**STK11/LKB1 deficiency promotes neutrophil recruitment and proinflammatory cytokine production to suppress T cell activity in the lung tumor microenvironment**

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**SUPPLEMENTAL FIGURE LEGENDS**

**Supplementary figure 1. Characterization of tumor bearing lungs from *Kras* and *Kras/Lkb1* mouse models**

**A**. Total lung weights of the mice (*Kras*: n=8 or *Kras/Lkb1*: n=8) used in Figure 1, 2A and 2B. **B**. Total $CD45^+$ cell counts in *Kras* (n=8) versus *Kras/Lkb1* (n=8) tumors. **C**. Counts of additional myeloid cell populations: eosinophils, Ly-$6C^{hi}$ monocytes and $CD103^+$ dendritic cells (DC) in *Kras* (K:n=8) versus *Kras/Lkb1* (KL:n=8). **D**. Total counts

of NK cells and B cells in K (n=8) or KL (n=8) tumors. *p<0.05.

**Supplementary figure 2. Tumor-associated neutrophils produce proinflammatory cytokines and T cell suppressive factors**

**A**. Expression of immune modulating factors in the sorted tumor-associated neutrophils in control, *Kras* (K) or *Kras/Lkb1* (KL) tumors. Row-scaled, log-transformed FPKM values are shown, colored blue/red for low/high expression, respectively. Differential expression is shown as fold-change values, colored blue/red for under/over-expression compared to controls. **B**. MFG-E8 and IL-10 in BALFs from control (n=5), K (n=8) or KL (n=8) mice. **p<0.01, ***p<0.001. **C**. IL-6 production in culture supernatants after 48hr incubation from sorted $5x10^4$ tumor cells ($CD45^-EpCAM^+$) and tumor-associated neutrophils (TAN) from untreated KL tumors (n=2). **D**. Intracellular staining of LGALS9 in tumor cells and neutrophils (TAN) by flow cytometry. Representative plot from untreated KL tumors.

**Supplementary figure 3. CXCL7 and G-CSF were increased with IL-1α treatment in mouse KPL cell lines**

**A**. CXCL7 and G-CSF levels in culture supernatants measured 24hr after IL-1α

stimulation (0, 5 and 20ng/ml) of three *Kras* mutated, *p53*-deficient, *Lkb1*-deficient (KPL) cell lines. **B**. Total lung weights for the mice (K: n=6 and KL: n=6) analyzed in Figure 2C.

**Supplementary figure 4. Tumor-associated neutrophils contribute to T cell suppression in the KL tumor microenvironment**

**A**. Schema for identifying tumor-associated neutrophils in *Kras/Lkb1* tumors after anti Ly-6G/Gr-1 treatment. **B**. Total lung weights of untreated mice (n=6) and treated (Ly-6G ab) mice (n=6). **C**. TAN count in KL tumors after the neutrophil depletion (untreated: n=6 and treated (Ly-6G ab): n=6). **D**. Cytokine levels in BALFs from KL mice after neutrophil depletion (untreated: n=6 and treated (Ly-6G ab): n=6). **E**. CD4 and CD8 T cell counts and function in KL tumors after neutrophil depletion (untreated: n=6 and treated (Ly-6G ab): n=6).

**Supplementary figure 5. Functional loss of LKB1 in human isogenic cell lines demonstrate similar proinflammatory profile with mice.**

**A**. LKB1 levels by western blot in cells stably transfected with sh-NT or sh-LKB1 or reconstituted with wild type or Kinase dead LKB1 (LKB1 KD). **B**. PD-L1 levels in A549

cell line reconstituted with empty vector or WT or LKB1 KD. **C**. Levels of G-CSF and CXCL7 in culture supernatants from *LKB1* wild type or deficient cell lines. *p<0.05, **p<0.01, ***p<0.001. **D**. G-CSF and CXCL7 levels in culture supernatants measured 24hr after IL-1α stimulation (0, 5 and 20ng/ml) of three *LKB1* deficient cell lines. **E**. IL-6 levels in culture supernatants measured 12hr after IL-1α stimulation (0, 0.5 and 5ng/ml) of *LKB1*-knocked down and *LKB1*-intact cell lines.

**Supplementary figure 6. Immune analysis of *Kras/Lkb1* mice after 2 week IL-6 neutralizing antibody treatment and survival after combinational treatment with anti IL-6 and anti PD-1 antibodies.**

**A**. Total lung weights of untreated mice (n=7) and anti IL-6 antibody treated (IL-6 ab) mice (n=8) for immune analysis in figure 4. **B**. Tumor associated macrophages (TAM), CD4 T cells, CD8 T cells counts and CD8/Foxp3 ratio in *Kras/Lkb1* mice (untreated: n=7 and IL-6 ab: n=8). **C**. Numbers are 12, 8, and 11 for anti IL-6, anti PD-1, and anti IL-6+ anti PD-1 antibody combination.