vesicles labelled with FM 1-43. These data suggest that VMS astrocytes respond to a decrease in pH by releasing ATP via vesicular exocytosis.

507-Pos

The Role of Cell Adhesion Molecule 1 (CADM1) in Nerve-Mast Cell Communication

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It has long been demonstrated that the nervous and immune systems are not disparate entities. The nerve-mast cell relationship served as prototypic association, and unequivocal evidence has been considerably presented for the consistent anatomical association and the functional interaction between nerves and mast cells. We found that nerve-mast cell communication can occur bidirectionally in the absence of intermediary cells using in vitro coculture approach and calcium imaging analysis. We have studied the molecular mechanism in nerve-mast cell communication and showed that substance P was an important mediator from superior cervical ganglia (SCG) to mast cells and induced the degranulation to mast cells attached with SCG neurites. In addition, ATP released from antigen-stimulated mast cells was found to activate SCG neurites attached with mast cells. To investigate the adhesion molecules involved in the nerve-mast cell communication, we here focused an adhesion molecule of immunoglobulin superfamily, CADM1, which is expressed on bone marrow-derived mast cells from wild type mice. When mast cells with or without CADM1 were cocultured with SCG and dorsal root ganglia (DRG) neurons, the number of CADM1-expressing mast cells attached to neurites was much higher than CADM1-deficient cells. The transfection with CADM1 to CADM1-deficient mast cells recovered the attachment to neurites. The responding rate of mast cells with CADM1 attached to neurites following specific activation of neurons by scorpion venom was higher than ones without CADM1. Ectopic expression of CADM1 increased this proportion. CADM1 was also found to be locally concentrated at points of contact between neurites and mast cells. These results suggested that CADM1 on mast cells not only functions as simple glue in nerve-mast cell interaction but also promotes development of a microenvironment to communicate efficiently each other.

508-Pos

Tunneling Membrane Nanotubes Generate Local Calcium Signals and May Actively Propagate Calcium Signals Between Cells

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Cells have long been known to employ gap junctions and synapses to communicate with their neighbors. A new mechanism has recently been proposed following the discovery of tunneling membrane nanotubes (TNTs) between cells [1]. TNTs are dynamic membrane protrusions with lengths up to several tens of microns and diameters of 50-800nm, which permit the exchange of membrane components and cytoplasmic molecules between neighboring cells. Ca^{2+} diffusion along TNTs has been proposed as a means of intercellular communication [2], yet our modeling simulations show that passive diffusion alone is insufficient to account for efficient transmission of Ca^{2+} between cells. Instead, we observe local spontaneous and inositol trisphosphate (IP_3)-evoked mediated Ca^{2+} signals within the length of TNTs formed between cultured SHSY-5Y neuroblastoma cells. Moreover, immunostaining demonstrates the presence of both ER and IP_3 receptors along the TNT. We propose that IP_3Rs are involved in actively propagating intercellular Ca^{2+} signals along TNTs, acting as amplification sites to overcome limitations of passive diffusion in a chemical analog of electrical transmission of action potentials along axons.

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Epithelial Channels & Physiology

509-Pos

Effects of Kcne Subunit Deletion on Polarized Trafficking of the KCNQ1 Potassium Channel *in Vivo*

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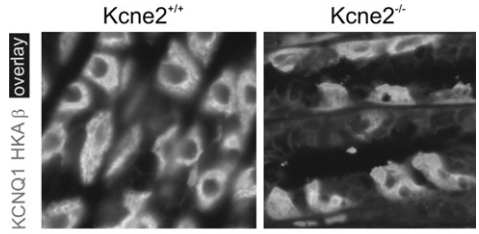
The KCNQ1 potassium channel alpha subunit generates essential K^+ currents in human heart and in a range of polarized secretory epithelia. The polarity of KCNQ1 trafficking varies between different epithelia, but neither the importance nor the mechanism for this polarity are well understood. KCNQ1 co-localizes apically with the KCNE2 beta subunit in gastric parietal cells but basolaterally with KCNE3 in colonic crypts. Both KCNE2 and KCNE3 convert KCNQ1 to a constitutively active channel. Here, genetic deletion of *Kcne2* in mice resulted in 5-fold upregulation of Kcne3, formation of Kcnq1-Kcne3 complexes, and basolateral Kcnq1 targeting in parietal cells, and gastritis cystica profunda stemming from achlorhydria and earlier hyperplasia. In contrast, *Kcne2*$^{-/-}$*Kcne3*$^{-/-}$ mice exhibited apical parietal cell Kcnq1 localization. Thus, in parietal cells, apical Kcnq1 localization is required for gastric acid secretion, and the apical localization *per se* does not require Kcne2. Kcne3, if present, actively targets Kcnq1 basolaterally, ultimately causing a preneoplastic condition which in humans could predispose to gastric cancer.



Apical (left) versus basolateral (right) localization of KCNQ1 (red) in gastric parietal cells of *Kcne2*$^{+/+}$ (left) versus *Kcne2*$^{-/-}$ (right) mice. Green: H^+/K^+-ATPase β subunit (apical marker).

510-Pos

Regulation of Delta-Enac Ion Channels by the Neuronal-Specific Sgk1.1 Kinase

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The epithelial sodium channel (ENaC) is a voltage-independent ion channel that plays a fundamental role in kidney transepithelial sodium transport and extracellular volume homeostasis. Previous work from our group and others have identified a novel ENaC subunit that is prominently expressed in neurons but not in kidney epithelia. The physiological role of delta-ENaC channels in neurons is unknown, but it could be involved in the regulation of membrane resting potential and hence of neuronal excitability. Kidney ENaC activity is increased by the serum and glucocorticoid-induced kinase 1 (SGK1). Recently, a new neuronal-specific isoform of SGK1, named SGK1.1, has been identified. We have tested whether SGK1.1 regulates delta-ENaC activity. Co-injection of SGK1.1 and delta-ENaC channels in *Xenopus* oocytes increased sodium current by two-fold. SGK1.1 increased delta-ENaC plasma membrane expression by 1.6-fold. *In situ* hybridization experiments confirmed the co-expression of delta ENaC and SGK1.1 in pyramidal neurons of the human cerebral cortex, indicating that this regulation could be physiologically relevant. In summary, we have identified a new regulator of delta-ENaC ion channels that could play a role in the control of neuronal resting potential and excitability.

511-Pos

A Multidomain Model For Electrodiffusion and Water Flow

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Fluid flow and its coupling to electrodiffusion is involved in many physiological systems from the kidney to the lens of the eye, where it has been studied in some detail (Journal of Membrane Biology (2007) 216:1-16). We formulate a mathematical model that describes electrodiffusion and water flow in three dimensions with resolution and scale appropriate for analysis of tissues. The mathematical model presented can be seen as a coarse-grained version of a model used in (PNAS(2008) 105:6463-6468) to model cellular and subcellular electrodiffusion. We shall discuss the relationship of the general model to other macroscopic models in electrophysiology, and show preliminary computations and applications.

Calcium Signaling Pathways

512-Pos

Orai3 and the Selective Activation of the Arc Channel by Arachidonic Acid

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