ATP acting through P2Y receptors causes activation of podocyte TRPC6 channels: role of podocin and reactive oxygen species

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Podocytes are highly polarized cells that cover the external surface of the glomerular capillary. Podocyte foot processes attach to the capillary basement membrane and are also connected to each other through specialized junctions known as slit diaphragms (33). The extracellular portions of slit diaphragms are formed from the interacting ectodomains of adhesion molecules such as nephrin and Neph1, which collectively comprise a porous matrix through which water and small solutes pass as a result of hydrodynamic and diffusive driving forces. The perselective properties of slit diaphragms normally prevent significant movement of albumin and comparable sized macromolecules into the urinary space inside Bowman’s capsule. While slit diaphragms and foot processes are often depicted as static structures, there is evidence that dynamic processes within foot processes can alter the passage of solutes through slit diaphragms (13, 35) and may in this way contribute to regulation of glomerular filtration rate (GFR). Even more dramatic changes in the shape of podocytes may allow for a stronger attachment to the glomerular capillary in the face of injury or stress, although this typically occurs at the expense of normal glomerular filtration (29).

GFR is regulated by a number of feedback mechanisms that operate over several time scales (14, 15). A mechanism of particular importance is tubuloglomerular feedback (TGF), a process in which cells of the macula densa detect changes in distal tubule flow rate and luminal Na+ content and initiate signals in response that ultimately act on glomerular cells to control GFR (26, 48). While a vast body of work on TGF has focused on regulation of vascular smooth muscle in the afferent and efferent arterioles (41, 42, 45, 46), recent studies have provided evidence that TGF generates a Ca2+ wave that propagates from smooth muscle through extra- and intraglomerular mesangial cells, into endothelial cells, and finally, some 20–40 s later, into podocytes (34). Importantly, the propagation of this Ca2+ wave was suppressed by extracellular ATP scavengers, and by blockade of P2 purinergic receptors (34). In recent years it has become clear that connexin and pannexin hemichannels can allow for regulated ATP release from a wide variety of cells (5, 31). It is notable that glomerular endothelial cells (GEnCs) express connexin 40, which mediates release of ATP and propagation of Ca2+ waves, in part by extracellular diffusion of ATP (50). Since only a short diffusion distance would be required for ATP secreted from endothelial cells to act on podocytes, this provides a potential mechanism for propagation of the final phase of the glomerular Ca2+ wave observed in TGF. Something like this would appear to be necessary, since podocytes and GEnCs lie on opposite sides of the GBM and therefore cannot be connected by gap junctions.

The purpose of the present study is to examine the actions of ATP on canonical transient receptor potential-6 (TRPC6) channels in podocytes. TRPC6 channels are Ca2+-permeable cationic channels that play a role in G protein-mediated signaling in a wide variety of cell types (6). Podocyte TRPC6 channels in podocytes are expressed in foot processes in a complex with other slit diaphragm proteins, including podocin and nephrin (1, 7, 17, 40). However, TRPC6 is also detected in the major processes and in the podocyte cell body (7), where it probably exists in different macromolecular complexes (1, 4, 7, 22). TRPC6 is of particular interest because mutations in these channels result in familial nephrotic syndromes (11, 40, 55). Moreover, podocyte TRPC6 channels are upregulated in several acquired glomerular diseases (32), and podocyte-specific overexpression of wild-type or mutant TRPC6 channels in mice results in proteinuria and glomerulosclerosis (28). There-
for ATP, ADP, UTP, and UDP at 100 and 200 μM suramin (52).

We now report that ATP evokes a concentration-dependent increase in current through TRPC6 channels in immortalized mouse podocyte cell lines, and in primary rat podocytes that are still attached to the GBM in explanted decapsulated glomeruli. The effects of ATP are blocked by the pan-P2 antagonist suramin as well as by inhibition of G protein signaling, and mimicked by P2Y agonists such as ADP and UTP. These effects of ATP are also blocked by TRPC6 knockdown using siRNA and by TRPC6 blocking agents. We also report that podocin is required for robust responses to ATP in podocytes, and we present evidence suggesting that reactive oxygen species play a role in the overall signal transduction cascade leading from P2Y receptors to TRPC6.

MATERIALS AND METHODS

Podocyte cell culture, glomerular isolation, immunoblot analysis, and siRNA procedures. An immortalized mouse podocyte cell line (MPC-5) was obtained from Dr. Peter Mundel of Harvard Medical School and maintained as described previously (23). Podocyte differentiation and expression of podocyte markers were induced by removal of γ-interferon and temperature switch to 37°C for 14 days. For glomerular isolation, male Sprague-Dawley rats (150–200 g from Charles River Laboratories) were anesthetized with isoflurane and euthanized according to NIH guidelines as approved by the University of Houston Institutional Animal Care and Use Committee. Glomeruli were immediately isolated using a sieving procedure described previously (1, 2, 44). Isolated glomeruli were plated for 24 h at 37°C in RPMI-1640 medium supplemented with 10% fetal bovine serum and 100 U/ml penicillin-streptomycin on collagen-coated glass coverslips. By that time they adhered sufficiently tightly to the substrate to allow analysis by whole cell recordings. In some experiments, panels of proprietary siRNAs directed against TRPC6 or podocin, and non-targeted siRNAs for use in control experiments, were obtained from Santa Cruz Biotechnology and transfected into isolated cultured mouse podocytes or isolated rat glomeruli immediately after isolation using Oligofectamine (Invitrogen) in serum-reduced medium according to the manufacturer’s directions, as described previously (1, 2, 20–24). Analyses of ATP effects by whole cell recording were carried out 24 h after transfection with siRNAs. Immunoblot analyses were carried out as described in previous studies (1) using rabbit anti-TRPC6 from Alomone Laboratories (Jerusalem, Israel) and rabbit anti-podocin from Actis Antibodies (San Diego, CA).

Electrophysiology. Methods for conventional whole cell recordings from podocytes were carried out by standard methods that have been

![Fig. 1. ATP activates cationic currents in immortalized mouse podocyte cell lines. A: whole cell currents recorded from a podocyte during ramp voltage commands (~80 to +80 mV in 2.5 s) before (left) and after (right) application of 200 μM ATP. Note marked increase in rectifying cationic current after ATP application. B: concentration-response relationship for ATP-evoked currents measured at +80 mV, at the end of ramp voltage commands. Points are fitted with the Hill equation, with EC50 at 9.5 μM. Points are means ± SE (N = 3 cells). C: cationic currents before and after ATP application in cell pretreated with the P2 antagonist suramin. D: currents at +80 mV before and after ATP application in control cells and in cells pretreated with 100 μM suramin (N = 9 cells per group). E: several nucleotides can activate cationic currents in immortalized mouse podocyte cell lines. Mean currents ± SE recorded at +80 mV are plotted for ATP, ADP, UTP, and UDP at 100 and 200 μM, as indicated (N = 5 cells per group).](http://ajprenal.physiology.org/)}
described in detail previously (1, 2, 20–22). Recordings were made with an Axopatch 1D amplifier (Molecular Devices) and analyzed using pClamp v 10 software (Molecular Devices). The bath solution contained 150 mM NaCl, 5.4 mM CsCl, 0.8 mM MgCl₂, 5.4 mM CaCl₂, and 10 mM HEPES, pH 7.4. Pipette solutions in all experiments contained 10 mM NaCl, 125 mM CsCl, 6.2 mM MgCl₂, 10 mM HEPES, and 10 mM EGTA, pH 7.2. The use of Cs⁺ in bath and pipette solutions prevents contamination by current flowing through K⁺ channels that are also expressed in these cells (23). The relatively high Ca²⁺ concentration in the bath solution markedly increases stability of whole cell recordings. We also note that replacing NaCl in bath solution with Na-gluconate does not affect the current-voltage characteristics or reversal potential of ATP-evoked currents in these cells. The relatively high Ca²⁺ concentration in the bath solution markedly increases stability of whole cell recordings. We also note that replacing NaCl in bath solution with Na-gluconate does not affect the current-voltage characteristics or reversal potential of ATP-evoked currents in these cells, indicating that Cl⁻ conductance is not contributing to the observed currents (data not shown). In some experiments, the pipette solution also contained guanosine 5’-O-(2-thiodiphosphate) (GDP-βS), a GDP analog resistant to hydrolysis and phosphorylation that competitively inhibits G protein activation by GTP (8). ATP in the absence or presence of other agents was applied by gravity feed through the recording chamber. Tricyclodecan-9-yl-xanthogenate (D-609) and tempol were applied to glomeruli 30 min prior to electrophysiological analyses. To monitor TRPC6, currents were periodically evoked by 2.5-s ramp voltage commands (−80 to +80 mV) from a holding potential of −40 mV. Whole cell currents were quantified at +80 mV. It is possible to compensate up to 80% of series resistance without introducing oscillations into the current output of the amplifier. Throughout, data are presented as means ± SE, and quantitative comparisons were analyzed using ANOVA followed by Tukey’s post hoc test with P < 0.05 considered significant.

Drugs and reagents. The pan-TRP channel inhibitor 1-[2-(4-methoxyphenyl)-2-[3-(4-methoxyphenyl)propoxy]ethyl]-1H-imidazole hydrochloride (SKF-96365) was obtained from Sigma. ATP, UTP, UDP, ADP, GDP-βS, tempol, suramin, and D-609 were also obtained from Sigma. The P2Y₂-selective agonist 4-thiouridine-5’-O-(β,γ-difluoromethylene) triphosphate used in one set of experiments was obtained from Tocris (catalog no. 4333).

RESULTS

Our initial experiments were carried out on the differentiated cells of an immortalized mouse podocyte cell line (MPC-5 cells) that we have used in several previous studies on TRPC6 (1, 2, 20, 21). Cationic currents were evaluated during application of slow duration (2.5 s) ramp voltage commands (−80 mV to +80 mV). Application of ATP by gravity-fed bath superfusion evoked large cationic currents that showed substantial outward rectification under our recording conditions (Fig. 1A) and which reversed rapidly upon washout (not shown). The effects of ATP were concentration dependent, with half-maximal currents typically occurring at ~10 μM (Fig. 1B), and with maximal responses observed at 100 μM (Fig. 1B). Pretreating podocytes with 100 μM suramin completely eliminated responses to ATP (Fig. 1, C and D), suggesting that they are mediated by P₂ receptors.

The P₂ receptor can be subdivided into seven forms of ionotropic P₂X receptors, and a family of eight metabotropic receptors, known as P₂Y₁, P₂Y₂ and P₂Y₆ have been detected in rodent podocytes (10). ATP can activate P₂Y₁ and P₂Y₂ receptors, whereas UTP can activate P₂Y₂ and P₂Y₆ receptors. Note, however, that the later are not inhibited by suramin. UDP preferentially activates P₂Y₆, whereas ADP preferentially activates P₂Y₁ (52). We observed that cationic currents qualitatively similar but consistently smaller than those evoked by ATP could be activated by 100 μM or 200 μM of ADP, UTP, or UDP (Fig. 1E). Responses were also evoked by the synthetic

![Fig. 2. ATP activation of podocyte cationic currents requires G protein signaling. Whole cell recordings of ATP-evoked currents in immortalized mouse podocytes. A: example of recording made using an electrode filled with normal solution. B: example of recording made using electrode filled with normal solution supplemented with 50 μM GDP-βS, an agent that prevents GTP binding and thereby abolishes G protein signaling. Bar graph in C shows summary of several repetitions of these experiments (N = 5 cells per group). In this and subsequent bar graphs, mean current measured at +80 mV is plotted, and error bars represent SE.](http://ajprenal.physiology.org/ by 10.22033.6 on October 29, 2017)
agonist 4-thiouridine-5′-O-(β,γ-difluoromethylene) triphosphate at concentrations where it is selective for P2Y2 receptors (9) (data not shown). For all of these nucleotides, response amplitudes were similar when they were evoked at 100 or 200 μM, suggesting that they comprise the top of the concentration-response curves. These data suggest that the functional P2Y1, P2Y2, and P2Y6 receptors are expressed in mouse podocytes, consistent with earlier investigations on transcript expression (10). ATP evoked larger responses than any of the other nucleotides, which suggests that its effects are caused by simultaneous activation of multiple subtypes of receptors expressed in these cells, most likely P2Y1 and P2Y2 (since it is not able to activate P2Y6).

Irrespective of the relative contributions of the various subtypes of P2Y receptors, responses to ATP were not seen when recording electrodes contained 50 μM guanosine 5′-O-(2-thiodiphosphate) (GDP-βS), a GDP analog resistant to hydrolysis and phosphorylation that competitively inhibits G protein activation by GTP (8) (Fig. 2). We have previously shown that this pipette solution also blocks responses to angiotensin II (ANG II), although activation of TRPC6 by hypotonic stretch persists under those recording conditions (1). These data indicate that podocyte responses to ATP are mediated by G protein-coupled metabotropic receptors in the P2Y family (10).

The ATP-evoked cationic current appears to flow through endogenously expressed TRPC6 channels. Currents activated by ATP were completely blocked by bath application of 10 μM SKF-96365, a nonselective pan-TRP channel inhibitor (Fig. 3A). Podocytes express TRPC5 and TRPC6 subunits (7, 20, 49), and those two types of channels are both blocked by SKF-96365 (49). However, they are differentially sensitive to micromolar concentrations of La3+, as TRPC6 can be completely inhibited by micromolar La3+, whereas TRPC5 is actually activated by La3+ at that concentration (19, 49). We observed that 50 μM La3+ rapidly and completely blocked currents evoked by 200 μM ATP, suggesting that they are mediated by channels containing TRPC6 subunits, and indicating that TRPC5 channels cannot be making a significant contribution to the ATP-evoked currents in these cells (Fig. 3B). Consistent with this, we observed that transient siRNA knockdown of TRPC6 using procedures described previously (1, 2, 20) abolished podocyte responses to ATP, whereas cells continued to respond to ATP after treatment with a control siRNA (Fig. 4). The effectiveness of the siRNA was confirmed by immunoblot (Fig. 4D).

Previous studies have shown that P2Y1, P2Y2, and P2Y6 receptors are preferentially coupled to Gq (52) and therefore have the potential to activate phospholipases that feed into TRPC6 (12). The role of phospholipases in TRP channel activation is unclear, and further studies are needed to clarify this point.

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**Fig. 3.** ATP-evoked cationic currents are blocked by TRP inhibitors in immortalized mouse podocyte cell lines. A: cationic currents evoked by 200 μM ATP are blocked by 10 μM SKF-96365, a nonselective inhibitor of TRP family channels, including TRPC6 and TRPC5. B: ATP-evoked cationic currents are completely blocked by 50 μM La3+, an agent that blocks TRPC6 but not TRPC5. C: summary of several repetitions of this experiment (N = 5).

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**Fig. 4.** Podocyte responses to ATP are mediated by G protein-coupled metabotropic receptors in the P2Y family (10).
signaling must be assessed with caution, because several of the most commonly used phospholipase inhibitors, such as U-73102, are direct inhibitors of certain TRP channels, including TRPC6 (Ref. 27 and unpublished observations). However, we have observed that tricyclodecan-9-yl-xanthogenate (D-609) can be used for experiments on TRPC6 channels, since it does not block responses evoked by diacylglycerol analogs. D-609 inhibits phosphatidylinositol-specific forms of phospholipase C (PLC) as well as certain forms of phospholipase A2.

We observed that pretreatment with 100 μM D-609 for 30 min abolished responses to ATP (Fig. 5), suggesting that signaling from P2Y receptors to TRPC6 channels in podocytes entails activation of phospholipases.

Previous studies have shown that TRPC6 channels of podocytes become active in response to signals that increase generation of reactive oxygen species (2, 20, 21), including rapidly acting signals such as ANG II (2). We observed that 30 min pretreatment with 10 mM tempol, a membrane-permeable superoxide dismutase mimetic, abolished responses to ATP (Fig. 6), suggesting a pathway similar to the one we previously described for ANG II (2). In a more recent study we observed that podocyte TRPC6 channels reside in multiprotein complexes that include the NADPH oxidase NOX2, which can generate ROS locally to facilitate TRPC6 activation in podocytes (22). The interaction between TRPC6 and NOX2 is indirect, and coimmunoprecipitation of these proteins requires the hairpin-loop inner membrane protein podocin (22). As with our previous studies on ANG II (2), we observed that podocin knockdown using a panel of siRNAs eliminated ATP activation of TRPC6 channels, whereas responses were readily detected in cells transfected with a control siRNA (Fig. 7). Immunoblot analysis showed that podocin siRNA produced strong reductions in podocin expression but had no effect on TRPC6 (Fig. 7D).

It is possible that changes in gene expression and cell physiology occur when podocytes are immortalized and propagated as a cell line. If the response to ATP is physiologically relevant, one would expect to see it in primary podocytes. To this end, we have employed an isolated decapsulated rat glomerulus preparation in which podocytes remain attached to the underlying glomerular basement membrane. This preparation does not require enzymatic digestion, and the podocytes on the external surface of the preparation can be readily seen using Hoffman modulation contrast optics. They are readily accessible to the recording electrode (Fig. 8A), the bath solution, and any agents that we may include in external culture media or recording solutions. We observed that bath application of ATP evoked robust increases in cationic current in this preparation, and these currents were completely blocked by subsequent exposure to 50 μM La3+ (Fig. 8B and C). Treating the isolated glomerulus preparation for 24 h with the same TRPC6 siRNAs that we used on the immortalized cell lines resulted in a loss of ATP responses of podocytes located along the outer margin of the preparation, whereas glomeruli treated with control siRNA continued to show robust responses to ATP (Fig. 9). Immunoblot analysis confirmed reduction in TRPC6 expression by siRNA (Fig. 9D). Collectively these data indicate that channel complexes containing TRPC6 subunits are required for ATP-evoked cationic currents in primary rat podocytes, as in the immortalized podocyte cell line.

**DISCUSSION**

In this study we have shown that ATP evokes robust activation of TRPC6 channels in immortalized mouse podocyte cell lines and in primary rat podocytes still attached to the glomerular basement membrane in ex vivo glomeruli. The effects of ATP are mediated by a G protein-coupled pathway from P2Y receptors, through a phospholipase, to the TRPC6 channels. At some point, most likely downstream of phospholipases (22), the transduction cascade generates ROS, which contribute to TRPC6 activation. In addition, the cascade re-
quires podocin, which appears to function as a scaffold to allow for spatial colocalization of the various transduction components within cholesterol-rich membrane proteins (1, 17, 22). In short, the transduction cascade is qualitatively similar to the one used in these cells by ANG II and AT1R receptors, which we have described recently (2).

Responses to ATP are generally larger than responses to ANG II at concentrations that evoke maximum responses (2). The robustness of the response to ATP may occur because its signals are simultaneously transduced through multiple forms of P2Y receptors (especially P2Y1 and P2Y2) (10), whereas ANG II signals to TRPC6 are only transduced by ATR1. Responses to UTP, UDP, and ADP suggest the presence of multiple functional P2Y receptors in these cells, which is largely consistent with a recent study (18). It should bear noting, however, that this last study did not detect Ca\(^{2+}\) influx in response to UDP. Collectively these observations also suggest that treatments that reduce ATP-evoked Ca\(^{2+}\) overload into foot processes through this pathway could be especially effective therapeutic strategies. In this regard, a previous study has shown that sustained exposure to ATP can cause cell death in podocytes (10).

In principle, Ca\(^{2+}\) overload in foot processes could be reduced by agents that inhibit TRPC6 channels, or possibly by agents that inhibit ROS generation by NADPH oxidases (54). The present results raise the possibility that P2Y antagonists might also reduce Ca\(^{2+}\) overload, assuming they could be tolerated. In this regard, P2Y\(_1\) receptors expressed in podocytes have been shown to mediate Ca\(^{2+}\) influx (18) and are also expressed in proximal tubules where they have been proposed to play a role in regulation of bicarbonate transport (3). P2Y\(_1\) knockout mice are viable, but kidney function has not been assessed in these animals. P2Y\(_2\) receptors are expressed in podocytes and in several different nephron segments and play a complex role in regulation of renal electrolyte and water transport (51). P2Y\(_6\) is also expressed in renal vasculature, although it is not responsive to ATP (53). There is evidence suggesting that locally released ATP may modulate gating and steady-state surface expression of the epithelial sodium channel ENaC in the distal nephron (30, 47, 43, 36, 37) and may also regulate collecting duct aquaporin channels (25). As a result, there is a net salt-resistant increase in mean arterial pressure in P2Y\(_2\) knockout mice that appears to be associated with changes in multiple homeostatic systems (51) and which is consistent with the idea that global P2Y\(_2\) activation results in a steady diuresis (39). In addition, P2Y\(_2\) knockout mice actually appeared to be more susceptible to various indexes of kidney damage by 8 wk after subtotal (5/6) nephrectomy, including an increase in albuminuria compared with wild-type mice subjected to the same stress, although there was no increase in glomerulosclerosis in these experiments in the knockout mice (38). These results would tend to suggest that P2Y\(_1\) or P2Y\(_2\) might be the most promising therapeutic targets for glomerular disease, with the caveat that the P2Y\(_2\) knockout

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**Fig. 5.** Phospholipase signaling is required for ATP activation of TRPC6 channels in immortalized mouse podocytes. A: after establishing a response to ATP, bath application of 100 μM D-609 reversed activation of the currents. D-609 can inhibit phosphatidylserine-specific PLC, as well as some forms of PLA2. In pilot experiments we have shown that D-609 does not block TRPC6 activation by diacylglycerol analogs, in contrast to several other widely used phospholipase inhibitors. B: summary of a slightly different experiment in which cells were pretreated with control solution or 100 μM D-609 for 30 min prior to testing of response to ATP by whole cell recording (N = 6).
mice used in the studies cited above are complete, global (in every tissue) and constitutive (including during embryonic development) (16). Therefore it may not be straightforward to compare the physiology of those mice to what might occur with subtotal pharmacological blockade in a system that developed normally.

One question that emerges pertains to the source of ATP that might activate podocyte P2Y receptors during normal physiol-
ogy. Glomerular endothelial cells are able to secrete ATP through connexin and/or pannexin hemichannels (50), and we favor this as a mechanism for propagation of Ca$^{2+}$ waves to podocytes during TGF. The question of whether it is adenosine or ATP that carries the initial signals from the macula densa to the afferent arteriole (45, 46) is immaterial as to how the Ca$^{2+}$ wave is subsequently propagated into the rest of the glomerulus. We know from Lucifer yellow dye-filling experiments that podocytes are not connected to other cells by gap junctions (unpublished data) and therefore orthograde signals must pass into podocytes, and possibly from one podocyte to another, by means of diffusible messengers. ATP is a prime candidate for this, based on previous studies on the effects of suramin and ATP scavengers on propagation of Ca$^{2+}$ waves through the glomerulus during TGF (34). Obviously, ATP is also freely filtered, and there would be minimal diffusional barriers for ATP released from glomerular endothelial cells to podocytes. ATP can also be modified by extracellular nucleotidases once

![Fig. 8. ATP evokes cationic currents in podocytes in isolated rat glomeruli. A: modulation contrast optics view of isolated de-capsulated rat glomerulus with patch electrode attached to a podocyte located on the outer margin of the preparation. B: example of typical ATP-evoked current, and complete blockade of this response by 50 μM La$^{3+}$ in the continued presence of ATP. C: summary of this experiment (N = 5 cells per group).](http://ajprenal.physiology.org/)

![Fig. 9. TRPC6 knockdown completely inhibits ATP responses in podocytes in isolated rat glomeruli. Glomeruli in this ex vivo preparation were transfected with control siRNA (A) or siRNA targeting TRPC6 (B) for 24 h. Cell culture medium was changed several times, and glomeruli were then transferred to recording chamber, where whole cell recordings were made from podocytes on the outer margin of the preparation. C: summary of the results of this experiment (N = 5 cells per group). D: immunoblot analysis showing effectiveness of siRNA procedures in isolated glomerulus preparation.](http://ajprenal.physiology.org/)
it is secreted and can thereby produce ADP, which is also an effective agonist in podocytes. The sources of UTP or UDP, if any, are not known.

Finally, we should note that podocin knockdown abolished the ability of ATP to evoke cationic currents in podocytes. This is consistent with previous studies showing that podocin potentiates chemical activation of TRPC6 by diacylglycerol analogs (1, 17). We have recently reported that podocin is required for colocalization of TRPC6 channels and NOX2 in podocytes (22), which can allow for a locally generated source of ROS to modulate TRPC6 gating as part of a physiological transduction cascade without the need for toxic increases in cytosolic ROS. Thus our observations with podocin knockdown are consistent with the observation that tempol (a ROS quencher) also blocks ATP activation of TRPC6 in podocytes. If ATP-evoked cationic currents are abolished by treatments that inhibit or knockdown TRPC6, and ATP causes the largest activation of TRPC6 of any stimulus that we have examined. Ectonucleotide signaling to podocytes may therefore play a role in normal glomerular filtration or in the pathophysiology of glomerular disease.

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ATP REGULATION OF PODOCYTE TRPC6 CHANNELS


