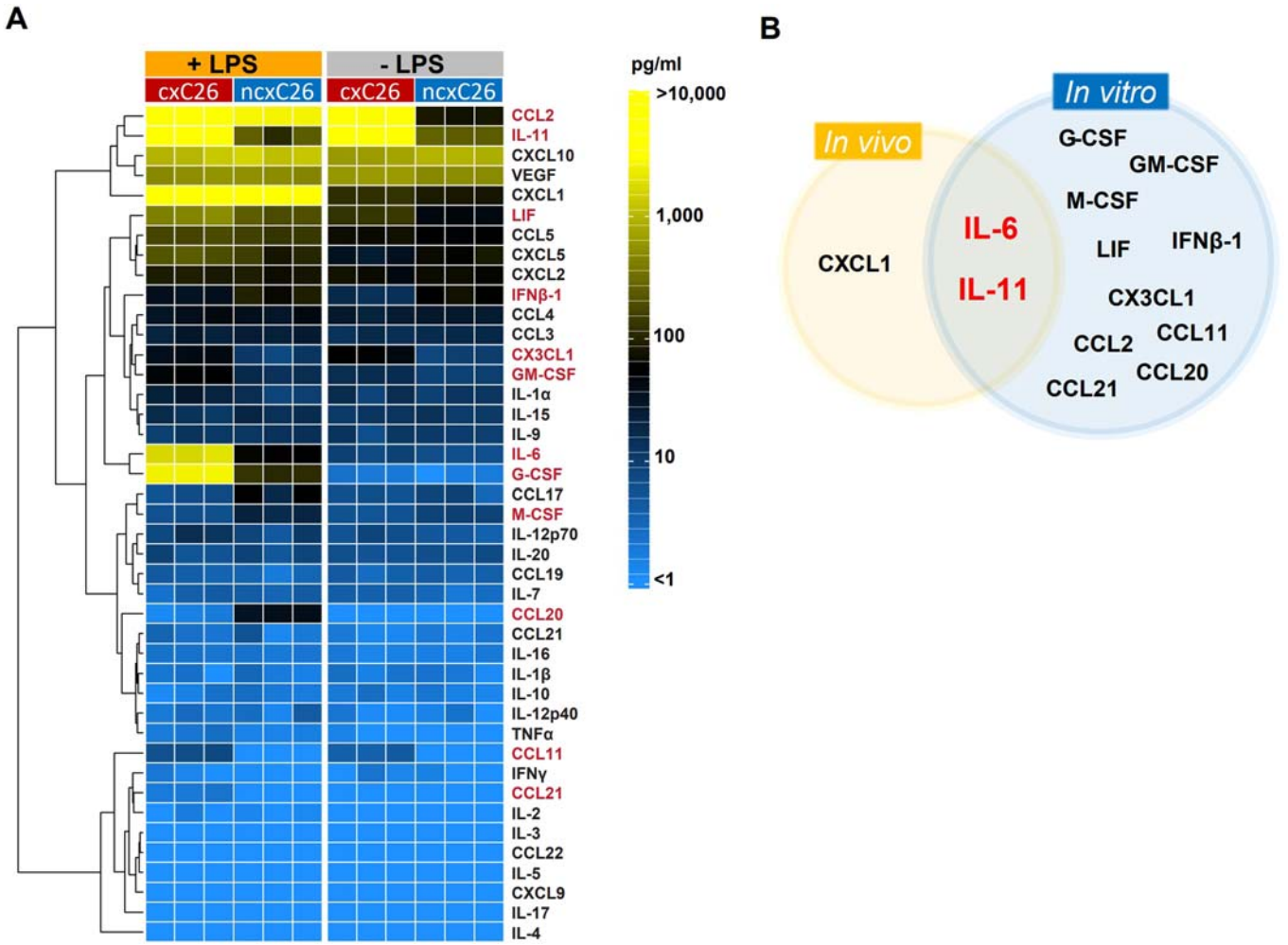


Expanded View Figures



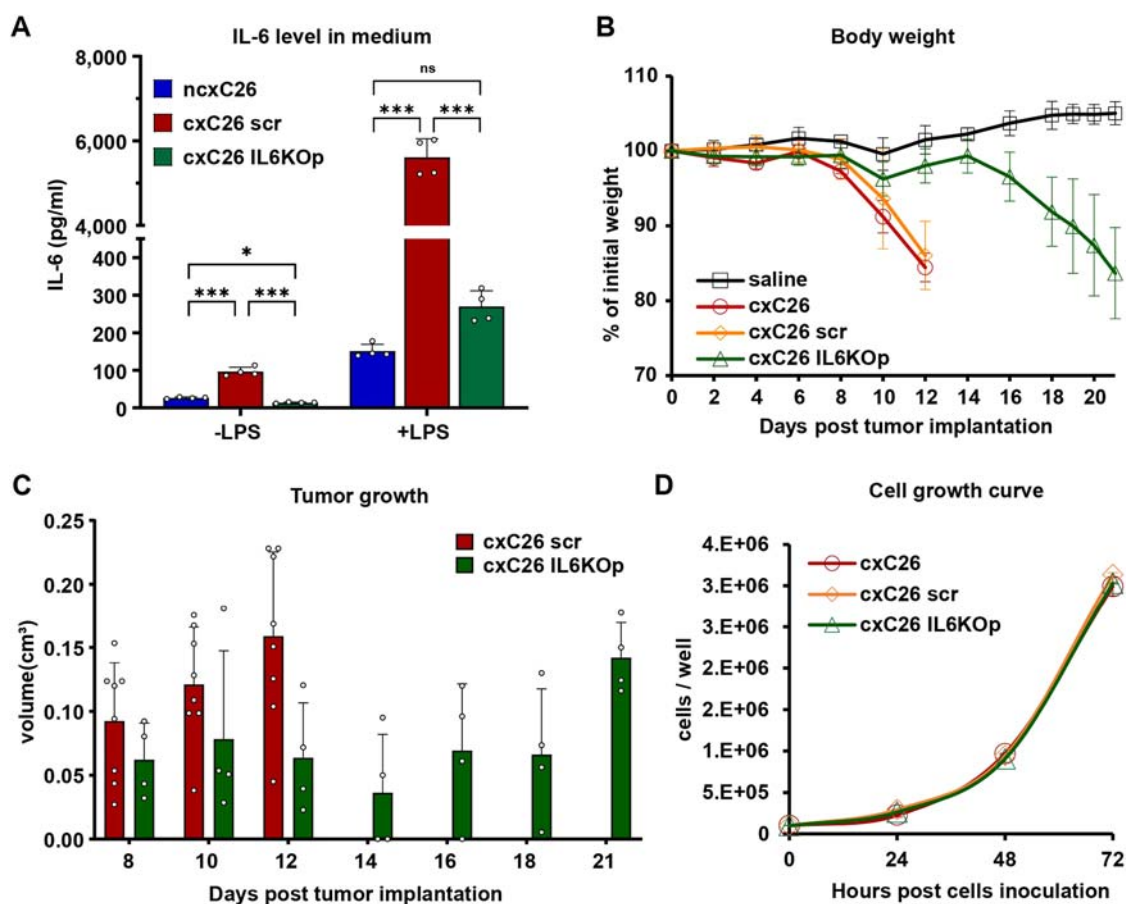


Figure EV2. Characterization of cxC26 IL-6 KO pool (IL6KOp).

(A) Levels of IL-6 in conditioned media of cxC26 scr (CRISPR/Cas9 scrambled gRNA control) and cxC26 IL-6 KO pool with or without LPS (2 μ g/ml) treatment for 24 h. (B) Body weight. (C) Tumor growth. CD2F1 mice were inoculated with 1×10^6 cxC26, cxC26 scr, or cxC26 IL-6 KO pool cells. (D) Growth curves of cxC26, cxC26 scr, and cxC26 IL-6 KO pool cells in vitro. $n = 3$ per group. Data information: (A, B) $n = 4$ for per group. (C) $n = 8$ for cxC26 scr, $n = 4$ for cxC26 IL6KOp (D) $n = 3$ for per group. All data (A–D) are shown as the mean $\pm$ s.d. Significance of the differences: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ between groups by one-way ANOVA. ns not significant.

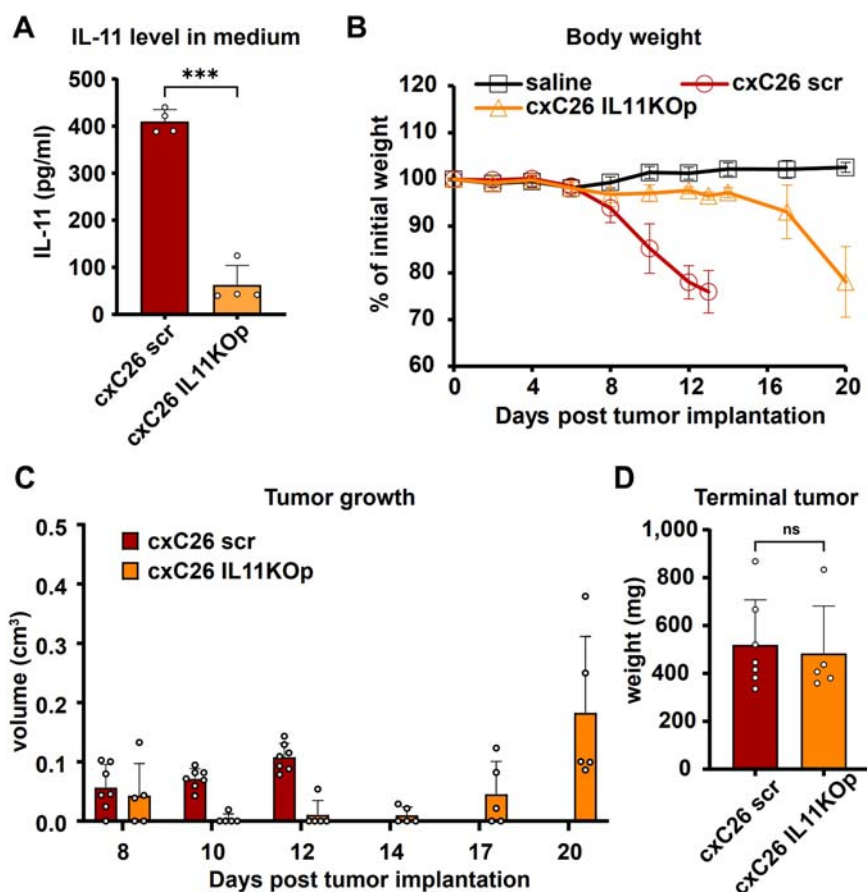


Figure EV3. Characterization of *IL-11* knockout in cxC26 cells.

(A) Levels of IL-11 in conditioned media of cxC26 scr and cxC26 IL-11 knockout pool (KOp). (B) Body weight. (C) Tumor growth. (D) Tumor mass at the terminal time point. CD2F1 mice were injected with saline or inoculated with 1×10^6 cxC26 scr or cxC26 IL-11 KOp cells. Data information: All data (A–D) are shown as the mean $\pm$ s.d. Significance of the differences: *** $P < 0.001$ between groups by Student's *t*-test. ns not significant. $n = 5$ for saline, $n = 7$ for cxC26 scr, $n = 5$ for cxC26 IL-11 KOp.

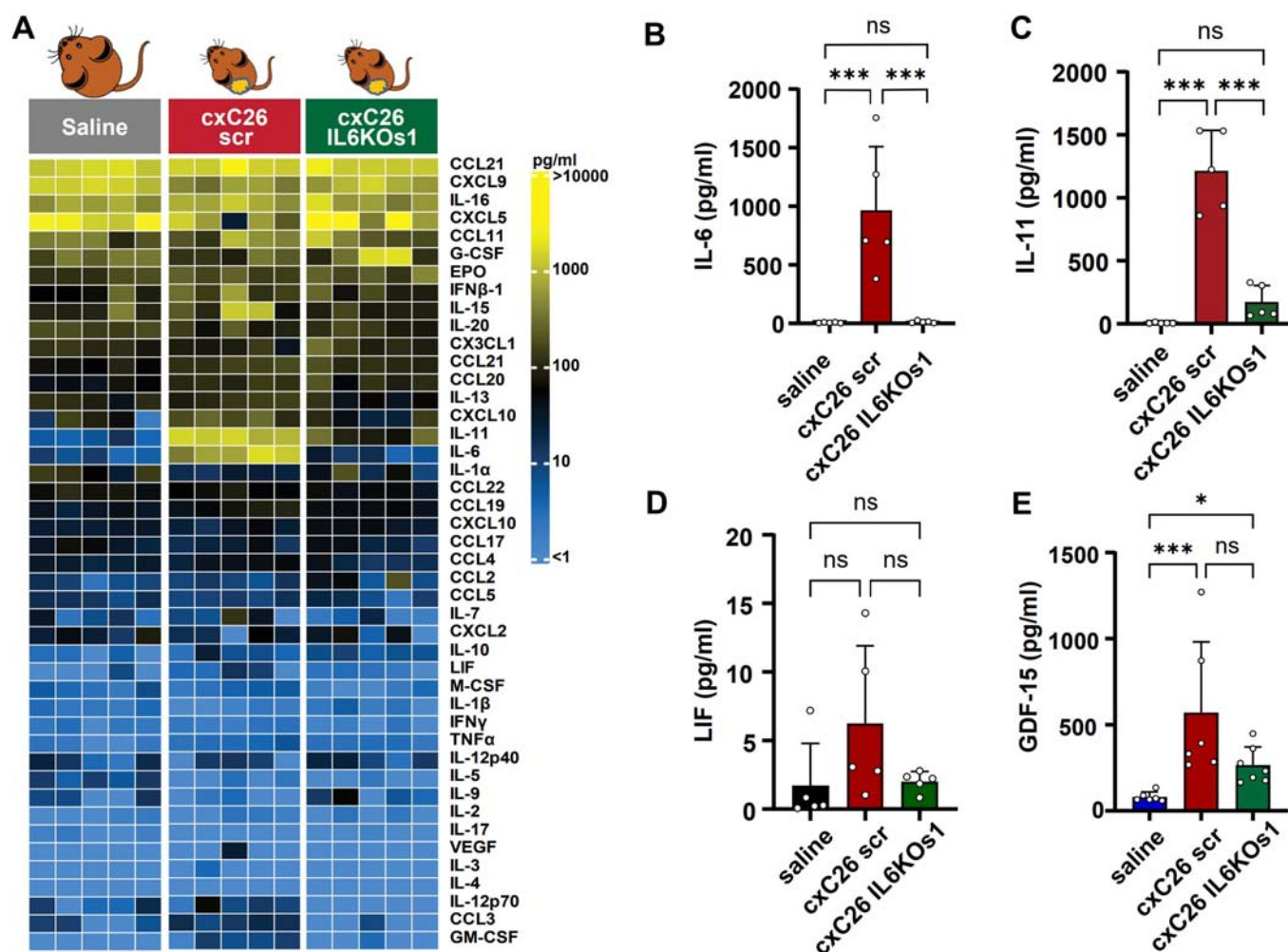
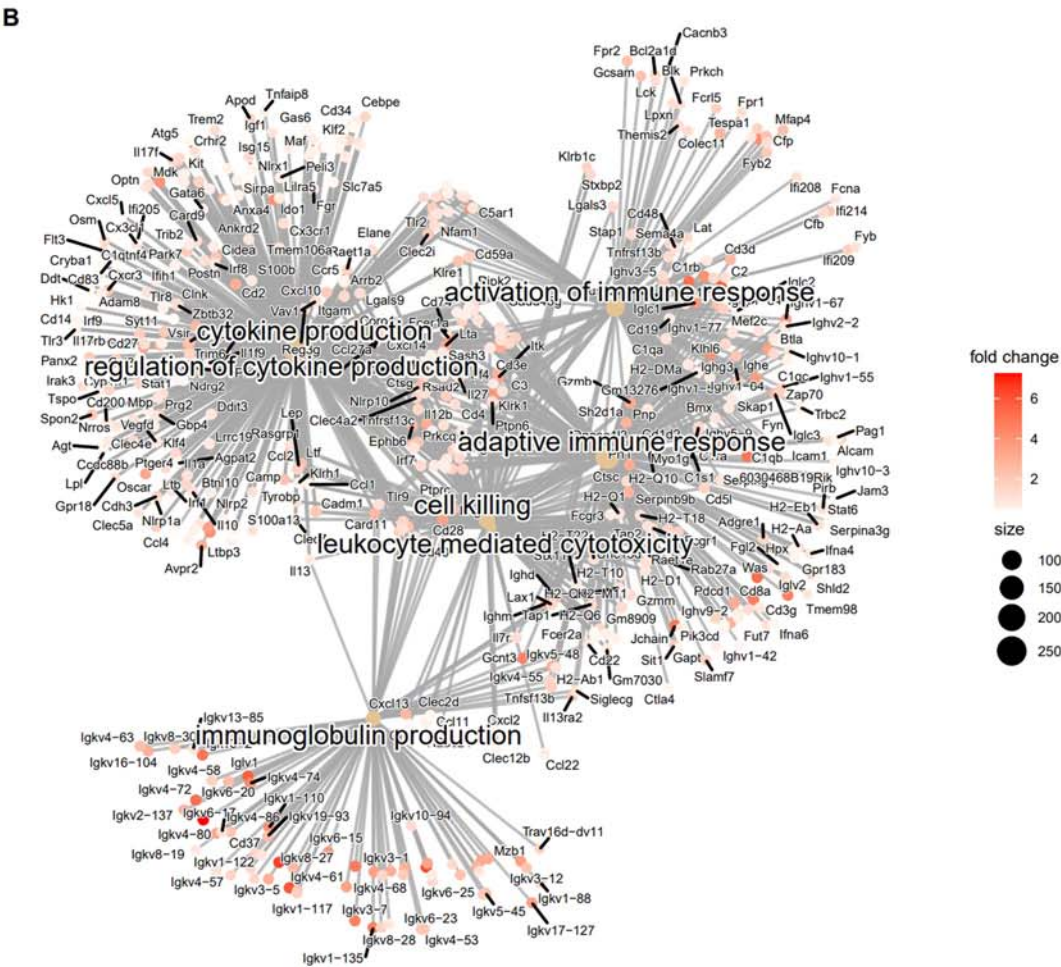
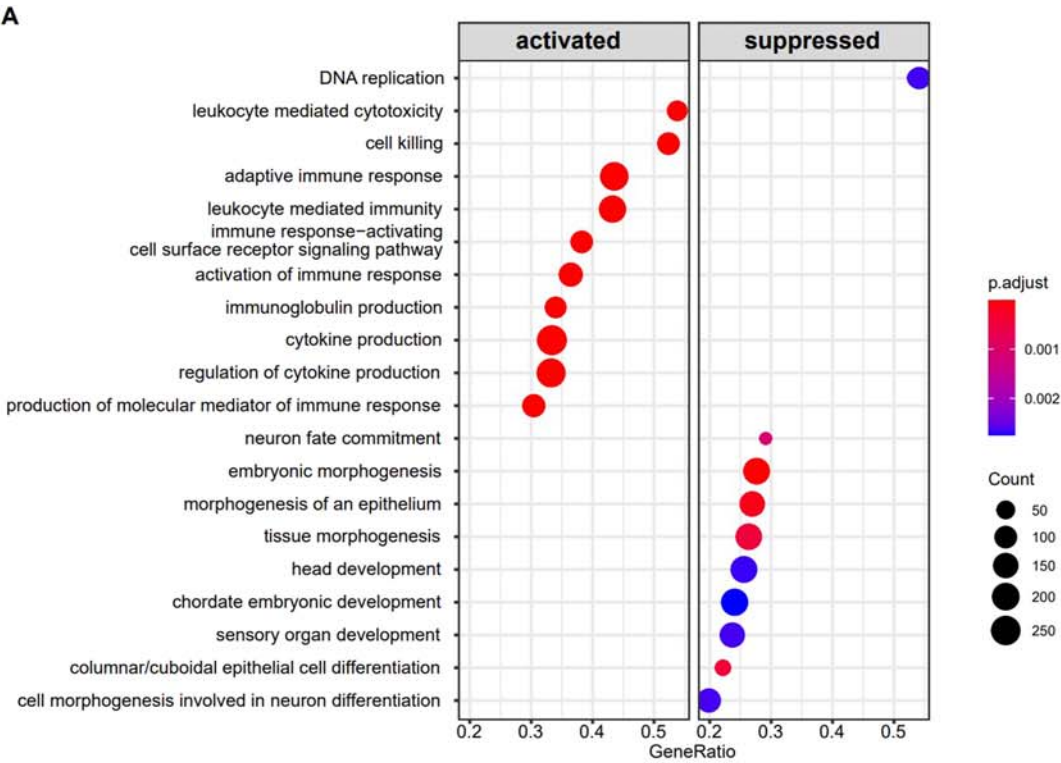


Figure EV4. Circulating cytokine profile in mice bearing the cx26 IL-6 KO tumor.

CD2F1 mice were injected with saline or inoculated with 1×10^6 cx26 scr or 1×10^7 cx26 IL-6 KO s1 cells. (A) Heatmap for circulating cytokine levels and concentration of circulating (B) IL-6, (C) IL-11, and (D) LIF at the terminal time point. (E) Circulating GDF-15 concentration at the terminal time point. Data information: (A–D) $n = 5$ per group. (E) $n = 6$ for saline and cx26 scr, $n = 7$ for cx26 IL-6 KO s1. (B–E) are shown as the mean $\pm$ s.d. Significance of the differences: * $P < 0.05$, *** $P < 0.001$ between groups by one-way ANOVA. ns not significant.



**Figure EV5. Alteration of gene expression by disruption of IL-6 in the cxC26 tumor.**

(A) Elevated and suppressed biological processes in the cxC26 IL-6 KO s1 tumor compared to the cxC26 scr tumor. (B) Network plot of the terms that are the most significantly changed biological processes in the cxC26 IL-6 KO s1 tumor. ClusterProfiler was used for calculating GeneRatio and adjusted *p* value (FDR) for identifying the significantly changed biological process and drawing the RNA-seq data. *n* = 4 for cxC26 scr and cxC26 IL-6 KO s1.