KV4 and ANO1 / TMEN16A chloride channel expression profiles distinguish between atypical and typical smooth muscle cells in the mouse renal pelvis

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Previous intact preparation experiments and calcium imaging have suggested that atypical smooth muscle cells (SMCs) in the proximal renal pelvis are likely to be the pacemaker cells that drive pyeloureteric peristalsis (Lang *et al*., 2007). However, their electrical characteristics, location and mechanisms of pacemaker generation remain obscure. Standard perforated-patch patch clamp, intracellular microelectrode recording and immunohistochemistry techniques were used. In some experiments a transgenic mouse with enhanced yellow fluorescent protein (eYFP) exclusively expressed in cells containing α-smooth muscle actin (α-SMA) were used.

Single atypical eYFP-α-SMA$^+$ SMCs could be distinguished electrophysiologically from typical eYFP-α-SMA$^+$ SMCs by the absence of a voltage-operated transient 4-aminopyridine-sensitive ('A-type' KV4) K^+ current (I_{KA}) and the absence of spontaneous transient outward currents (STOCs) arising from the opening of large conductance Ca^{2+}-activated K^+ (BK) channels. Both typical and atypical SMCs displayed spontaneous transient inward currents (STICs) flowing through niflumic acid (NFA)-sensitive Cl^- channels. However, 25% of typical SMCs also displayed a large NFA-sensitive Cl^- current which displayed relatively slow kinetics of activation and deactivation, presumably reflecting a relatively high internal Ca^{2+} concentration. Atypical SMCs also fired prolonged large inward currents (LICs), which were cation-selective and blocked by La^{3+} or ryanodine. Immunostaining for ANO1/ TMEN16A Cl^- channel subunits was found predominately in the distal regions of the renal pelvis, co-localizing with intense immunostaining for α-SMA. In contrast, α-SMA$^-$ interstitial cells (ICs) were distinguished by the presence of a Xe991-sensitive KV7 current, a small I_{KA} current, tetraethylammonium-sensitive BK channel STOCs and Cl^--selective STICs blocked by NFA. Intense TMEN16A immunostaining also located to a population of Kit$^-$ α-SMA$^-$ ICs in the proximal and mid regions of the renal pelvis.

We conclude that (i) KV4$^+$, BK STOC$^+$, α-SMA$^+$ SMCs are the typical SMCs that facilitate muscle wall contraction, (ii) TMEM16A or KV7 immunoreactivity may be useful makers of Kit$^-$ ICs in the urogenital tract, and (iii) KV4$^-$ α-SMA$^+$ atypical SMCs firing cation-selective LICs are likely to be the pelviureteric pacemakers.

Lang RJ, Hashitani H, Tonta, MA, Parkington, HC & Suzuki H. (2007) Spontaneous electrical activity and Ca^{2+} transients in typical and atypical smooth muscles and interstitial cells of Cajal-like cells of mouse renal pelvis. *Journal of Physiology* **583**, 1049-1068