Carotid body vascularization relies on O_2-sensing cells-derived VEGFA.

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Oxygen (O_2) and nutrient delivery to tissues require an intricate network of physiological mechanisms regulating tissue perfusion to meet metabolic demands and cellular function. The carotid body (CB) emerges as a pivotal arterial chemoreceptor, finely attuned to detecting alterations in blood composition and oxygen levels, thereby ensuring adequate oxygen delivery to tissues and organs to support cellular function and survival. To achieve its function, the CB must receive a relatively high blood flow compared to surrounding tissues. Despite its significance, our comprehension of the specific mechanisms governing CB vascularization remains limited. Previous investigations have demonstrated that HIF-2α overexpression in CB glomus cells leads to CB hypertrophy, whereas HIF-2α inactivation detrimentally affects CB development. HIF-2α mediates the upregulation of vascular endothelial growth factor A (VEGFA), a key regulator of vascularization during development and under pathological conditions, such as cancer. In this study, we elucidate that targeted inactivation of VEGFA in CB O_2-sensing cells results in defective vascularization of the CB parenchyma, concomitant with an augmentation in the number of CB O_2-sensing cells. Consequently, we observed an enhancement of the acute hypoxic ventilatory response to hypoxia compared to control mice. Notably, systemic adaptation to chronic hypoxia remains unaffected in VEGFA-deficient mice; however, a diminished number of proliferating cells within the CB parenchyma (TH-/BrdU+) suggests impairments in the differentiation of CB progenitor cells into new endothelial cells. These collective findings underscore the pivotal role of CB O_2-sensing cells in releasing VEGFA to foster their own vascularization, thereby facilitating the sensing of oxygen levels in the blood. An in-depth understanding of the mechanisms governing CB vascularization promises valuable insights into its function and potential implications for various physiological and pathological conditions.