Letter by Papangeli et al Regarding Article, “The ERG–APLNR Axis Controls Pulmonary Venule Endothelial Proliferation in Pulmonary Veno-Occlusive Disease”

To the Editor:

We have read with great interest the article by Lathen and colleagues titled “The ERG–APLNR Axis Controls Pulmonary Venule Endothelial Proliferation in Pulmonary Veno-Occlusive Disease,” and congratulate the authors for their thorough approach using human samples and modern genetic techniques. However, there are 2 key points that, in our opinion, deserve attention.

First, following a literature review, the authors conclude that “These studies point to the concept that Aplnr signaling has direct and unique effects on the venous circulation.” However, the majority of the cited studies do not describe venous-specific mechanisms. Cheng et al demonstrated that apelin administration decreased both the mean arterial pressure and the mean circulatory filling pressure in rats, summarizing that “apelin is an arterial and venous dilator in vivo.” Cox and colleagues used a bead chemotaxis model on frog embryos; although apelin-soaked beads induced sprouting from the cardinal vein region, the response to apelin was comparable to vascular endothelial growth factor–soaked beads and did not exclude nonvenous endothelial cells responding to apelin. Last, the authors invoke work by Eyries and colleagues that used the zebrafish cefulin fin amputation model to study the apelin contribution on regenerative angiogenesis.

Second, the selective induction of Aplnr in response to adenoviral infection of the adult mouse lung, using Microfil injected into the right ventricle to effectively delineate the pulmonary arterial tree. We found robust expression of Aplnr in the pulmonary arteriolar endothelium by using 2 independent approaches: (1) in situ hybridization (given the paucity of a robust Aplnr antibody) and (2) green fluorescent protein expression from the recently developed AplnrCreER:RosamTmG mice. The larger pulmonary arteries did not express Aplnr, as reported by Lathen and colleagues. Although we cannot fully exclude the possibility of a secondary, yet unidentified apelin receptor that may be mediating the effects of apelin in pulmonary arterial hypertension, our findings provide strong evidence that Aplnr, given its robust expression in the pulmonary arterioles, can certainly be the key receptor that mediates the effects of apelin in pulmonary arterial hypertension.

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The referenced work by Lathen and colleagues provides interesting insights into a novel mechanism of pulmonary veno-occlusive disease; nevertheless, we believe that the roles of Aplnr in the pulmonary vasculature extend beyond the pulmonary venous system, and would like to ensure that the pulmonary arteriole expression of Aplnr is not understated.

Disclosures

None.

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References


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