SUPPLEMENTAL INFORMATION

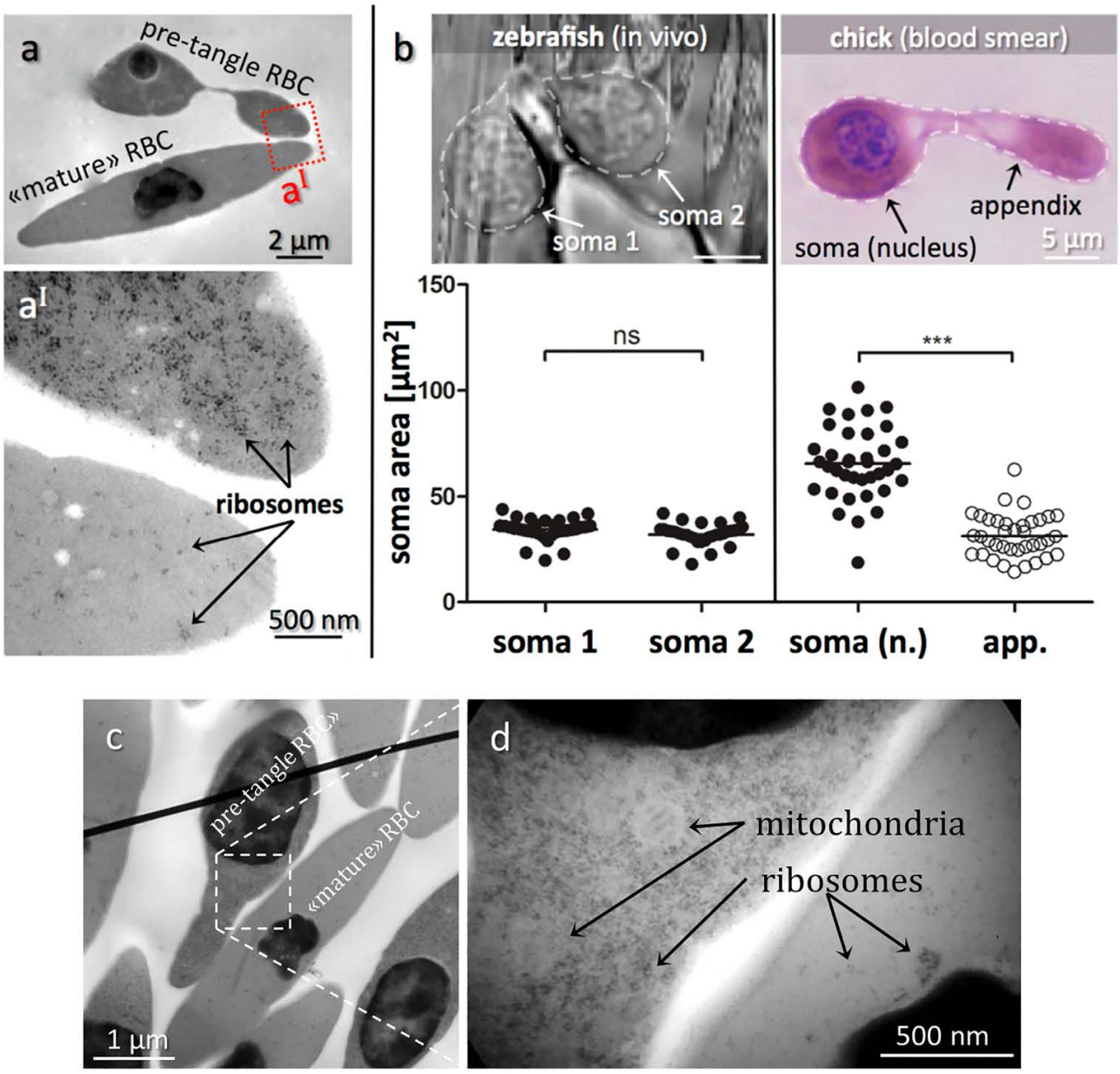
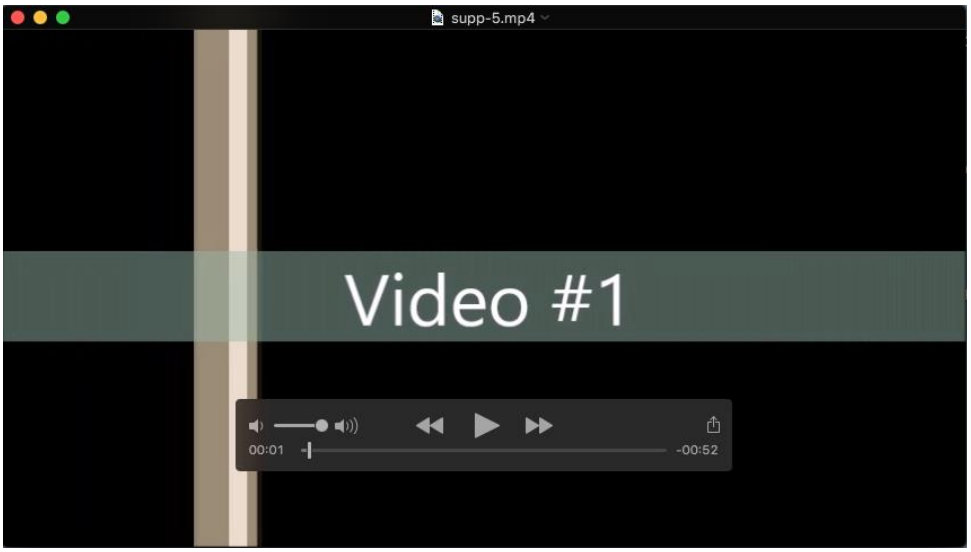


Fig. S1. Transmission electron micrographs of RBCs in blood of fish and chick embryos. (a) Electron micrographs comparing pre-tangle and mature chick RBCs. (a′) Zoomed region indicated in (a) in a pre-tangle RBC (top) contains abundant free ribosomes in contrast to the mature RBC (bottom). Other side-by-side comparisons of pre-tangling versus mature chick RBCs as shown in (c + d) confirmed the far higher quantity of ribosomes and mitochondria in immature RBCs relative to fully differentiated cells. (b) Comparing somata sizes of dumbbell-shaped zebrafish and chick RBCs. In the zebrafish, both somata are nucleated and of similar size. In contrast, only one soma is nucleated in the chick RBC, which is significantly larger in size than the other soma. ***P<0.001.

Movie 1. Formation of transluminal pillars and bifurcations. Time-lapse confocal imaging of the developing vasculature in the CVP of *Tg(fli1a:eGFP)* zebrafish between 28- 32 hpf. GFP-signal is represented in black. The vascular front rapidly expands by sprouting angiogenesis and joins to form the pole. Two arrows (red, green) indicate the appearance of two transluminal pillars. Such pillars are then integrated into the CVP and remain there for many hours or even days. They are the main site where *RBC splitting* occurs.

Movie 2. Exemplifying videos #1-4 of *RBC splitting* in the zebrafish embryo. RBCs are tangling up and splitting at a vascular pole. Time interval is indicated as min:sec. The videos were all captured between 39-45 hpf.



Movie 3. Examplifying videos #1-3 of tangled RBCs in the chicken chorioallantoic membrane (CAM) at d10. At day 10 after incubation (d10), the chick CAM contains high numbers of capillary beds. In these regions, dumbbell-shaped RBCs tangle up at vascular structures.