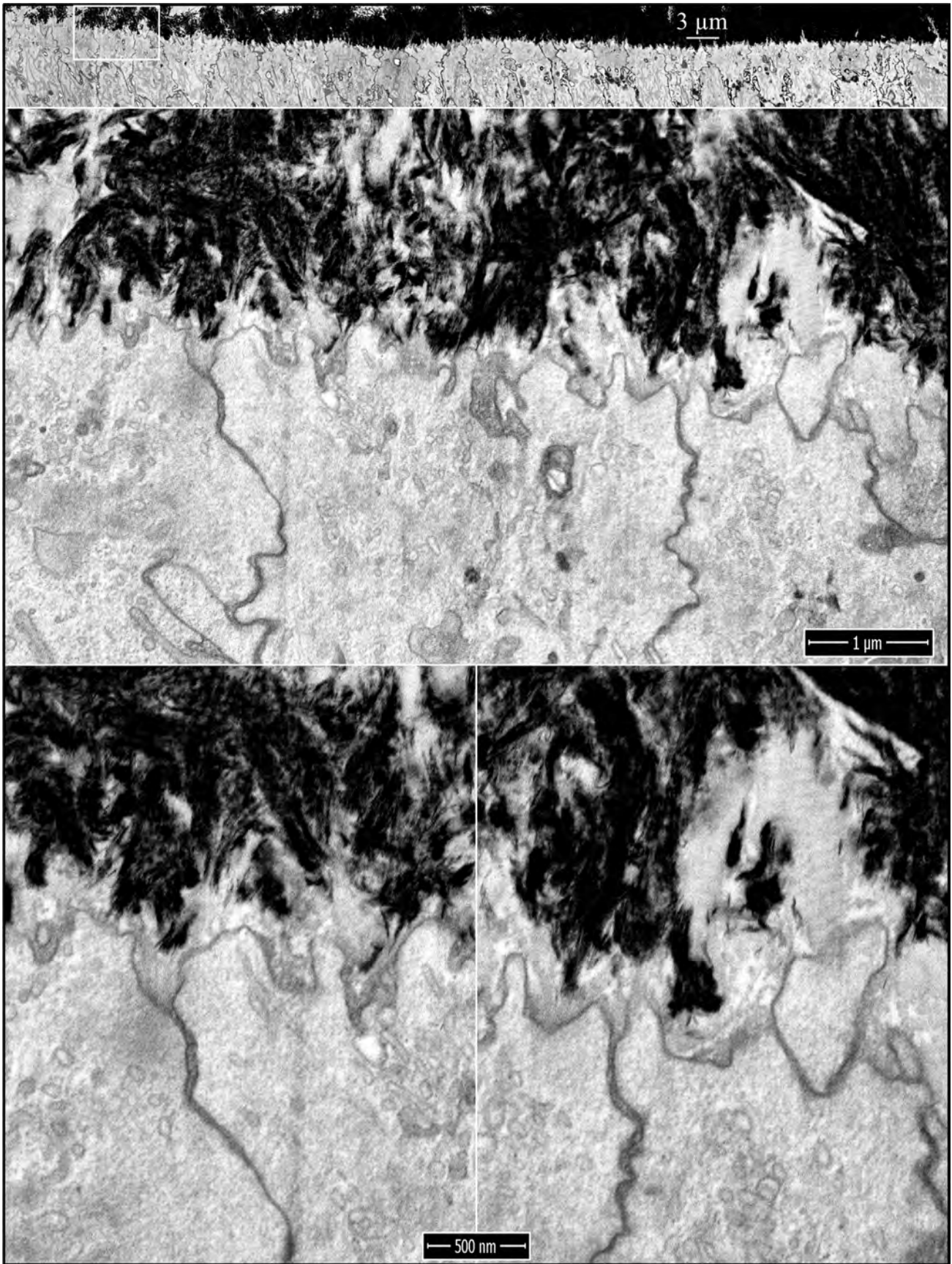


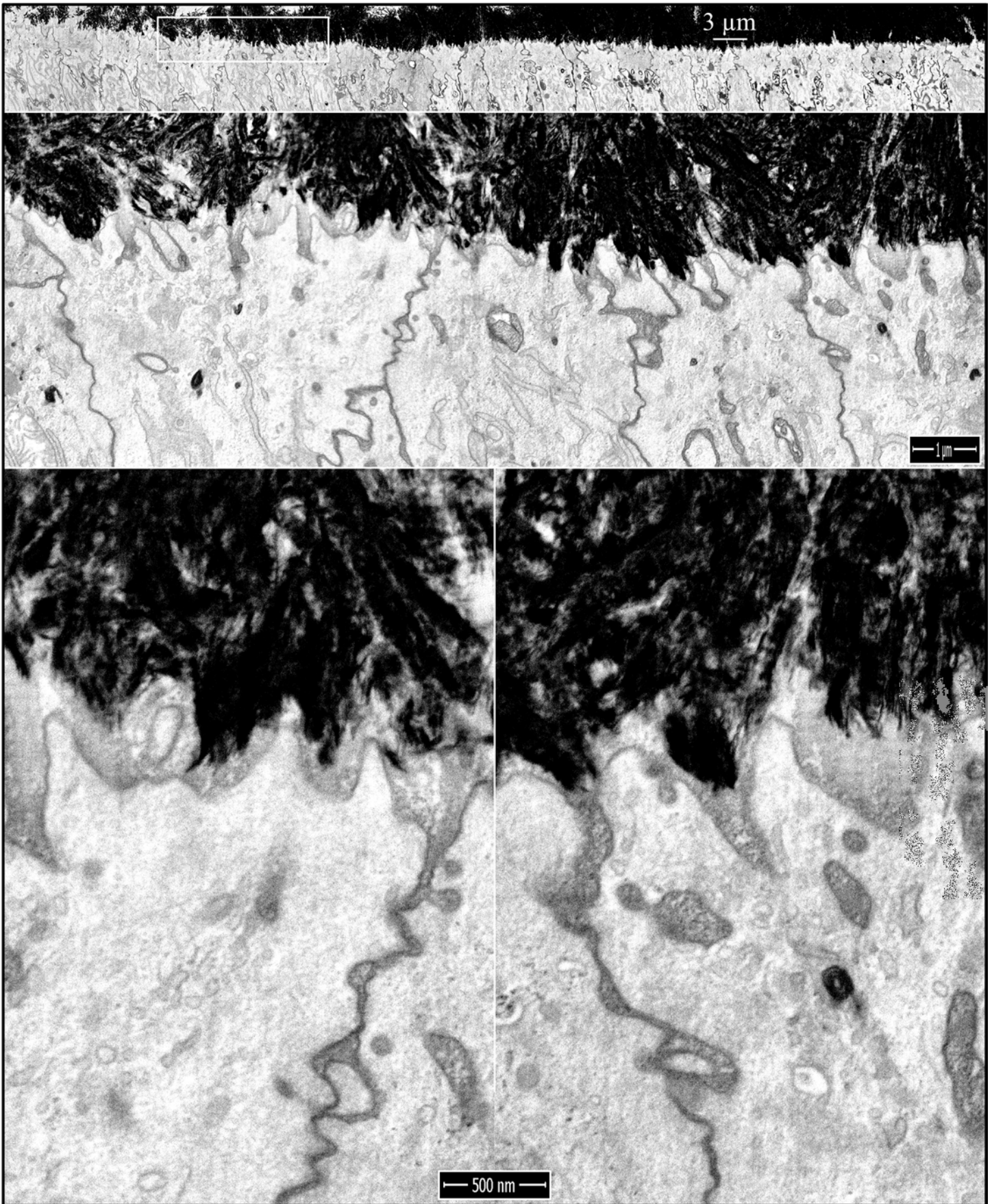
**Figure S24 Region 3.** Montage of *Ambn/Amelx* double null FIB-SEM images (2500x TLD) showing a lack of enamel initiation despite progression of dentin mineralization to almost 10  $\mu\text{m}$  in thickness (Fig. S34). **Key:** Am: Ameloblast; Od: Odontoblast; pD: predentin; SI: stratum intermedium.



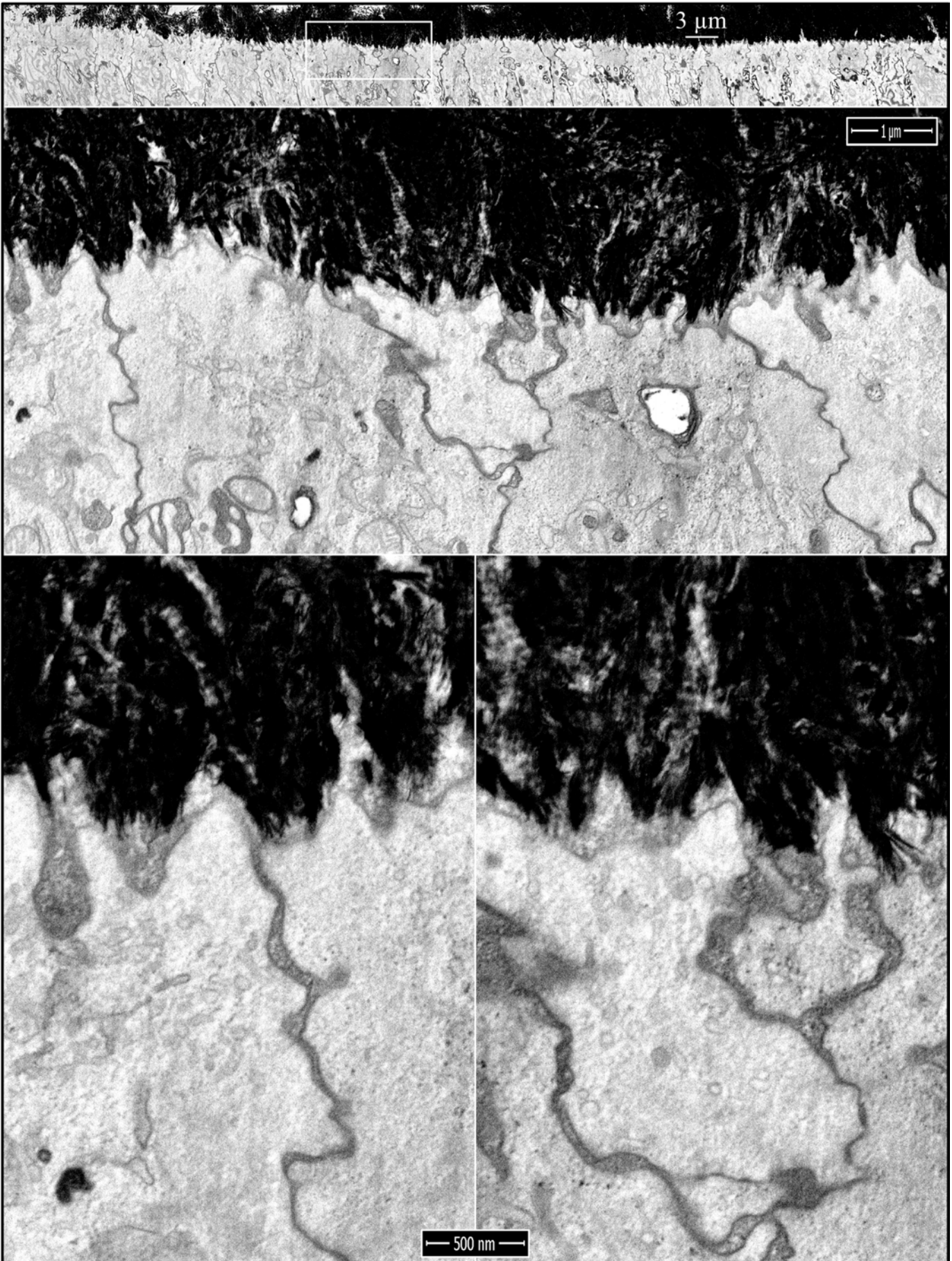
**Figure S25 Region 3a.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images. Note the expansion of dentin mineral, often extending along collagen fibers and extending near the ameloblast membrane.



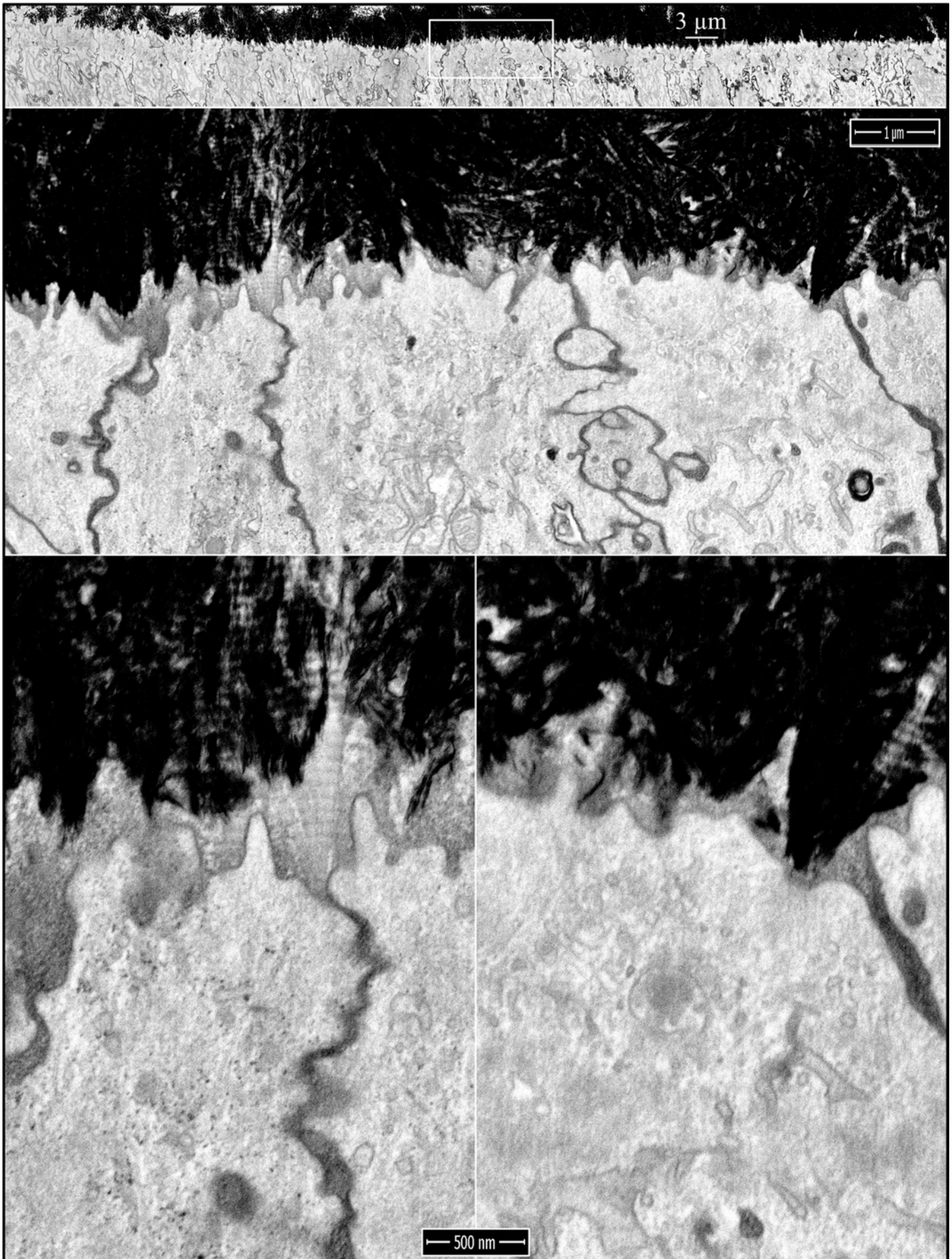
**Figure S26 Region 3b.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images. Note dentin mineral has coalesced into a continuous layer and closely approximates the ameloblast membrane. The initiation of characteristic enamel ribbons would normally occur approximately at this position.



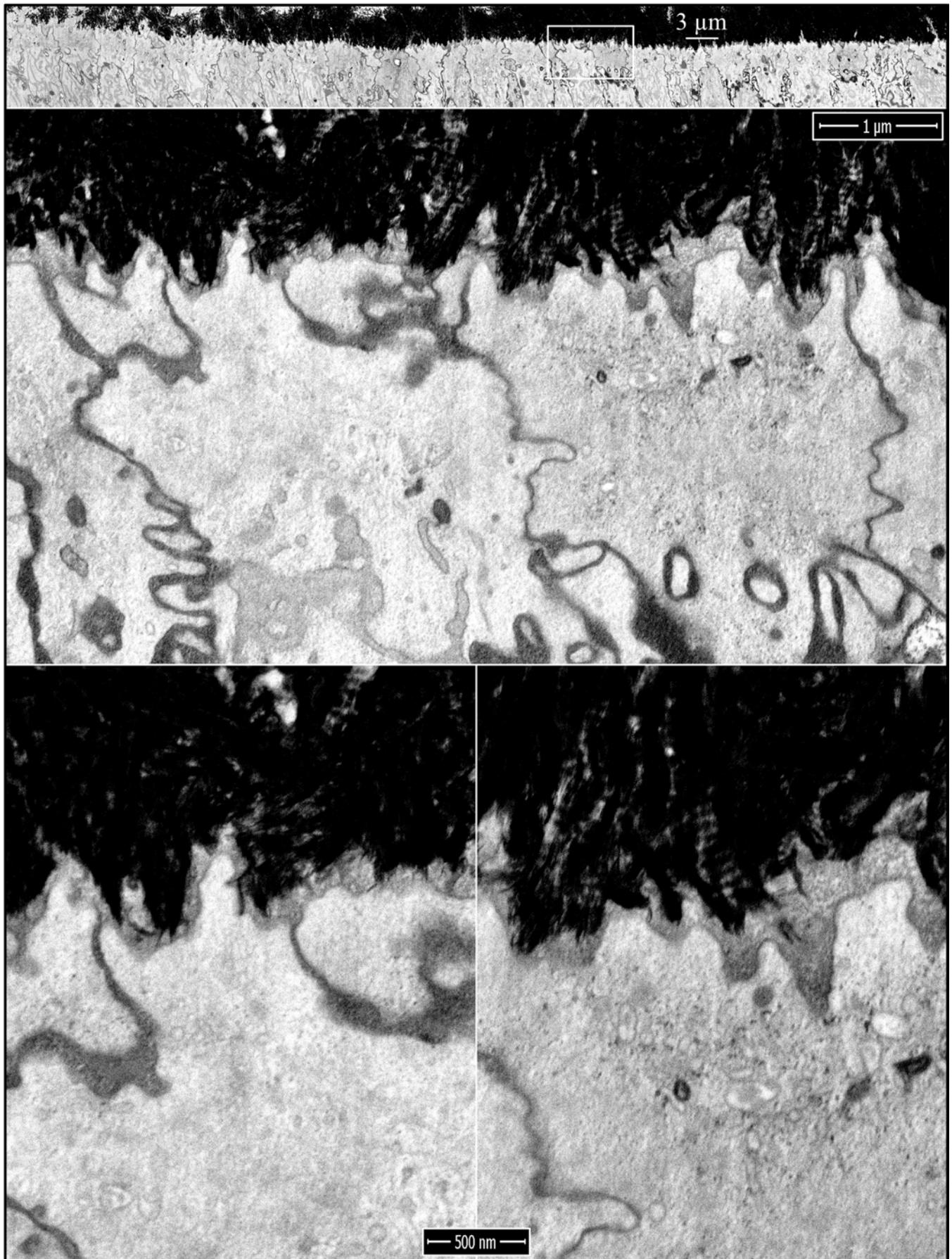
**Figure S27 Region 3c.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.



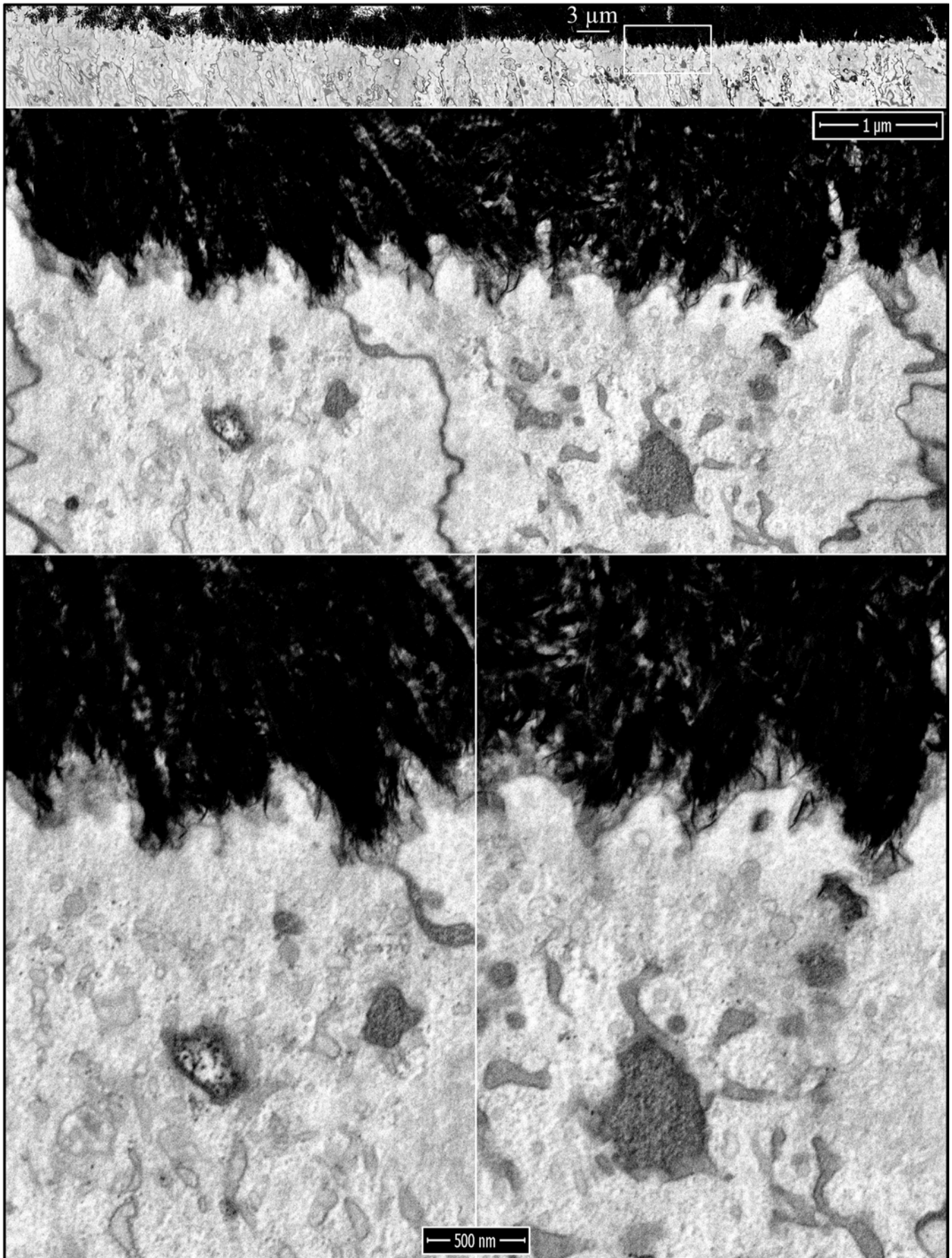
**Figure S28 Region 3d.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.



**Figure S29 Region 3e.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.

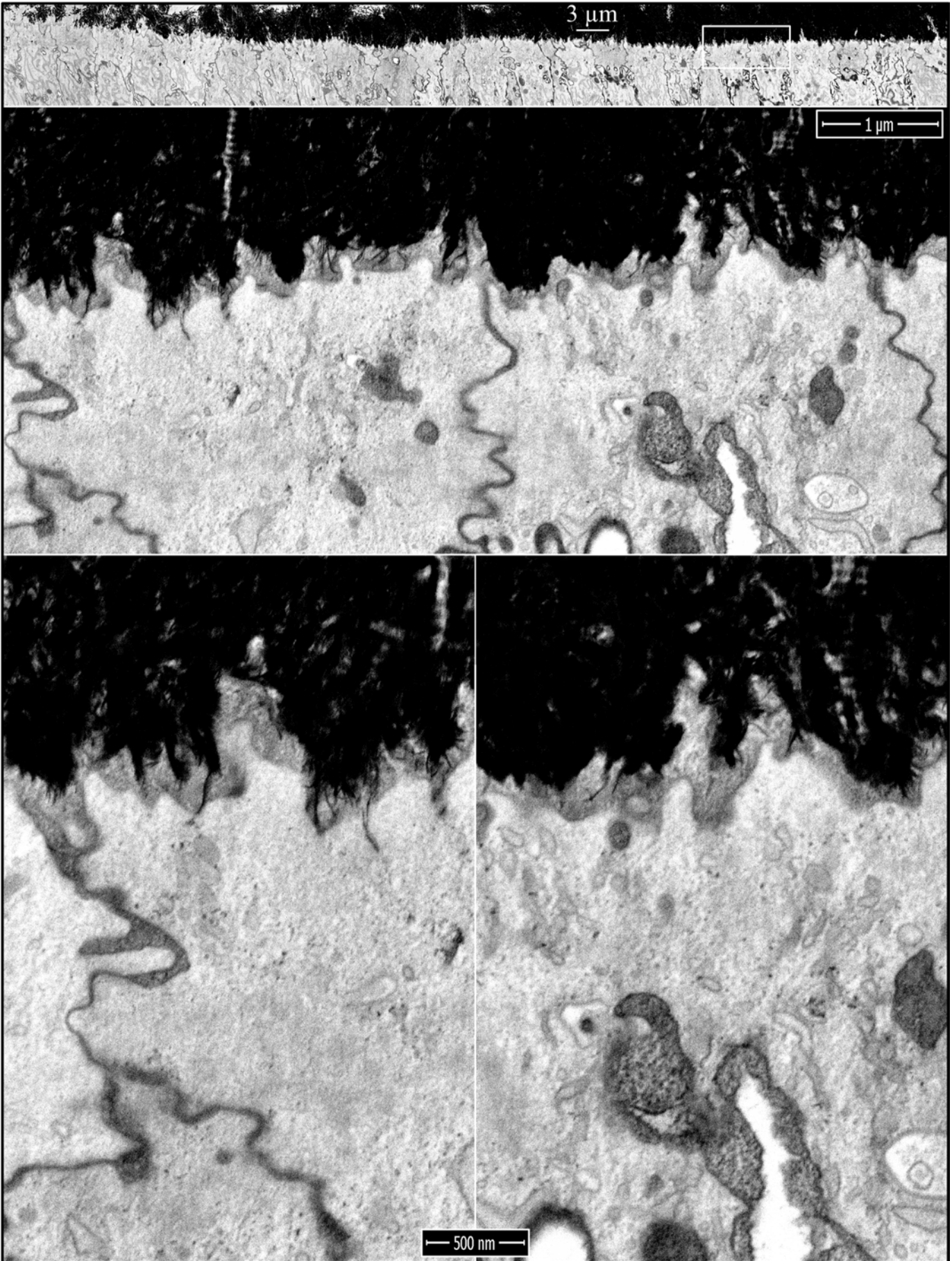


**Figure S30 Region 3f.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.

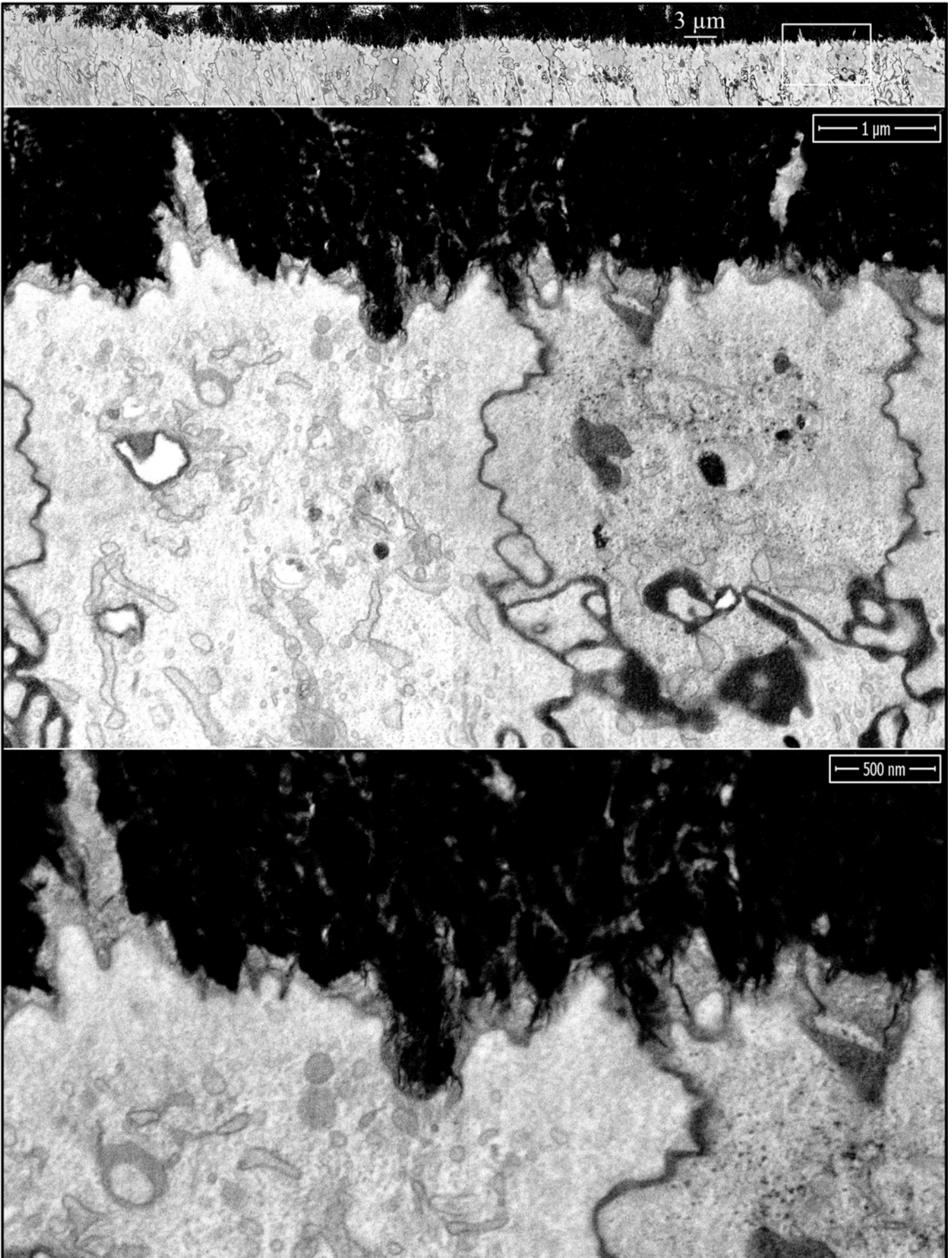


**Figure S31 Region 3g.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.

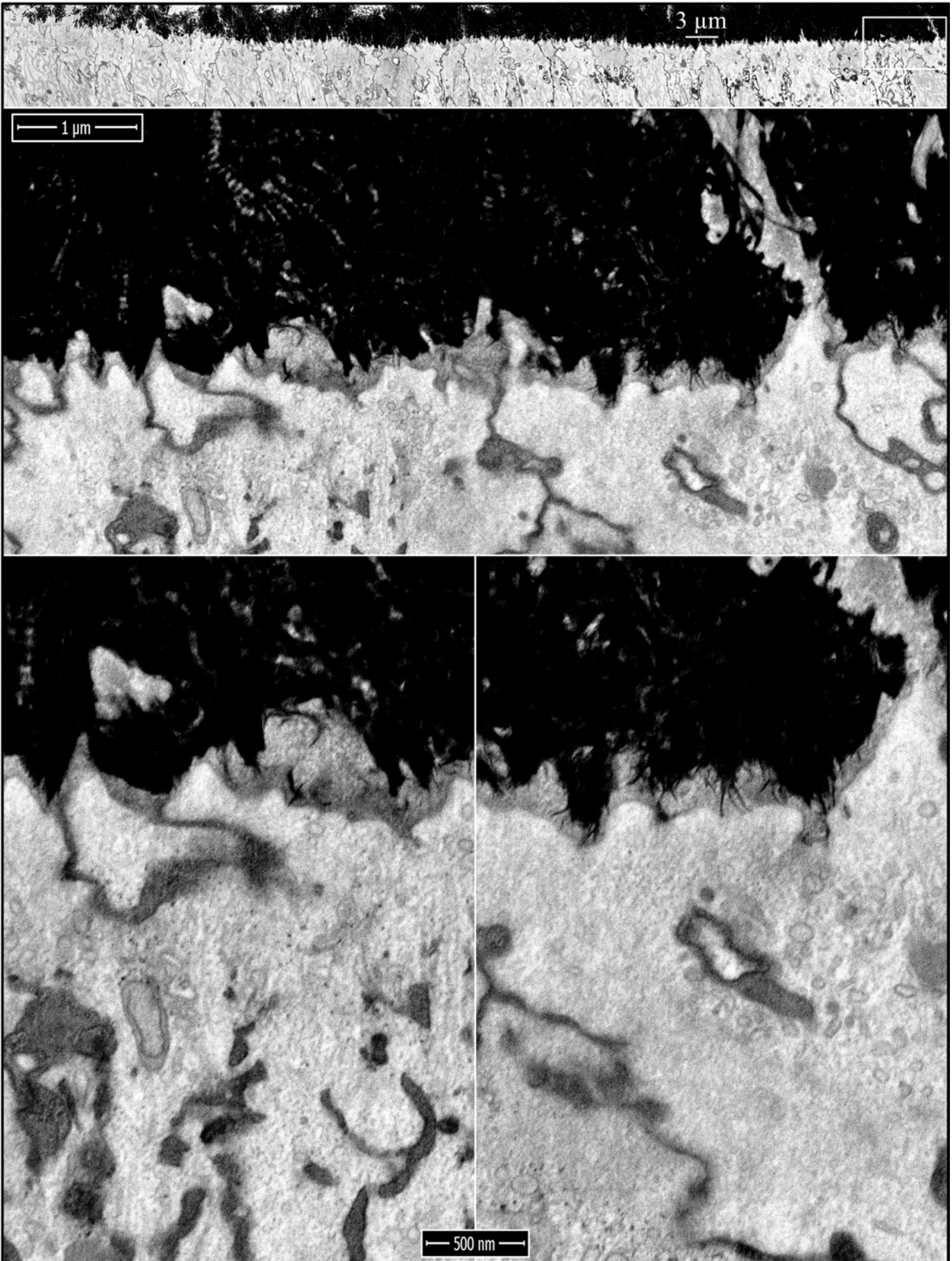




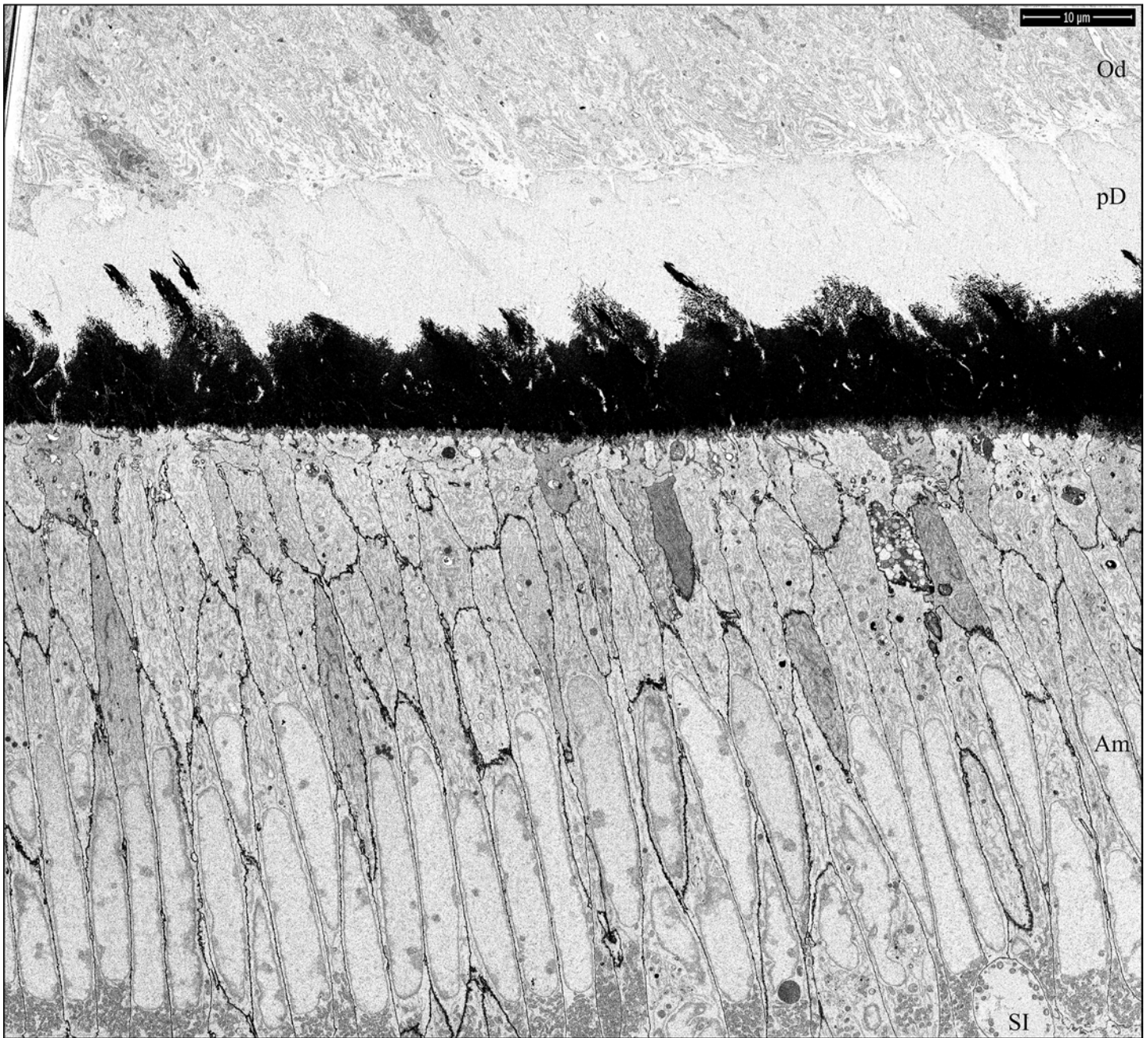
**Figure S32 Region 3h.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.



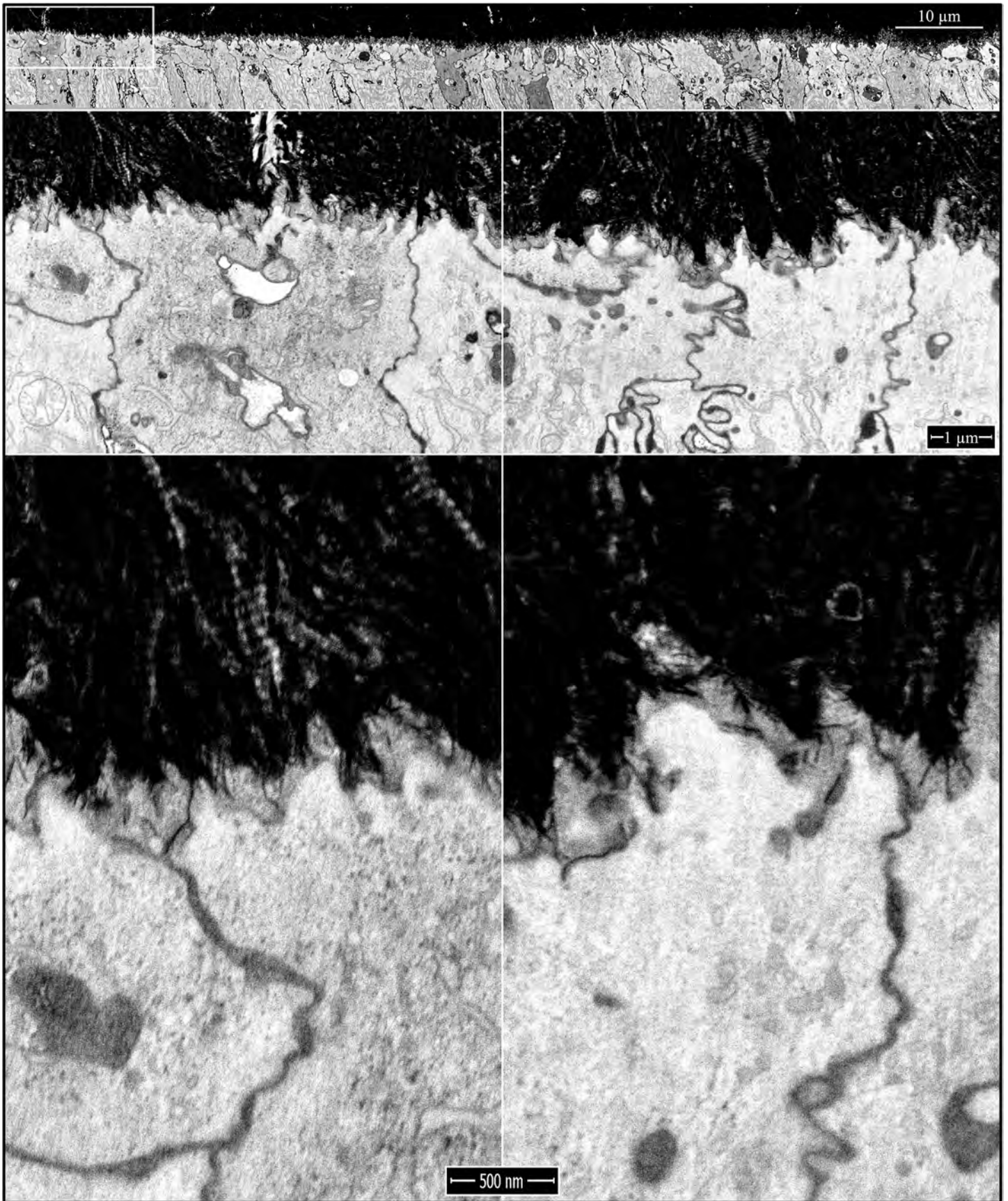
**Figure S33 Region 3i.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.



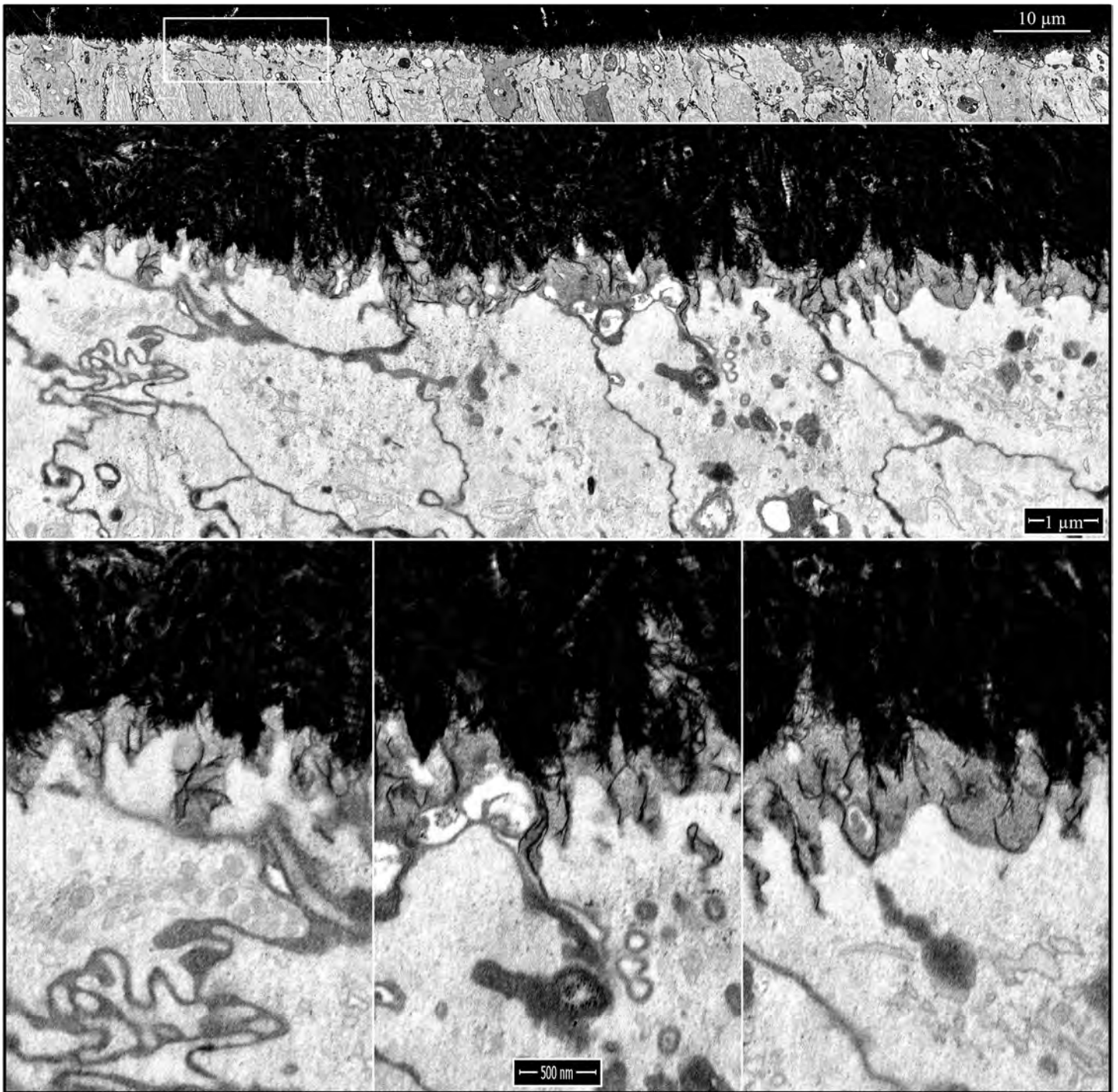
**Figure S34 Region 3j.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.



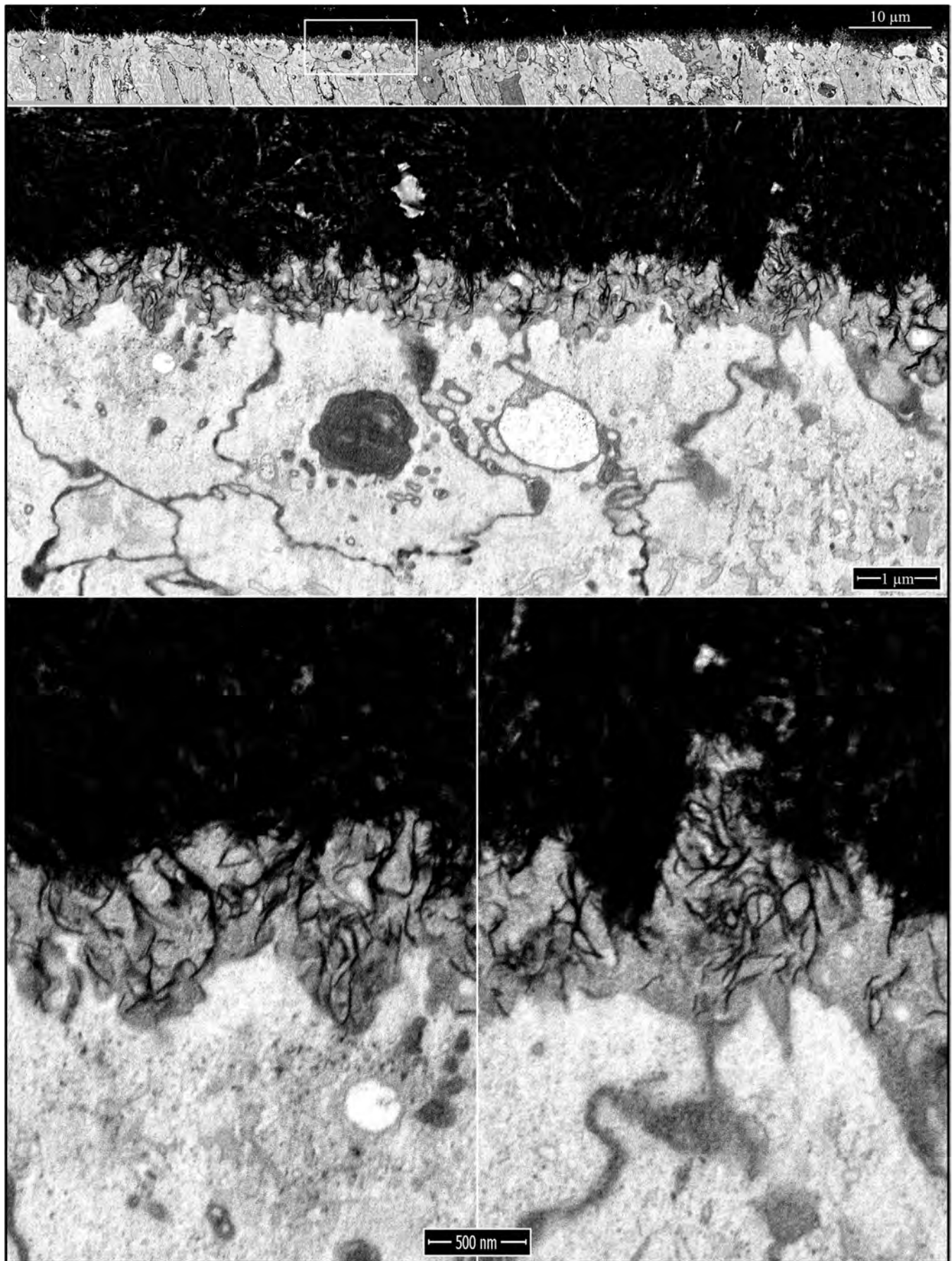
**Figure S35 Region 4.** Montage of *Ambn/Amelx* double null FIB-SEM images (2500x TLD) showing the region immediately incisal to Region 3 (Figs. S24-S34) showing a lack of enamel initiation despite progression of dentin mineralization to high density and 15-20  $\mu\text{m}$  in thickness. Moving incisally, the ameloblasts increasingly show increasing signs of cell pathology. **Key:** Am: Ameloblast; Od: Odontoblast; pD: predentin; SI: stratum intermedium.



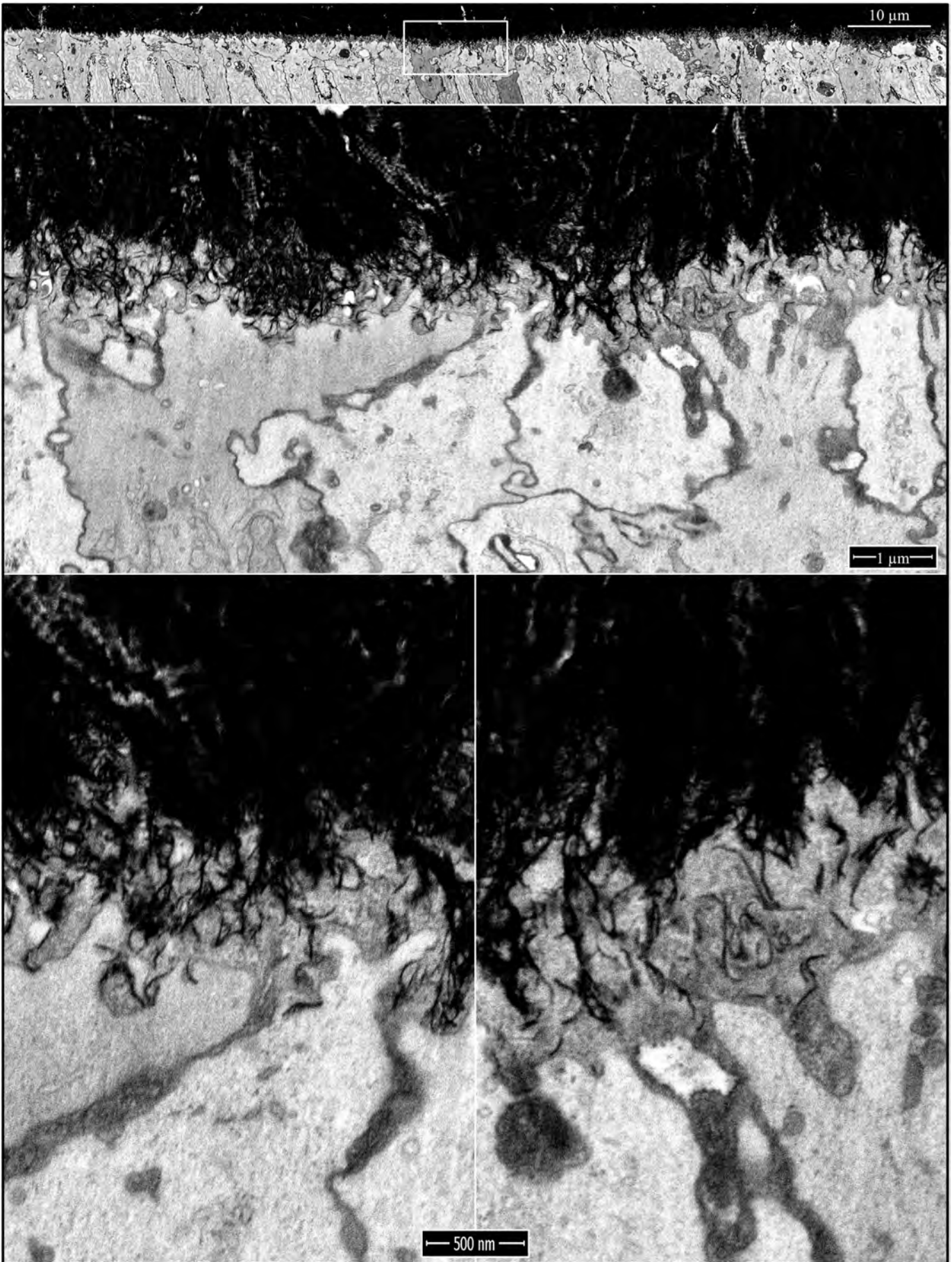
**Figure S36 Region 4a.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.



**Figure S37 Region 4b.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.

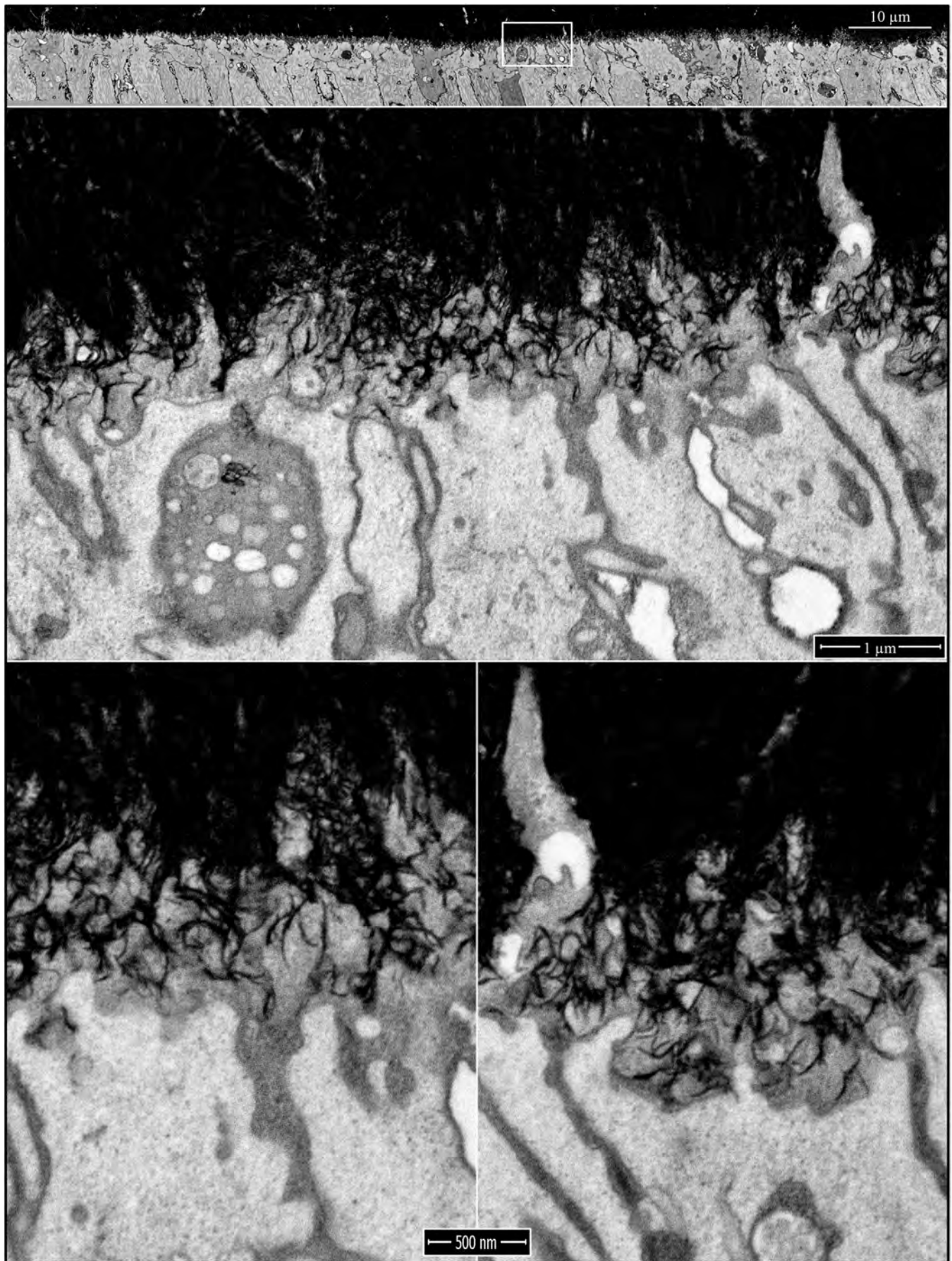


**Figure S38 Region 4c.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. Note the large dark and light vacuoles within the ameloblasts at the time strange curled ribbon-like deposits form. **Bottom:** 35000x TLD images.

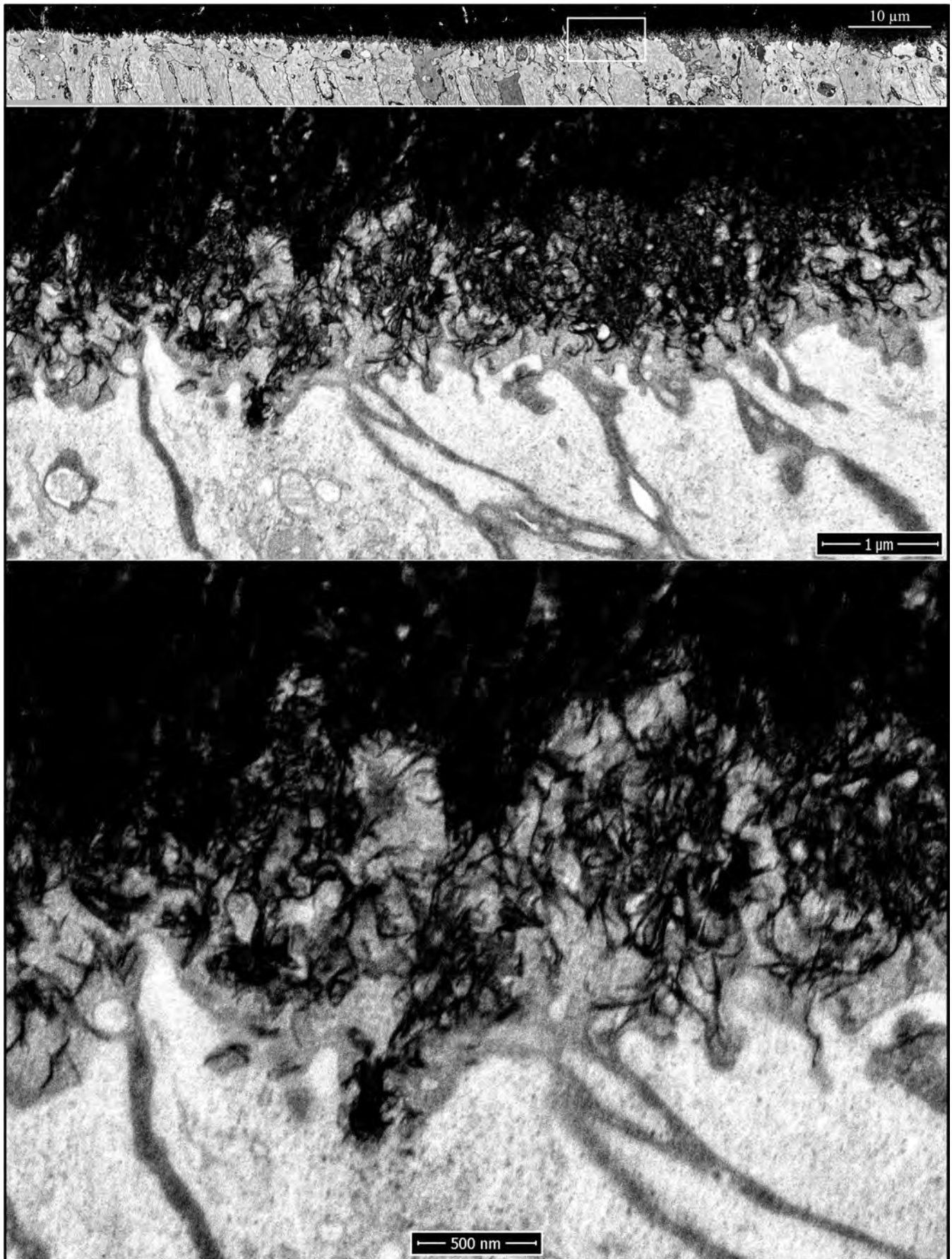


**Figure S39 Region 4d.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.

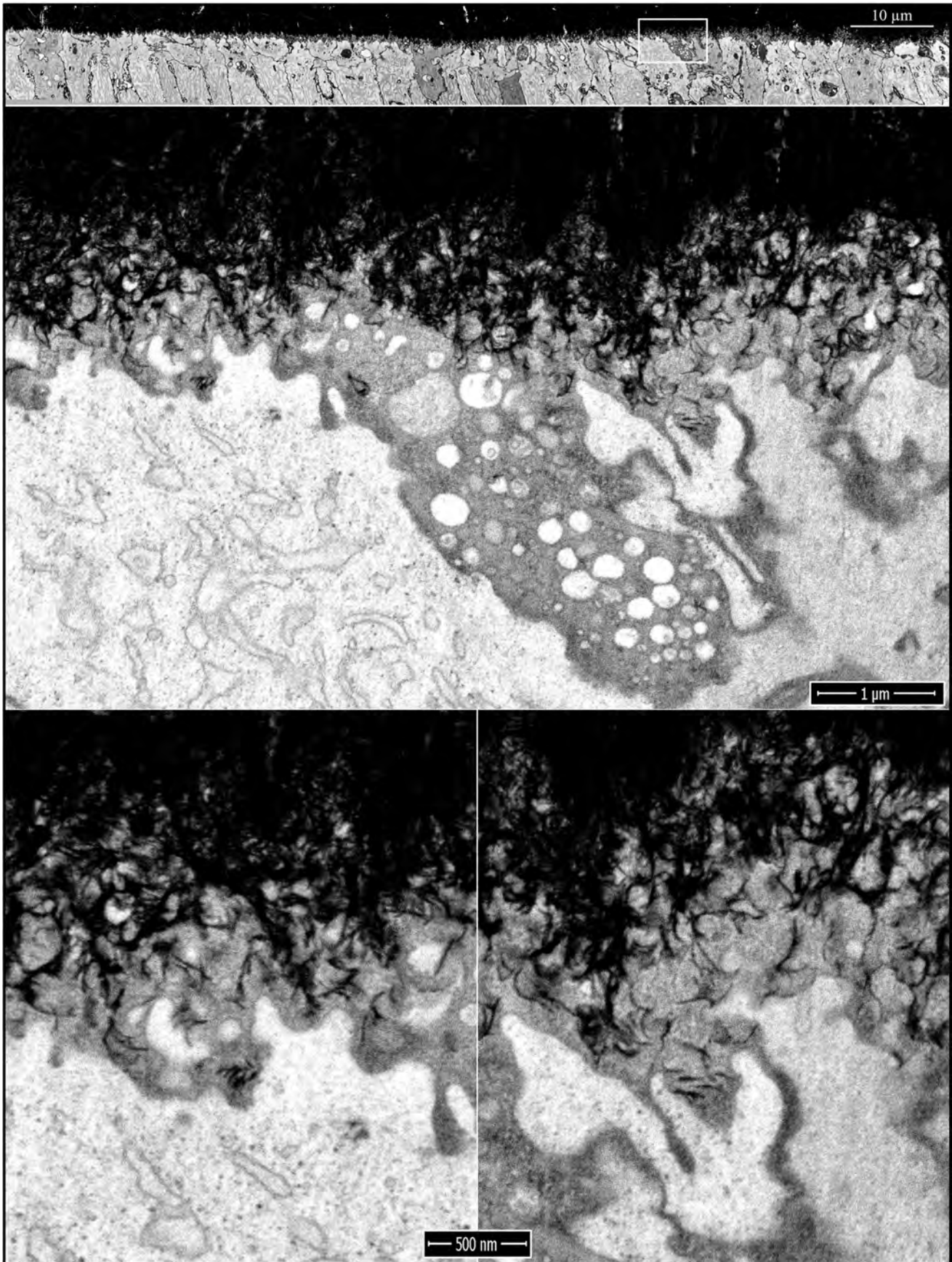




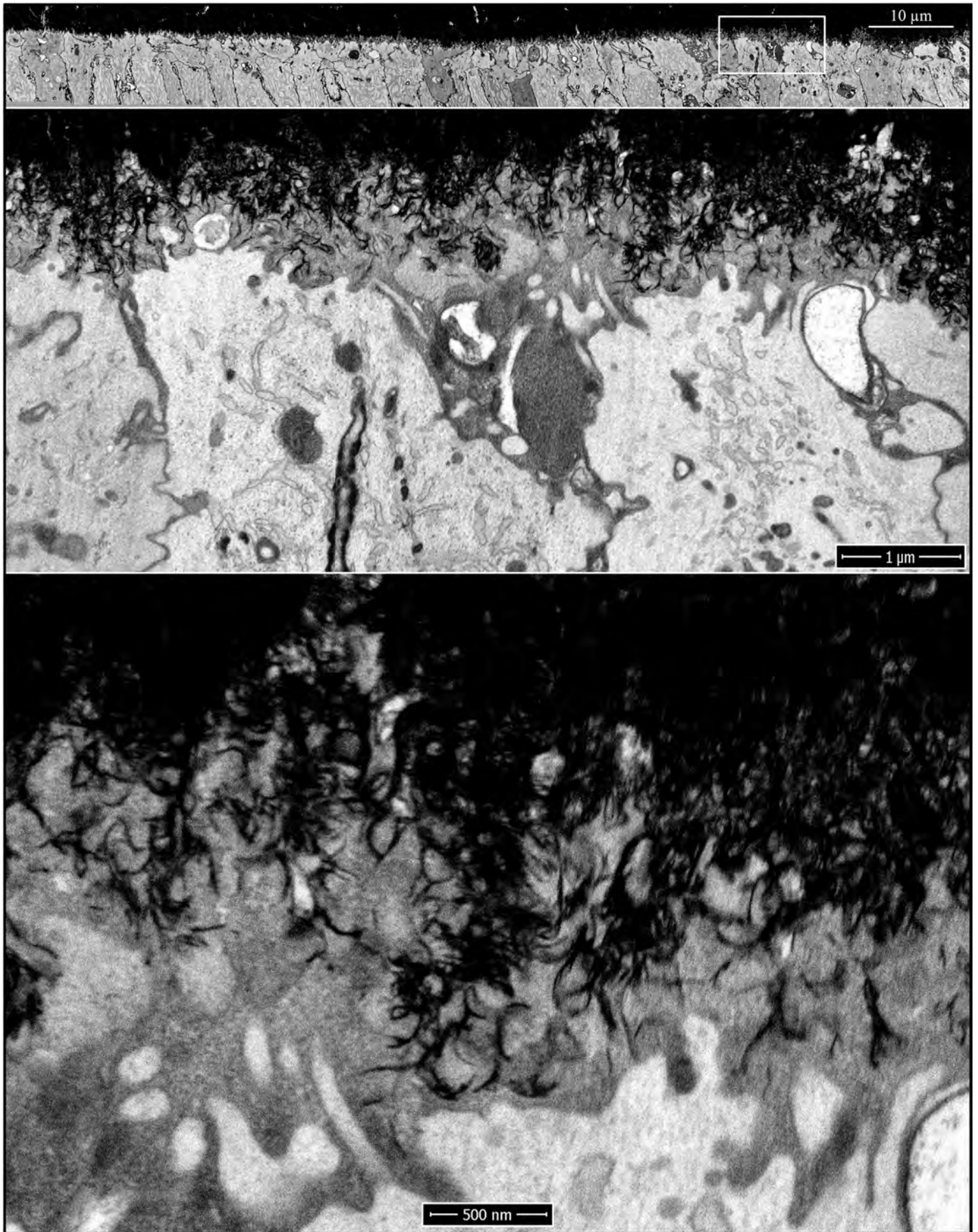
**Figure S40 Region 4e.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. Note the large vacuole containing smaller vacuoles or vesicles. **Bottom:** 35000x TLD images.



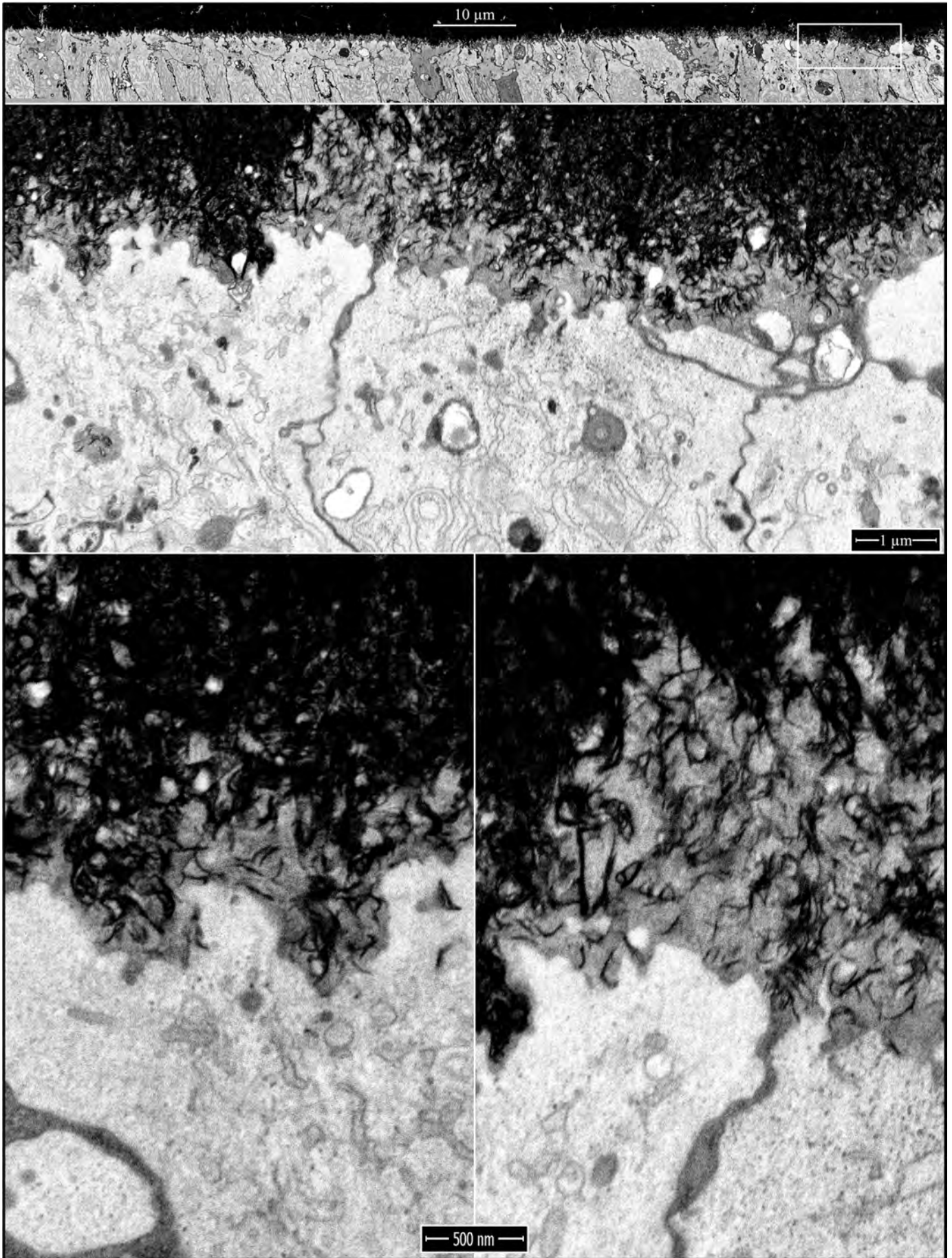
**Figure S41 Region 4f.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images. Disorganized, mineral crust, not oriented toward the ameloblast membrane forms on dentin.



**Figure S42 Region 4g.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area showing ameloblast cell pathology associated with the deposition of a mineral crust on the dentin surface. **Bottom:** 35000x TLD images showing the initial mineral crust that is deposited in place of a characteristic field of initial enamel.



**Figure S43 Region 4h.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.



**Figure S44 Region 4i.** *Ambn/Amelx* double null FIB-SEM images. **Top:** Montage of 10000x TLD images. **Middle:** Montage of 20000x TLD images from boxed area. **Bottom:** 35000x TLD images.