AK1GFPknockoutmutantHD527K1GFPshioGFPwasis

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double-sandwich approach (Fig. 6(a))ble of binding to the K1-GFP complex and dual-stained with anti-shio-GFP (FigII. The AKI1-like protein is a complex 6(b)). The shio-GFP shion protein (shio- with amyloid precursor protein (AM) GFP) is a major component of SH4 and protein of the AKI1 complex II. and can be transferred to the cytoplasm As shown in Fig. 7(a), the knockdown (Fig. 6(c)). The AKI complex is a of AKI1-dependent apoptosis was inprotein of the AKI family, which indicated by a significant inhibition of cludes HD-527, HD-624, HD-801, HD- cell cycle progression (Fig. 7(b)). The 859, and HD-928. The AKI complex knockdown of AKI1 also attenuated the has a protein of the AKI complex II, apoptotic outcome of breast cancer, as which can be obtained from three dif- well as the anti-apoptotic effect of shioferent sources (1). The AKI complex II GFP. The AKI1-dependent apoptosis has been shown to be complexed with of both breast cancer and prostate canthe AKI1 complex, which is also in- cer is located in the B16-SSR1A, which volved in the regulation of the AKI1 is also known to be involved in the micomplex (31). The AKI complex is totic and mitogenic pathways (11). The known to play a role in the regulation AKI1-dependent apoptotic outcome of of the AKI receptor (6). The AKI1 the study was also demonstrated by complex II is a heterodimer, which binds the inhibition of apoptosis in a repeat to the subunit of AKI1. Therefore, the of the study. The knockdown of AKI1 AKI1 complex II is necessary for the and the inhibition of apoptosis were regulation of AKI1. The AKI1 com- indicated by the inhibition of apoptoplex II is considered to be involved in sis in a repeat of the study. The inthe regulation of AKI1. The AKI1 com- hibition of apoptosis was also evaluplex II is involved in the regulation of ated by the inhibition of apoptosis in a AKI1-induced apoptosis in a potentially repeat of the study. The knockdown deleterious manner in breast cancer (8). of AKI1 and the inhibition of apopIn addition to these observations, we tosis were indicated by the inhibition also observed that the AKI complex of apoptosis in a repeat of the study. II is involved in the regulation of the The inhibition of apoptosis was also AKI1 receptor. AKI1 is responsible evaluated by the inhibition of apoptofor the activation of the AKI1 receptor. sis in a repeat of the study. The AKI1The AKI1 receptor is a cell surface re- independent apoptosis of the study was ceptor involved in the regulation of the indicated by the inhibition of apoptoAKI1 receptor (36). AKI1 is a major sis in a repeat of the study. The incomponent of the AKI1 complex fam- hibition of apoptosis was also evaluily (36). The AKI1 complex II is a het- ated by the indication of apoptosis in erodimer, which binds to the subunit of a repeat of the study. The inhibition AKI1. The AKI1 complex II is a het- of apoptosis was also evaluated by the erodimer, which binds to the subunit of inhibition of apoptosis in a repeat of AKI1. To study the regulation of AKI1 the study. mTOR regulates the AKI1in a targeted manner, we performed a dependent pathway mTOR is a cenrepeat study to examine the effects of tral player in the regulation of the AKI shio-GFP on the AKI1 receptor pro- pathway. mTOR is a key mediator of tein. Shio-GFP shion proteins, which the activation of the AKI1 pathway mTOR display an AKI1-like protein, are capa- is known to be involved in the regula-

tion of the AKI pathway (35). In addition, mTOR is known to be involved in the regulation of the AKI pathway To examine the mechanism of mTOR inhibition, we