**Supplementary Fig. 1: Aortic arch and conotruncal defects in VEGF$^{120/120}$ and VEGF$^{188/188}$ mice:** Intraventricular injection of ink (a) or Evans blue (c) to visualize the vascular malformations in VEGF$^{120/120}$ and VEGF$^{188/188}$ neonates, with schematic representation of the vascular malformations. For each set of two panels, the left panel displays a micrograph of the thoracic vessels, while the right panel schematically illustrates the vascular malformation. a,b, VEGF$^{188/188}$ neonate: the right subclavian artery (S; traced with yellow dashed line in a and indicated in yellow in b) originates aberrantly from the descending aorta and crosses the midline behind the esophagus and trachea. This “artera lusoria” is caused by abnormal regression of the right 4$^{\text{th}}$ arch artery and persistence of the right distal dorsal aorta. For better visualization of the vascular defects, the ductus arteriosus and pulmonary trunk were removed. c,d, VEGF$^{120/120}$ neonate with a right-sided aortic arch and descending aorta, a right-sided ductus arteriosus (D) and a left-sided brachiocephalic trunk. This condition is the “mirror”-image of the normal aortic configuration. e, Conotruncal alignment defect in E14.5 VEGF$^{188/188}$ embryo: the aorta runs anterior and parallel to the pulmonary trunk but both arteries connect to the correct ventricle. There is a subarterial ventricular septal defect because of malalignment of the conotruncal septum. f,g, Whole-mount LacZ staining of E9.5 VEGF$^{188/188}$ embryos, harboring a Tie1LacZ transgene, to visualize the vasculature (blue). Panel f shows a healthy VEGF$^{188/188}$ embryo, revealing normal development of the 1$^{\text{st}}$, 2$^{\text{nd}}$ and 3$^{\text{rd}}$ pharyngeal arches and their arteries and dorsal aorta. In panel g, a sick VEGF$^{188/188}$ embryo with circulatory collapse is shown, revealing hypoplasia of the first three pharyngeal arches and disintegration of their pharyngeal arch arteries and rostral dorsal aorta. The mouse in panel e was injected with ink. A (aorta); AV (atrio-ventricular channel); B (brachio-cephalic trunk); C (carotid artery); D (ductus arteriosus); E (esophagus); LV (left ventricle); P (pulmonary trunk); PTA (persistent truncus arteriosus); RA (right atrium); T (trachea); S (subclavian artery). Colour codes and abbreviations as in Fig. 1.