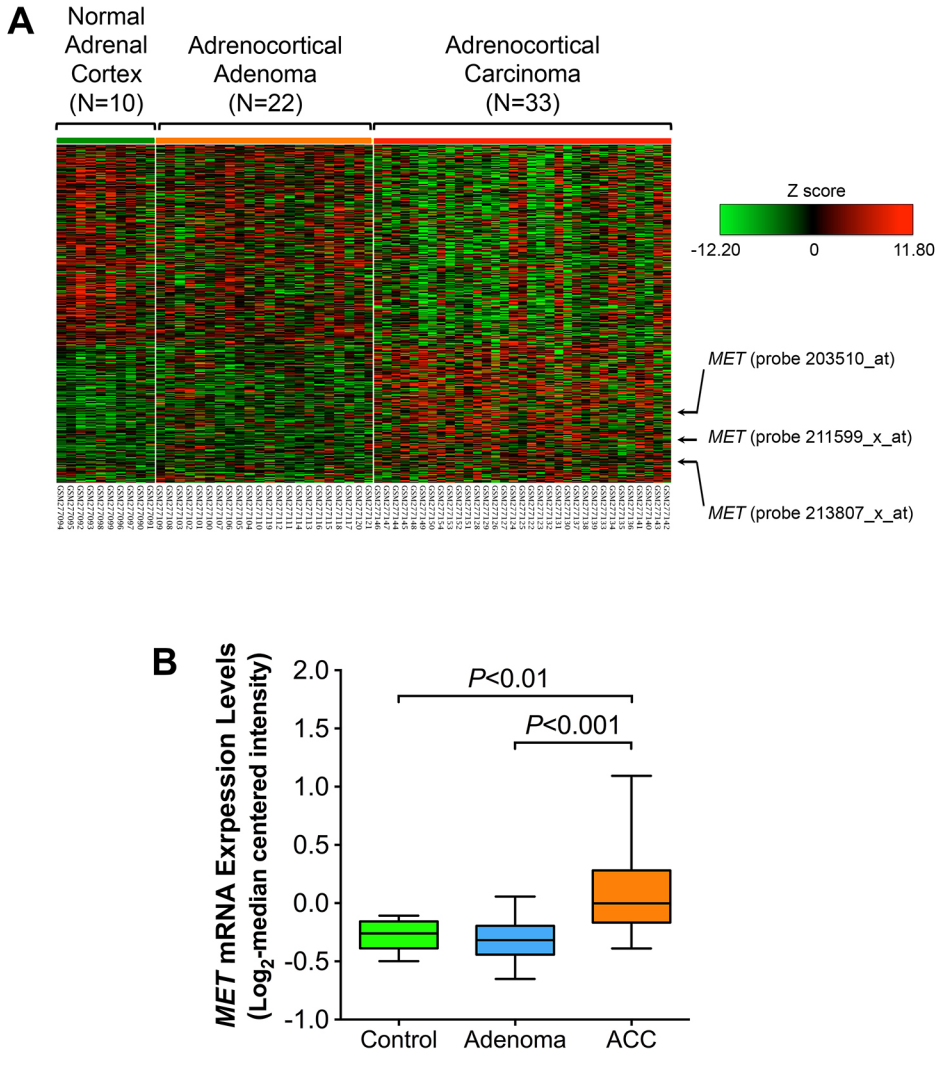
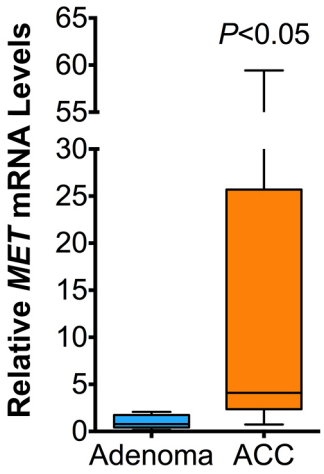
SUPPLEMENTAL FIGURES



Supplemental Figure 1 High *MET* expression in ACC patients.

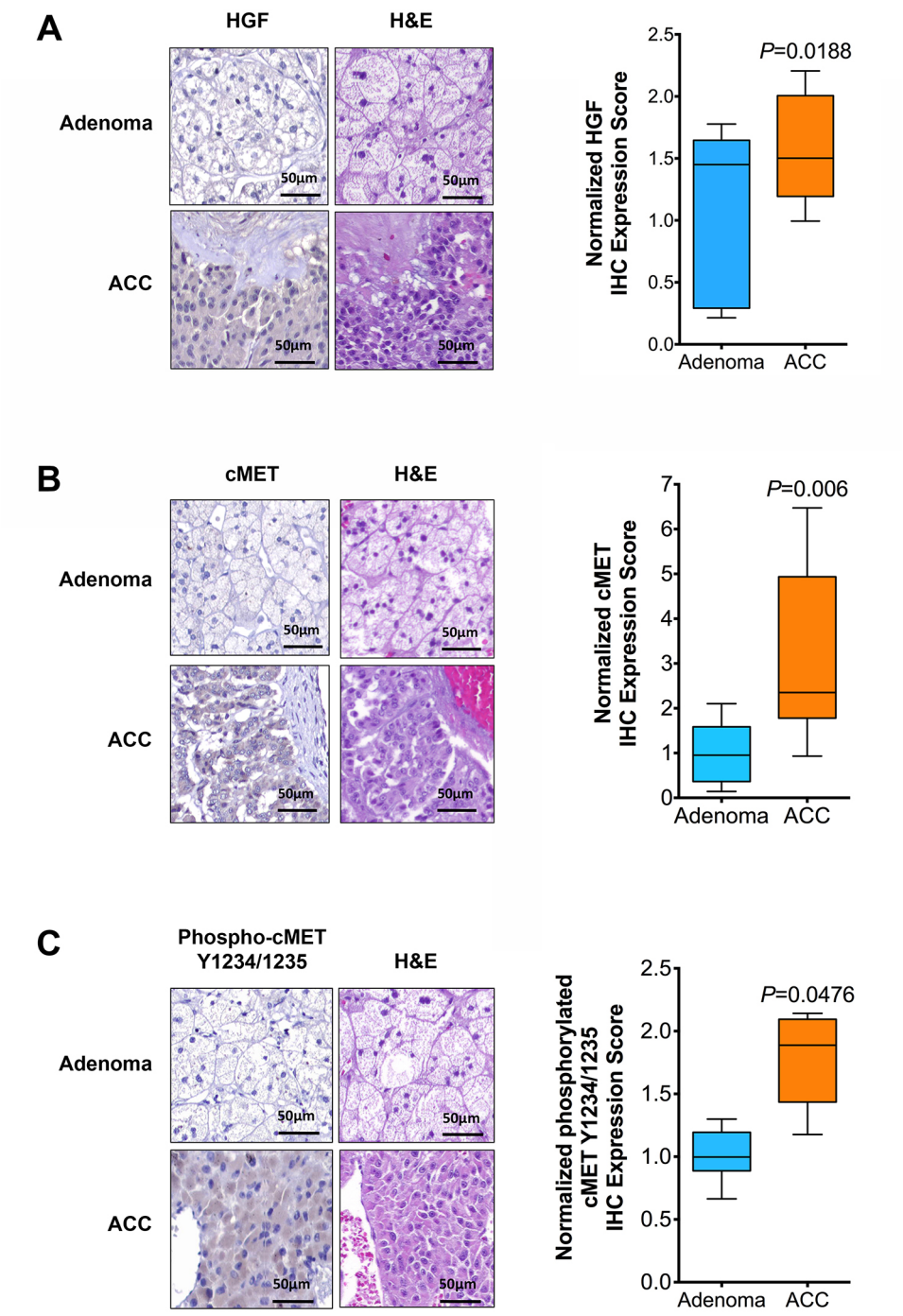
(**A**) Transcriptomic analysis of ACC dataset GSE10927 revealed higher *MET* mRNA levels in ACC (n=33) than in adrenocortical adenoma (n=22) and normal adrenal cortex

tissues (n=10). (**B**) mRNA levels analysis of ACC dataset GSE10927 revealed higher *MET* mRNA levels in ACC (n=33) than in adrenocortical adenoma (n=22) and normal adrenal cortex tissues (n=10).



Supplemental Figure 2 High *MET* mRNA expression levels in ACC.

Real-time PCR analysis of a representative set of tumor samples collected at MD Anderson Cancer Center demonstrated that *MET* mRNA expression was higher in ACC (n=8) than in adrenocortical adenomas (n=6).



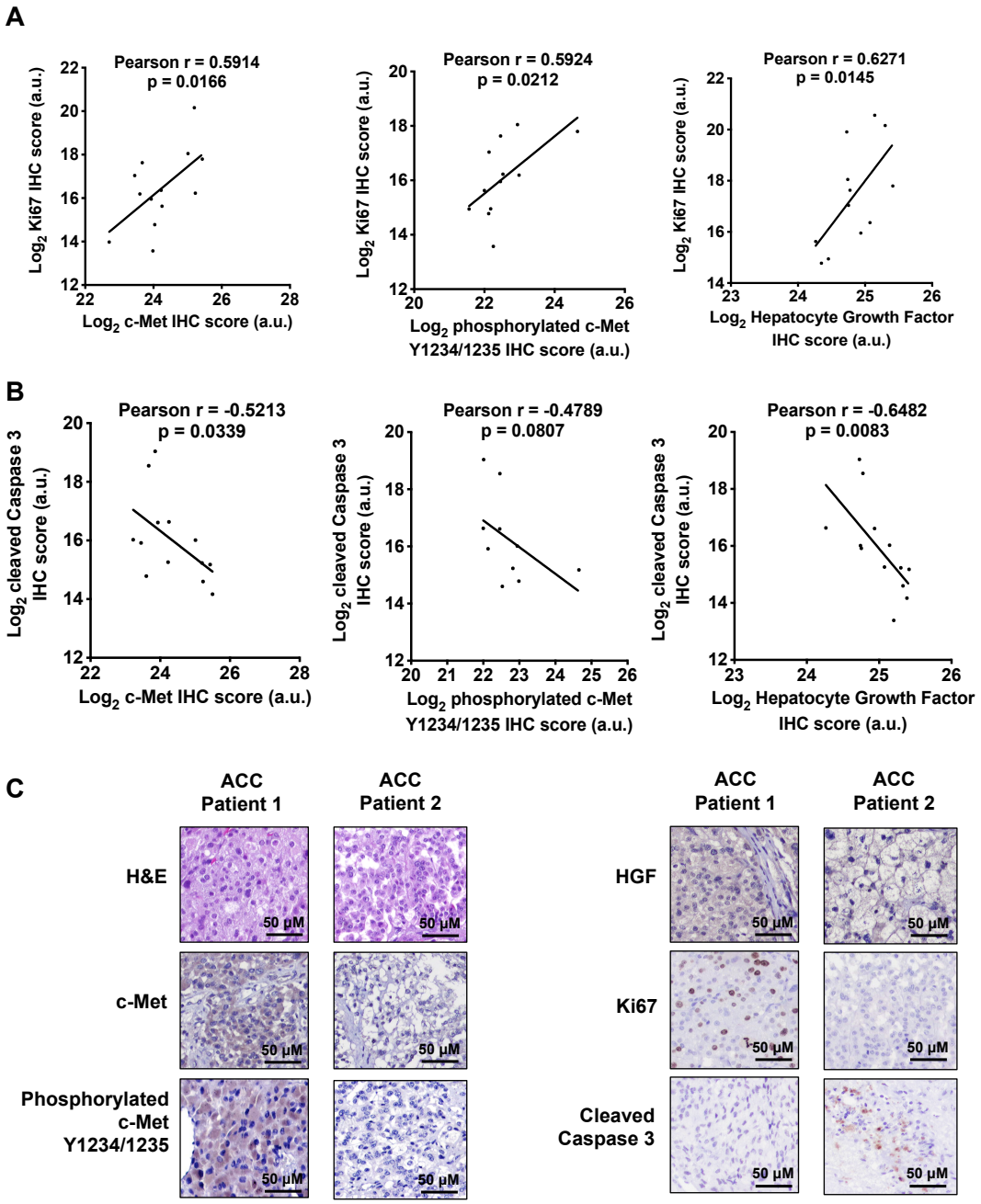
Supplemental Figure 3 cMET signaling is activated in ACC.

(**A**) Representative immunohistochemical (IHC) analysis of HGF and hematoxylin-eosin (H&E) staining of tissue microarray samples. The right panel shows the box plots of IHC

analysis scores of tissue microarray samples (13 ACC and 7 adrenal adenoma samples) indicating higher HGF protein levels in ACC than in adrenal adenomas.

(**B**) Representative IHC analysis of total cMET and H&E of staining of tissue microarray samples. The right panel shows box plots of IHC analysis scores of tissue microarray samples (13 ACC and 7 adrenal adenoma samples) indicating higher cMET protein levels in ACC than in adrenal adenomas.

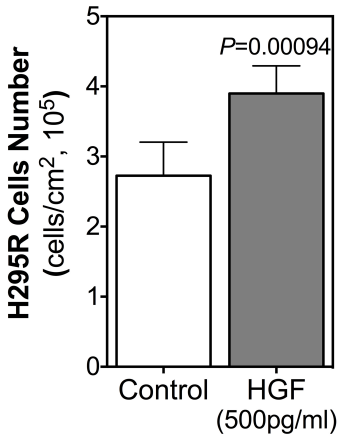
(**C**) Representative IHC analysis of phosphorylated cMET (Y1234/1235) and H&E of staining of tissue microarray samples. The right panel shows box plots of IHC analysis scores of tissue microarray samples (13 ACC and 7 adrenal adenoma samples) indicating higher cMET signaling activation in ACC than in adrenal adenomas.



Supplemental Figure 4 Increased HGF/cMET signaling is associated with enhanced proliferation and reduced apoptosis in tumors from ACC patients.

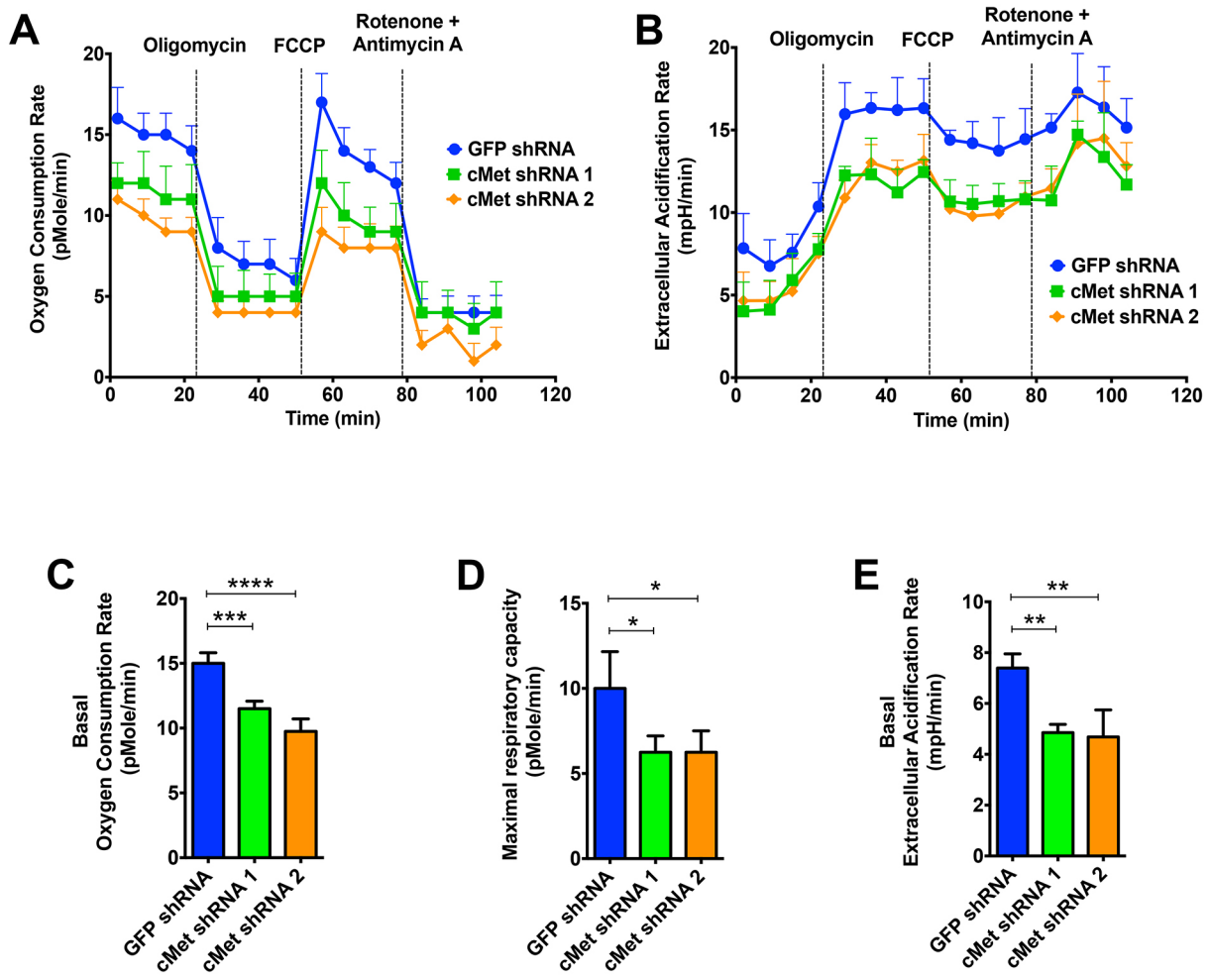
(**A**) Positive correlation between HGF/cMET signals and ACC proliferation (Ki-67 staining). (**B**) Inverse relationship between activation of the HGF/cMET pathway and apoptosis in ACC (cleaved caspase 3 staining). (**C**) Representative

immunohistochemistry images indicating the stimulatory impact of the HGF/cMET signaling pathway on ACC cell proliferation and survival. Patient 1 had high HGF, cMET and phosphorylated cMET in association with increased Ki-67 staining and low cleaved caspase 3, whereas patient 2 had the opposite associations. IHC, immunohistochemistry; a.u., arbitrary units; H&E, hematoxylin-eosin.



Supplemental Figure 5 HGF stimulates NCI-H295R ACC cell proliferation.

Cell proliferation was measured as the number of NCI-H295R cells after 6 days of culture in medium alone (control) or containing 500 pg/ml of recombinant human HGF that is in range with the average concentration serum HGF found in ACC patients and with the recombinant HGF EC50 found in the NCI-H295R cell viability experiments. The error bars represent 95% confidence intervals.



Supplemental Figure 6 HGF/cMET signaling is important for ACC cell energy metabolism.

(**A**,**B**) *MET* shRNAs decrease mitochondrial energy metabolism, as measured by the cell oxygen consumption rate (**A**), and glycolytic energy metabolism and lactate production, as measured by the extracellular acidification rate (**B**).

(**C**,**D**,**E**) *MET* shRNAs decrease the basal oxygen consumption rate (**C**), maximal respiratory capacity (**D**) and basal extracellular acidification rate **(E)**. FCCP, carbonyl cyanide 4-(trifluoromethoxy)phenylhydrazone; GFP, green fluorescent protein. The error

bars represent 95% confidence intervals; * $P<0.05$, ** $P<0.01$, *** $P<0.001$, and **** $P<0.0001$.