



Supplemental Figure 1.

A, Enrichment plots of gene expression signature for the mevalonate pathway using TCGA dataset. **B**, Genes and **C**, protein from Clark et al. (14) dataset analysis shows that expression of genes involved in the “mevalonate pathway” is significantly downregulated in ccRCC tumors vs. normal tissue. *HMGCS1*, 3-Hydroxy-3-Methylglutaryl-CoA Synthase 1; *MVK*, Mevalonate kinase; *PMVK*, Phosphomevalonate kinase; *FDPS*, Farnesyl Diphosphate Synthase; *MVD*, Diphosphomevalonate decarboxylase; *IDI1*, Isopentenyl-Diphosphate Delta Isomerase 1; *LSS*, lanosterol synthase; *DHCR7*, 7-Dehydrocholesterol reductase. **D-H**, Alteration frequency of *VHL*, *FDFT1*, *DHCR24*, *SQLE*, *LSS* genes in several kidney cancer genomic datasets using cBio Cancer genomic portal. *VHL*, Von Hippel-Lindau; *FDFT1*, squalene synthase; delta 24-sterol reductase; *SQLE*, squalene monooxygenase; *LSS*, lanosterol synthase. **I** and **J**, Metabolomics analysis of squalene levels in ccRCC tissue relative to adjacent normal kidney tissue samples from two independent cohorts (**I**, (6) and **J**, (16)). **K**, **L** and **M**, Representative photographs of A498, 786-O and HK-2 cells from proliferation assay at 96h showing insensitivity of ccRCC cell lines to atorvastatin treatment (5mM). Magnification (x100). (*=P<0.05, **=P<0.01, ***=<0.001, n.s=non-significant).