figure S6: NRG1 expression correlates with pre-adipocytic markers and is predominantly expressed in inflammatory cancer-associated fibroblasts in human bladder urothelial carcinoma. (A) Representative images of IHC staining of NRG1 in human MIBC TMA. Red line separates tumor and stroma compartments. (B) Graphs represent percentage of patients expressing low and high NRG1 levels in the tumor (top) and stroma (bottom), divided by the tumor stage (T2, T3, T4). (C-D) Analysis of single cell RNA sequencing data obtained from Chen et al., 2022 (25). (C) Imputed gene expression of MMP3 (left) and DPP4 (right) displayed as a function of expression density. (D) Imputed gene expression of MMP3 (left) and DPP4 (right) displayed in violin plots. (E) Data obtained from the TCGA BLCA data set, N=426 samples. Expression levels of NRG1 in bladder cancer stratified based on MMP3 (left) and DPP4 (right) expression. The low and high cutoffs were determined based on the median expression levels of DPP4 and MMP3 among the samples. 10 samples did not have the expression level provided and therefore could not be included. ****P < 0.0001. (F) Heatmap showing imputed gene expression of CAF subcluster 3 (C3_SLC14A1+) described in Ma et al. 2022 analysed in single-cell RNA sequencing data from Chen et al. 2022 (25). (G) Heatmap showing imputed gene expression of adipogenic CAFs (CAF_{adi}) described in (Luo et al. 2022) analysed in single-cell RNA sequencing data from Chen et al. 2022 (25).