

Pyeloureteric peristalsis: role of interstitial cells of Cajal (ICC)-like cells as secondary pacemakers

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The primary function of the pyeloureteric system is to remove urine expressed from the renal papillae of the kidney and propel it towards the bladder for storage before micturition. Failure of peristalsis results in stasis and hydronephrosis which, if uncorrected, leads to kidney failure. Pyeloureteric peristalsis has long been thought to arise from pacemaker atypical smooth muscle cells (SMC) located primarily in the proximal regions of the renal pelvis. However interstitial cells, with many of the morphological and rhythmic electrical properties of interstitial cells of Cajal (ICC), the established pacemaker in the intestine, are present in small numbers along the length of the ureteropelvic junction (UPJ) of many mammals including human and mouse. Single ICC-like cells (ICC-LC) of the mouse UPJ have a unique expression profile of voltage- and Ca^{2+} -activated ion channels when compared with ICC of intestine and urethra. They also generate spontaneous transient inward currents (STICs) that sum to produce large inward currents (LICs) which are cation selective and little affected by $1\ \mu\text{M}$ nifedipine or blockers of capacitative Ca^{2+} entry, La^{3+} and Gd^{3+} ($100\ \mu\text{M}$). However all spontaneous regenerative electrical activity in the intact mouse UPJ recorded with intracellular microelectrodes is blocked by $1\text{-}3\ \mu\text{M}$ nifedipine. We speculate that an influx of Ca^{2+} through L type Ca^{2+} channels appears to be essential to entrain the fundamental pacemaker signals (STICs) into a regenerative electrical response that can be recorded with an intracellular microelectrode. It is not yet clear whether these Ca^{2+} channels are located in typical SMC, atypical SMC or in ICC-LC, or how all three cell populations communicate to provide a coordinated propagating peristaltic contraction. However, pyeloureteric ICC-LC with their unique properties may well provide a selective pharmacological target when considering non-surgical interventions to alleviate hydronephrosis arising from UPJ remodelling during and after ureteric blockade or pyeloplasty.