Supplemental Figure 1. **^{64}Cu-ATSM retention is lower in ArKO liver and in ArKO liver tumors as quantified by autoradiography.** Same size liver or liver tumor slices were prepared from mice liver frozen immediately after the biodistribution study. The retention of ^{64}Cu-ATSM in liver and liver tumor slices was quantified by autoradiography on phosphor imager system. Activity in the liver tumor slices was significantly lower than that of normal liver ($p < 0.001$ for ArKO liver tumor vs. WT and $p < 0.01$ for ArKO tumor vs. ArKO).

Supplemental Figure 2. **Representative AVI files from PET/CT scans of a WT (A) and an ArKO liver tumor bearing mouse (B) obtained at 1 hour post injection of ^{64}Cu-ATSM. Quantitative analysis of liver and tumor activity (C)**. Note the intense uptake of the radiotracer in the liver of the WT mouse and in the tumor free aspect of the liver in the ArKO mouse (displayed as red). The accumulation of ^{64}Cu-ATSM in liver tumor is lower than unaffected liver (displayed as green). (C) Quantitative analysis of liver and liver tumor activity was performed by selecting multiple regions of interest on serial axial images. The results are expressed as mean±sem. Activity in the liver tumor was significantly lower than that of normal liver ($p < 0.0001$ for ArKO liver tumor vs. either WT or tumor free ArKO liver).

Supplemental Figure 3. **Representative AVI file from a PET/CT scan obtained 1 hour post injection of ^{64}Cu-ATSM into a mouse bearing MES-SA and MES-SA/Dx5 tumors.** The intense uptake is with the MES-SA tumor. Note the

markedly lower activity in the MES-SA/Dx5 tumor.

Supplemental Figure 4. **MES-SA/Dx5 highly expresses MDR1 compared with the parent line MES-SA and retains lower levels of ^{99m}Tc-Sestamibi: Functional validation of the model**

(A). MDR1 protein levels in whole cell lysates were determined by western blot. Actin was used as a loading control. MES-SA/Dx5 expresses much more MDR1 protein. (B). Functional assay of MDR1 function in MES-SA/Dx5 and MES-SA by comparison of ^{99m}Tc-MIBI retention in two cell lines. The results are expressed as mean±se. Data represent the average of two independent experiments with triplicates in each group. There was a 30% decrease in the retention of ^{99m}Tc-MIBI in the drug resistant MES-SA/Dx5 cell line ($p < 0.001$).