

Figure S1: Advanced liver tumors in induced $kras^{V12}$ double transgenic fish. Morphological and histological examinations of liver tumors were carried out in driver-effector fish induced with mifepristone (RU486) for 8 weeks or longer. Representative brightfiled and fluorescent images of liver morphology and histology of induced Driver-effector fish are shown. (A) One sample from 8 weeks of RU486 treatment. Histoplathological analysis revealed that hepatoblastoma (dotted area) which is made up of undifferentiated cells with large nuclei developed in mixed carcinoma in Driver-effector fish after 8 weeks of induction. In addition, these fish also showed invasion of tumor cells into blood vessels. (B) Examples from more than 8 weeks of mifepristone induction. 10% of induced driver-effector fish developed cyst fluid or malignant ascites in HCC. Detached HCC cells were found in the cysts and blood vessels. Black arrows indicated invasive tumor cells. Scale bars, 100 μ m.