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Characterization of transgenic mouse models for the study of microvascular mural cells

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Microvascular mural cells are increasingly of interest in multiple fields of research for their plasticity and their diverse functional roles in physiology and disease. They have been described as a heterogeneous cell population constituting a continuum of cell phenotypes along the micro--- and macrovascular bed with vascular smooth muscle cells at one end and pericytes at the other end of the spectrum. Identification and discrimination of microvascular mural cells, however, remains challenging. Neither of the commonly used markers recognizes all cell phenotypes, nor are they exclusively expressed by microvascular mural cells. Consequently, the lack of specific microvascular mural cell identification as well as their discrimination continues to be a compelling restriction for the understanding of the implication of microvascular mural cells in both physiological and pathological scenarios. The ability to address the role of microvascular mural cells in multiple developmental and disease scenarios crucially depends on the reliability of tools to report and subsequently manipulate gene expression in vivo. Along these lines, the two commonly used Ng2--- and Pdgfrb--- as well as the lesser described Tagln--- (SM22a---) Cre driver were crossed to both the dual fluorescent mT/mG and the ROSA26YFP reporter line, respectively. The analysis of microvascular mural marker distribution along the microvascular bed in postnatal retina provided a novel concept for microvascular mural cell phenotype definition and discrimination and suggested TAGLN to be the most suitable marker for the detection of all microvascular mural cell phenotypes, including midcapillary pericytes. Microvascular mural marker expression and their target cell specificity were further characterized spatiotemporally in embryonic and postnatal tissues revealing that, while markers were consistently expressed at most sites, multiple microvascular mural cell subpopulations exist in a tissue context---dependent manner. Hepatic stellate cells were the only exception to this observation with microvascular mural cell markers expressed dynamically based on quiescent or activated cell state. Finally, transcriptomic profiling of cardiac, pulmonary and renal microvascular mural cells suggested organotypically differentiated subpopulations that may exert tissue---specific functional roles. Taken together, this study spatiotemporally and functionally characterized available tools for specific microvascular mural cell gene manipulation, thereby providing a concept for specific cell phenotype definition and discrimination and contributed to a better understanding of micorvascular mural cell heterogeneity and functional plasticity in health and disease conditions.