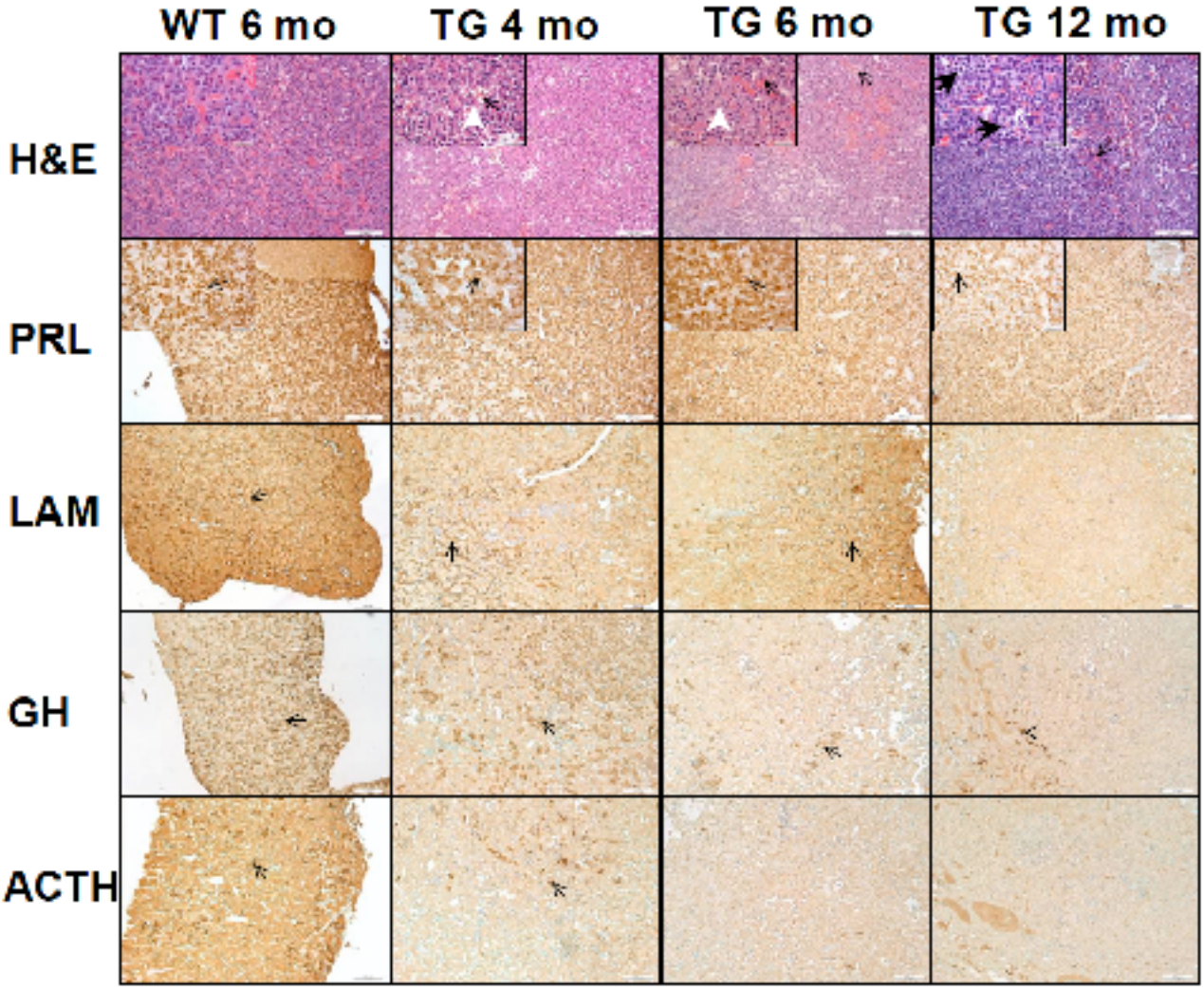

Supplementary Figure 2 Histological and immunohistochemical evaluation of wild-type (WT) and transgenic (TG) female mouse pituitary glands. The upper row of panels show representative hematoxylin-eosine (H&E) staining of pituitary glands of 6-month-old WT and 4-, 6- and 12 month-old TG mice. The thick black arrows indicate mitotic figures, white arrowheads vacuolized cells, and thin black arrows extravasated red blood cells. At 12 months, the small white arrow indicates a large cell with abnormally large nucleus, and the black bar the pseudocapsule. The second row of panels from the top shows PRL positive cells (arrows, brown cytoplasm). The 12-month TG sample (second row, right panel) presents another view from the same large adenoma with pseudocapsule as in the H&E staining with PRL positive cell in the nodule. The third row of panels from the top shows representative micrographs of laminin (LAM, arrow) staining. Notice the normal acinar pattern in WT mice, which is slightly disturbed in the 4 month-old TG females. At 6 months, unstained nodules are surrounded by almost normally stained areas, most probably corresponding to remnants of normal pituitary tissue. The macroscopic nodules in 12-month-old TG mice showed no laminin staining. The fourth and fifth rows of panels demonstrate that GH and ACTH positive cells (arrows) are seen in all TG pituitaries, but their density decreases when the pituitary glands become larger. Notice that the nodule in the 12-month TG sample did not stain for GH or ACTH.