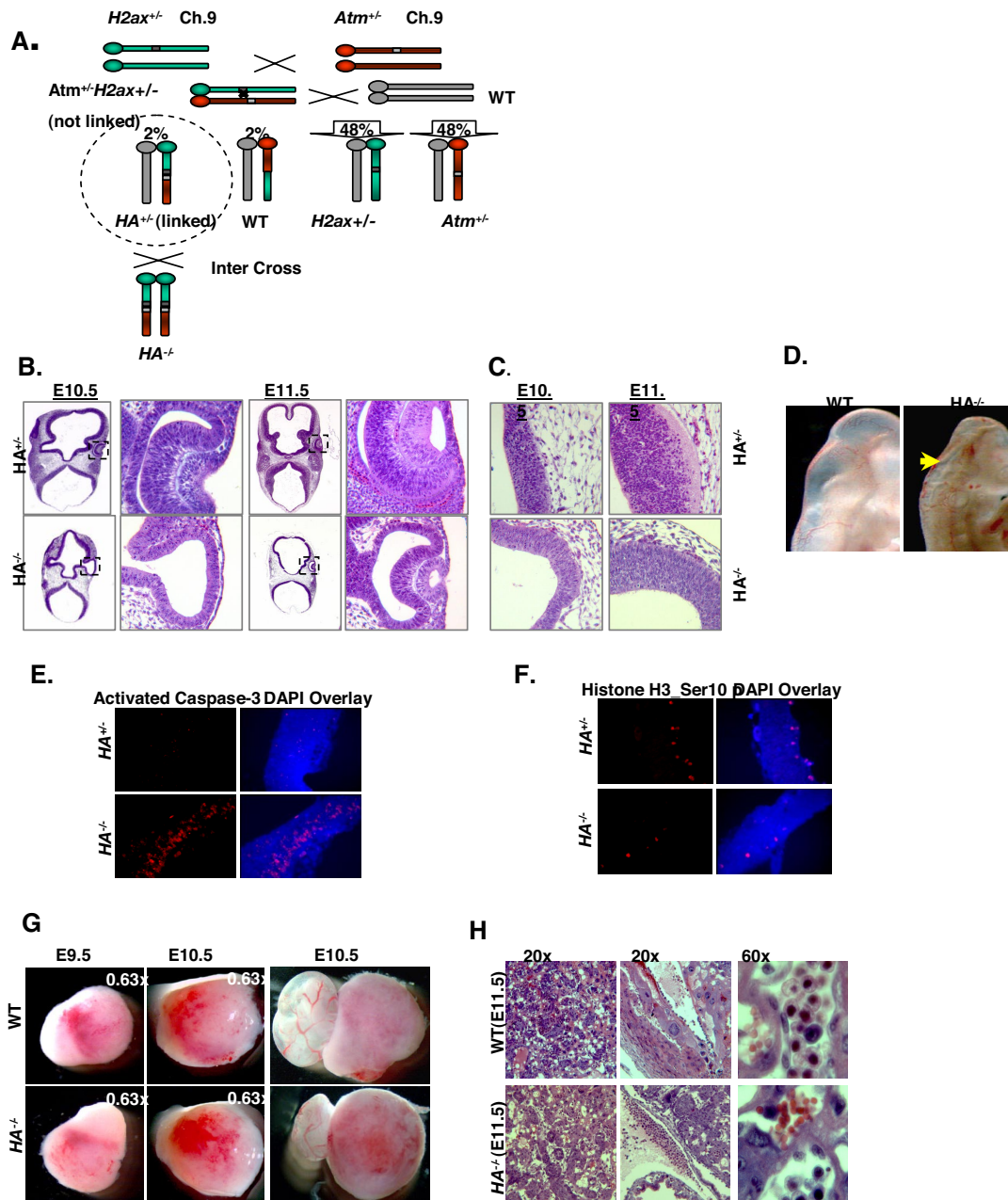


# Supporting Information

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**Fig. S1.** Generation and characterization of  $HA^{-/-}$  mice. (A) Breeding scheme used to generate  $HA^{+/-}$  and  $HA^{-/-}$  mice. Briefly,  $H2ax^{+/-}$  and  $Atm^{+/-}$  mice were bred together to generate  $H2ax^{+/-}Atm^{+/-}$  mice containing the  $Atm$  and  $H2ax$  mutations on different alleles (not linked) of chromosome 9. These founder mice were then crossed with multiple WT females. Because the two genes are 4 cm apart, this cross would genetically predict a 4% cross-over frequency of which half (2%) of the cross-overs would link the two mutant alleles and half (2%) would link the two WT alleles. As predicted, this breeding yielded 328 progeny of which 6 had the linked mutations ( $\approx 2\%$ ), consistent with the predicted cross-over frequency of 4% as outlined above. The founder  $HA^{+/-}$  mice were used to generate the cohort of  $HA^{+/-}$  and  $HA^{-/-}$  mice. Six initial  $HA^{+/-}$  mice were generated from three independent  $H2ax^{+/-}Atm^{+/-}$  (not linked) parents. (B) Hematoxylin/eosin (H&E)-stained transverse sections of E10.5 and E11.5  $HA^{+/-}$  and  $HA^{-/-}$  embryos (littermates). The dashed box indicates the optical cup region that is shown at the *Right*. The overview and the magnified pictures were taken used 4 $\times$  and 20 $\times$  objective lens, respectively. (C) Forebrain (20 $\times$ ) sections of E10.5 and E11.5  $HA^{+/-}$  and  $HA^{-/-}$  embryos. (D) Posterior views of E10.5 WT and  $HA^{-/-}$  embryos. The  $HA^{-/-}$  embryo shown has open neuronal tube (2 $\times$  objective lens). (E and F) Formalin-fixed, paraffin-embedded forebrain sections (20 $\times$ ) are stained with rabbit anti-cleaved Cap3 (E; Upstate) or rabbit anti-phosphorylated Ser-10 histone H3 antibody (F; Upstate) and Cy3-conjugated anti-Rabbit IgG secondary antibody. (G) Images of E9.5 and E10.5 WT and  $HA^{-/-}$  placentas with or without the yolk sac. (H) Histology analyses of the placentas from WT and  $HA^{-/-}$  embryos.