



**ESM Fig. 9** Screening of 3T3-L1 tet-907 cells. 3T3-L1 cells were transduced with lentivirus expressing IRE1 $\alpha$  K907A mutant under the control of the tetracycline-inducible promoter, followed by puromycin selection (2  $\mu$ g/ml). After 2 weeks, eighteen clones were selected. The expression levels of spliced *Xbp1* were measured in the presence or absence of doxycycline (5  $\mu$ g/ml) at **(a)** basal levels or **(b)** in response to 2  $\mu$ g/ml of tunicamycin treatment.