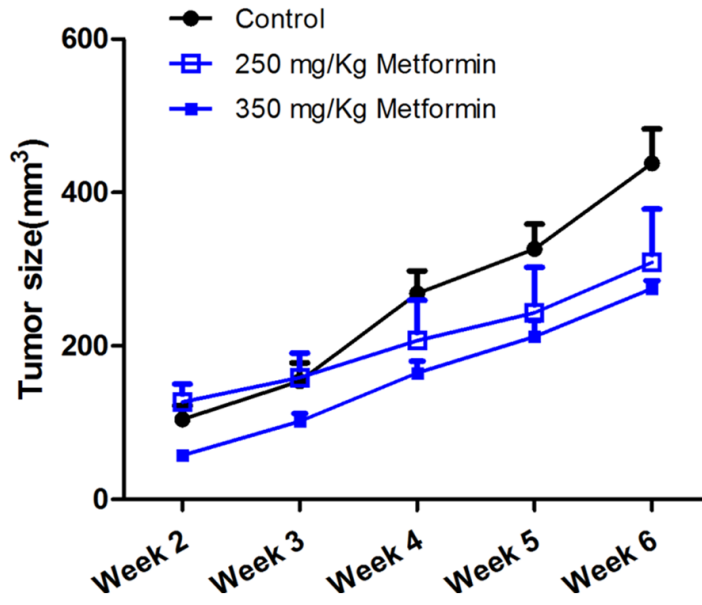
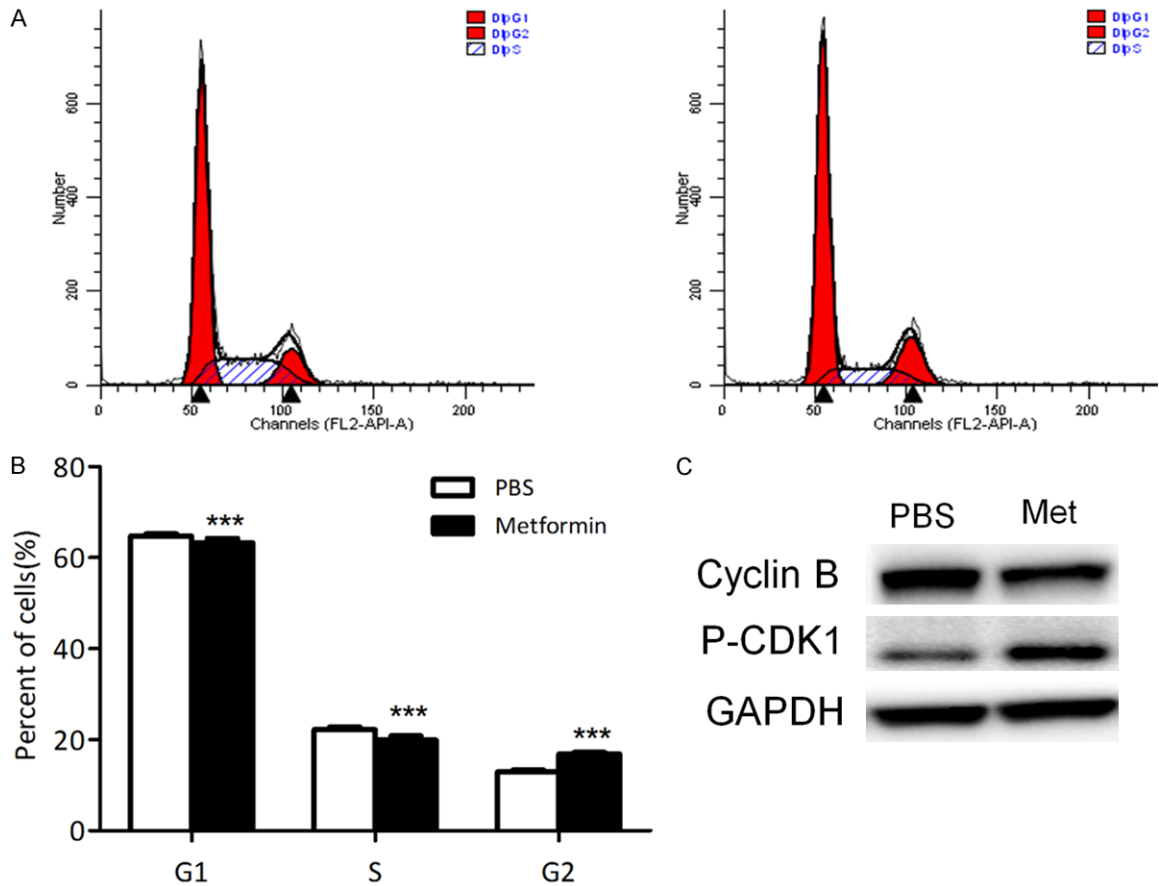


## Metformin inhibits salivary adenocarcinoma growth

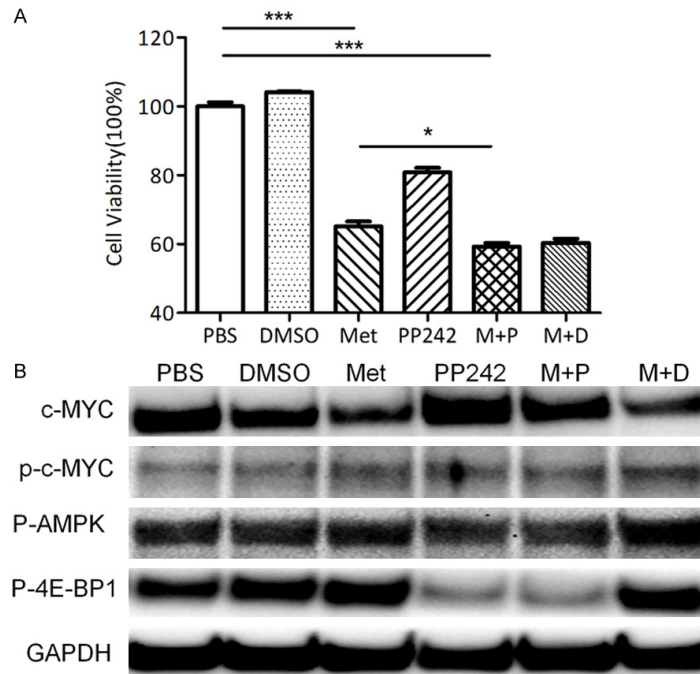


**Figure S1.** Metformin reduces HSY growth *in vivo* in a dose-dependent manner. Metformin were given to the mice through intraperitoneal injection at 2 different dosages. Tumor size of the 3 treatment groups (Control: PBS, metformin: 250 mg/Kg, metformin: 350 mg/Kg) were measured weekly.

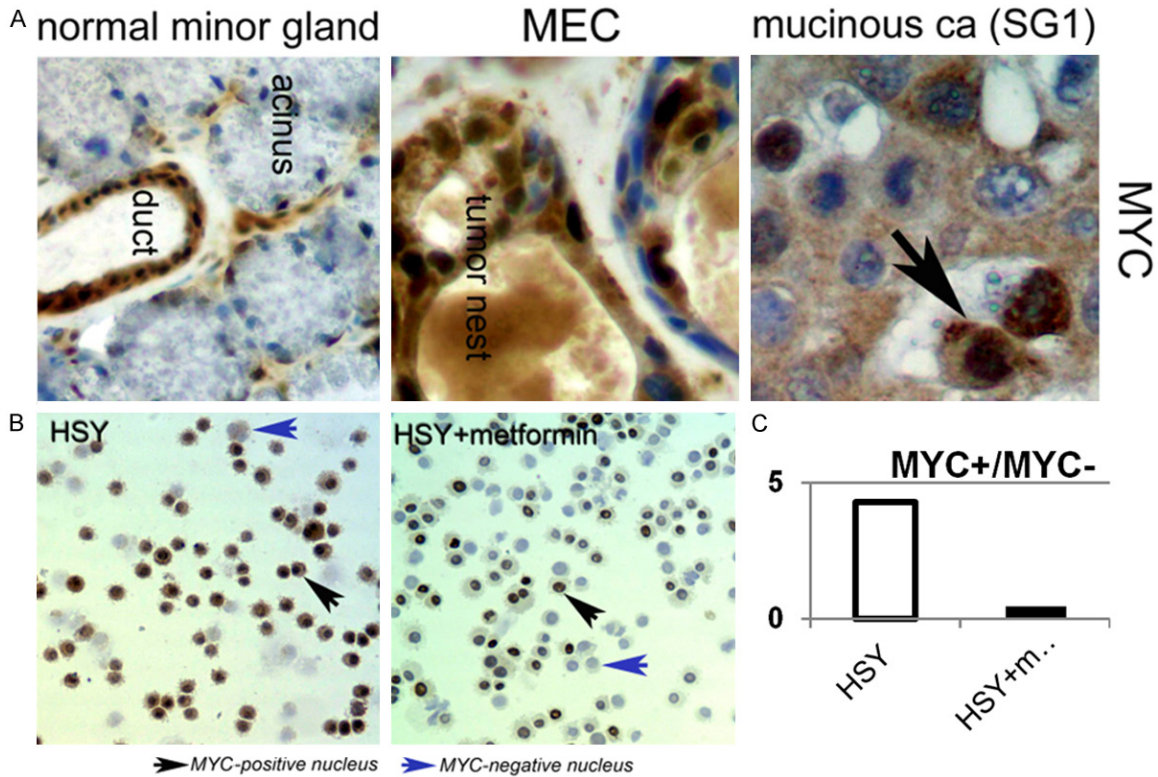


**Figure S2.** HSG cell cycle was arrested in G2 phase by metformin. A, B: Cells were treated with PBS or 4 mM metformin for 48 hours. PI was used to stain the cells. \*\*\*P < 0.01. C: HSG cells were treated for 48 h and the protein was harvested, then the cell cycle markers were tested by Western blot.

## Metformin inhibits salivary adenocarcinoma growth

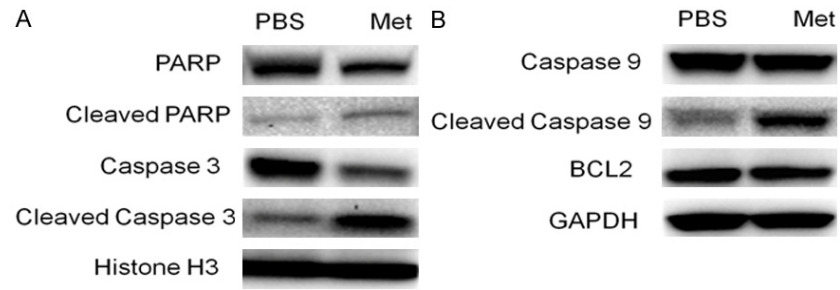


**Figure S3.** Metformin reduced c-MYC expression in human salivary gland cells. A: HSG cells were plated and treated same as HSY cells described in **Figure 3**. B: p-AMPK, p-4E-BP1 and MYC levels in HSG cell total proteins.

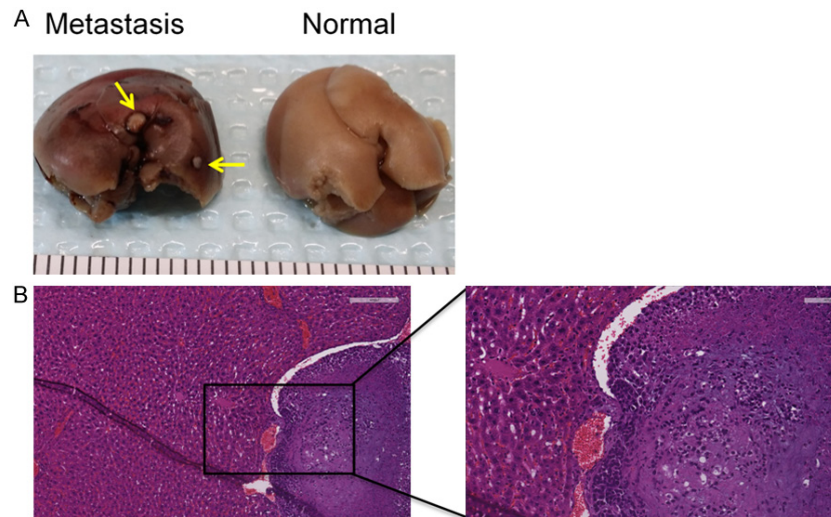


**Figure S4.** A: Sections of normal minor salivary gland (left), low-grade mucoepidermoid carcinoma (MEC, middle) and mucinous adenocarcinoma of the parotid (SG1, right) were stained for MYC by immunohistochemistry (positive cells are brown). B, C: HSY cells were incubated alone or with 10 mM metformin for 24 hours, then trypsinized and centrifuged onto glass slides, fixed in 10% formalin and stained by IHC. Photographed cells were counted (1100 per sample). Based upon nuclear expression, the ratio of MYC positive (MYC+) to MYC negative (MYC-) cells was calculated.

## Metformin inhibits salivary adenocarcinoma growth



**Figure S5.** Metformin stimulated apoptosis in HSG cells. HSG cells were treated with 4 mM metformin for 48 hours. Both nuclear and total protein were extracted to check the relevant apoptosis markers by western blot.



**Figure S6.** One out of 6 mice from PBS group demonstrated tumor metastases to the liver. A. Gross images of livers with and without metastasis lesion. B. H&E staining of liver metastasis.