Functional and Morphological Properties of Pericytes in Bladder Suburothelial Venules: Pacemaker Cells of Suburothelial Microcirculation

Introduction and Objective: Besides bladder outlet obstruction, growing evidence suggests that metabolic syndrome is also associated with overactive bladder. Therefore, it is likely that bladder ischemia, particularly in the suburothelial layer may be a primary cause of overactive bladder. The extensive plexuses of blood vessels that interconnect within the bladder wall and characterized by their winding arrangement is fundamental to maintain blood supply during filling phase. In addition to such morphological features, we have recently reported that suburothelial venules in the rat bladder exhibit regular spontaneous constrictions. Here, we aimed to identify the functional and morphological characteristics of the pacemaker cells driving spontaneous venular constrictions
Materials and Methods: Changes in diameters of suburothelial venules of the mouse bladder were measured using edge-tracking video microscopy, while intracellular Ca^{2+} dynamics were examined using fluo-4 fluorescence Ca^{2+} imaging. Electron microscopy and fluorescence immunohistochemistry were used to examine the morphological features of the suburothelial microvasculature.
Results: Stellate-shaped pericytes exhibiting spontaneous Ca^{2+} transients were abundant, synchronous Ca^{2+} transients within their network were accompanied with phasic vasoconstrictions. Nicardipine (1μM) disrupted the synchrony of spontaneous Ca^{2+} transients and greatly diminished their associated constrictions. Residual asynchronous Ca^{2+} transients were suppressed by CPA (10 μM), 2-aminoethoxydiphenyl borate (10 μM), SKF96365 (10 μM) or U-73122 (1 μM), while not affected by ryanodine (100 μM) or YM-244769 (1 μM), a specific blocker for NCX3. These data suggest that pericyte Ca^{2+} transients may rely on Ca^{2+} release from endoplasmic reticulum via $InsP_3$ receptor and also require Ca^{2+} influx through capacitative Ca^{2+} entry channels. Stellate-shaped pericytes interdigitating via their processes were immunoreactive against α-smooth muscle actin. Scanning electron microscopy revealed a network of stellate-shaped pericytes covering the venules, while transmission electron microscopy demonstrated that the venular wall consisted of endothelium and adjacent pericytes, lacking an intermediate smooth muscle layer. Pericytes were characterized by numerous caveolae and a distinct basal lamina.
Conclusions: Pericytes in bladder suburothelial venules are capable of generating spontaneous Ca^{2+} transients and contractile activity. They also appear to act as pacemaker cells driving the spontaneous venular constrictions that may be beneficial in maintaining the suburothelial microcirculation.