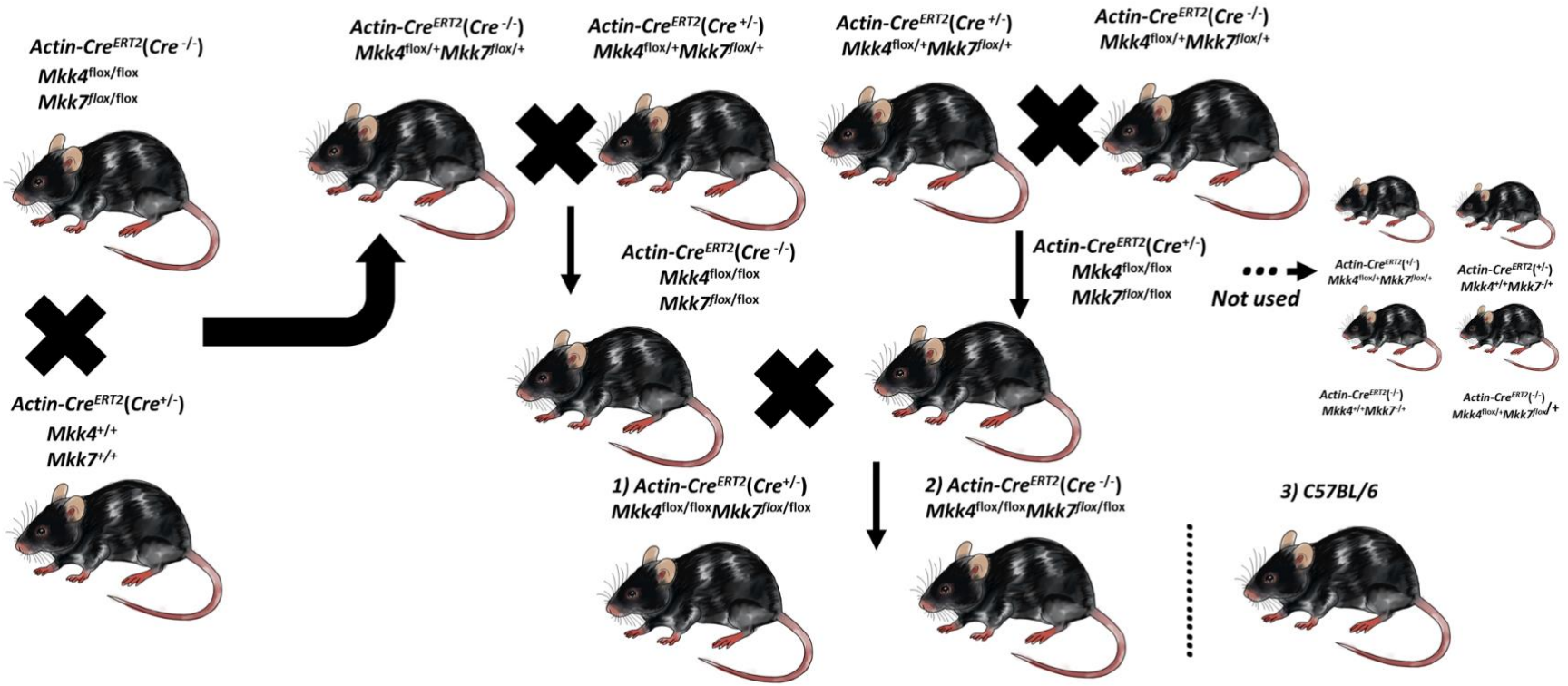

Figure S1. Generation of *Actin-Cre*^{ERT2}*(Cre*$^{+/-}$*),Mkk4*$^{flox/flox}$*,Mkk* $^{flox/flox}$ mice. Crossbreeding employed to get mice with the genotype handled in this investigation. Hemizygous *Actin-Cre*^{ERT2}*(Cre*$^{+/-}$*), Mkk4*$^{flox/flox}$*,Mkk7*$^{flox/flox}$ mice **(1)** was used to induce dual deletion of *Mkk4* and *Mkk7* genes after tamoxifen administration *Actin-Cre*^{ERT2} *(Cre*$^{-/-}$*), Mkk4*$^{flox/flox}$*,Mkk7*$^{flox/flox}$ **(2)** and wild-type C57BL/6 **(3)** mice were used in control groups.

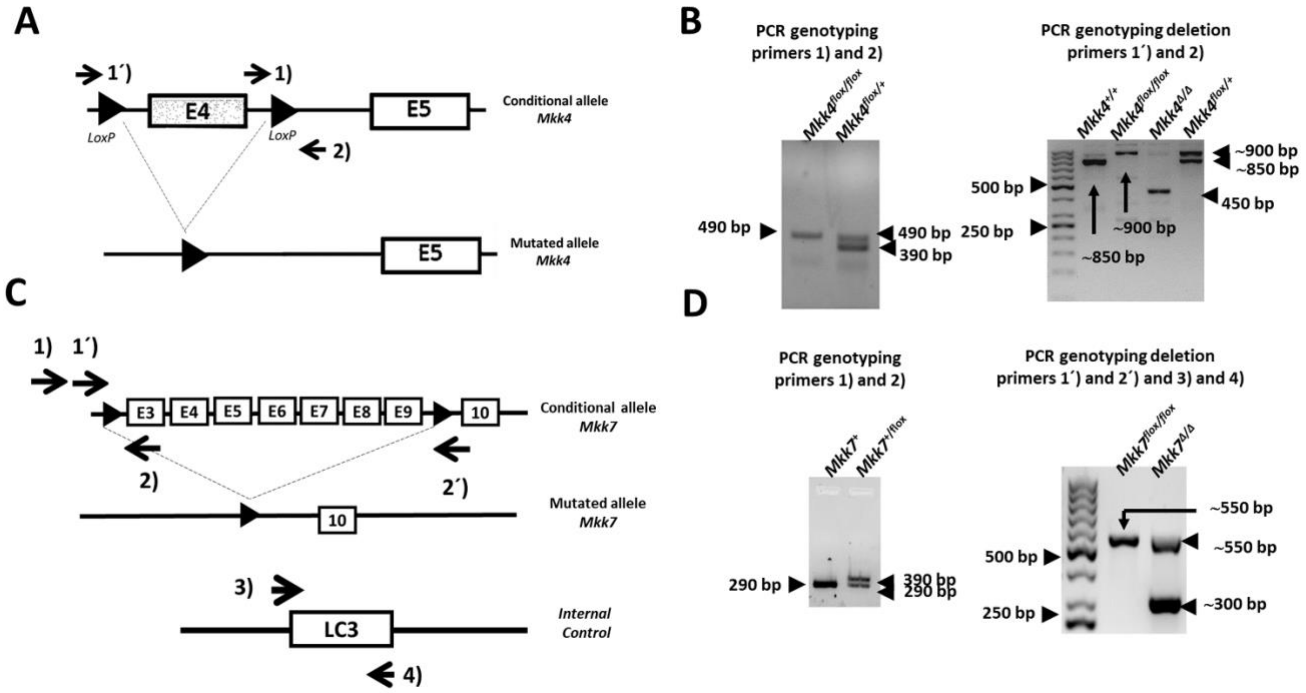

Figure S2. Strategy to genotype and to detect the deletion of *Mkk4* and *Mkk7* genes. A. Genomic region of conditional allele *Mkk4*, LoxP sequences flanked exon 4. Primers used for genotyping are 1) and 2). Primers employed for detecting deletion are 1´) and 2). **B.** In the left side, representative image of agarose gel for PCR genotyping test shows the band for $Mkk4^{+}$(390 bp) and $Mkk4^{flox}$(490 bp). On the right side, an image of agarose gel for PCR deletion test shows a band for $Mkk4^{+}$ (850 bp), $Mkk4^{flox}$ (900 bp) and $Mkk4^{\Delta}$ (450 bp). **C**. Genomic region of conditional allele *Mkk7*, LoxP sequences flanked exon 3 to exon 9. Primers used for genotyping are 1) and 2). Primers used for deletion are 1´) and 2´) plus a pair of primers 3) and 4) that amplifies a LC3 region, used as an internal control. **D.** Left, representative image of agarose gel for PCR genotyping test showing the band for $Mkk4^{+}$ (290 bp) and $Mkk4^{flox}$ (390 bp). The right agarose gel shows bands obtained for PCR deletion, $Mkk7^{\Delta/\Delta}$ genotype shows a band of 300 bp ($Mkk7^{\Delta}$) for deletion and 550 bp for Internal Control, $Mkk7^{flox/flox}$ genotype shows only a band of 550 bp (Internal Control).