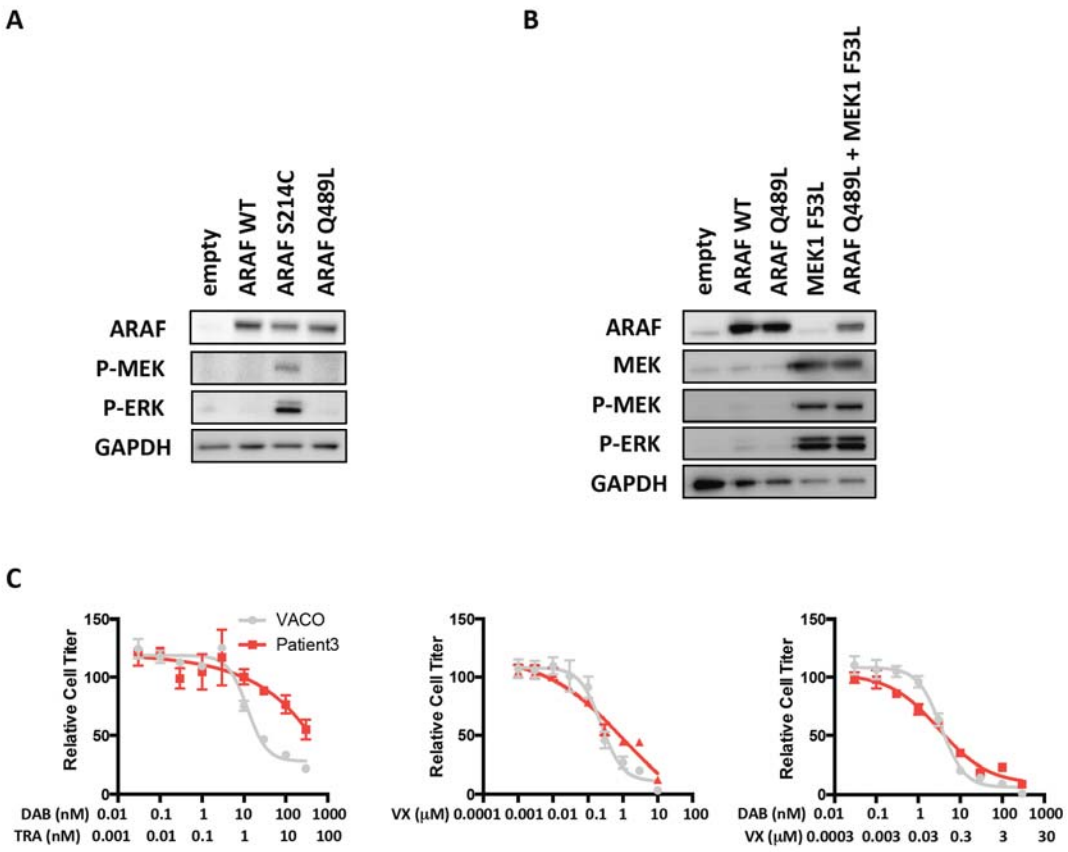

Figure S5: Role of ARAF Q489L and MEK1 F53L in resistance. (A) 293T cells expressing wild-type ARAF (ARAF WT), a S214C mutant ARAF known to be activating, Q489L mutant ARAF, or empty vector control were lysed and western blotting was performed with the indicated antibodies. (B) Western blot of 293T cells infected with empty vector, ARAF WT, ARAF Q489L, MEK1 F53L, and ARAF Q489L and MEK F53L in combination, as in (A). (C) VACO432 cells (VACO) and a tumor cell line derived from patient #3 (Patient3) were treated with the indicated concentrations of dabrafenib (DAB), trametinib (TRA), and VX-11e (VX) for 3d and relative cell titer was determined. Relative to VACO 432 cells, Patient3 cells display resistance to dabrafenib + trametinib, but retain sensitivity to VX-11e alone or in combination with dabrafenib.