macrophages developed many vacuoles in their cytoplasm. It is suggested that macrophages play important roles in phagocytosis of cell debris and wastes during the early stage of OA. On the other hand, F cells first increased in number by mitosis in the synovial intima to be densely arranged and later changed their morphology. F cells in OA model extended longer cytoplasmic processes and formed microvilli and microplicae on their cell surface. Under TEM, many rough endoplasmic reticulum were observed in the cytoplasm of F cells. These morphological changes of F cells may reflect their stimulated activities in secretion and absorption. It is suggested that the ultrastructural changes of synoviocytes reflect pathological conditions of synovial membrane, and synoviocytes play some important roles in pathogenesis of OA.

Ca^{2+}-activated K^+ channels involved in muscarinically stimulated salivary secretion in ruminant parotid acinar cells

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The aim of the present study was to characterize Ca^{2+}-activated K^+ channels responsible for muscarinically evoked K^+ efflux driven by HCO_3^- transport in bovine parotid acinar cells.

Net K^+efflux from perifused bovine parotid gland fragments was measured using flame photometry. Acetylcholine (ACh) perifused over the fragments for 3 min caused a transient net K^+ efflux in a concentration-dependent manner. The ACh (10μM) -induced K^+efflux was abolished by the muscarinic antagonist atropine (1 μM) and strongly inhibited by removal of $CaCl_2$ from the perifusing solution (with addition of 0.5 mM EGTA). The Ca^{2+} ionophore, A 23187 (3 μM) plus added Ca^{2+} was able to mimic the ACh-induced response. Net K^+ efflux evoked by ACh (10μM) or by A 23187 (3 μM) was inhibited by Ca^{2+}-dependent K^+ channel blockers, quinine (1 mM) and Ba^{2+} (1 mM), but not by tetraethylammonium (TEA) (10mM), a blocker of large-conductance, voltage-and Ca^{2+}-dependent K^+ channels (Maxi-K^+ channels). Removal of HCO_3^- (25mM) /CO_2 (5 %) from the perifusing solution abolished ACh (10 μM) or A 23187 (3 μM) -induced net K^+ efflux. In sharp contrast to the HCO_3^-/CO_2 requirement for the K^+ efflux in bovine parotid fragments, in the rat submandibular gland fragments there was no significant difference between the ACh (10μM) -induced K^+ efflux observed in normal and HCO_3^-/CO_2-free perifusate. Acetazolamide (1 mM), an inhibitor of carbonic anhydrase reduced the ACh-induced K^+ efflux by 30% in bovine parotid fragments.

In whole-cell patch clamp experiments, bovine parotid acinar cells exhibited both outwardly and inwardly rectifying conductances, attributable to TEA-blockable Maxi-K^+ channels and inward rectifier K^+ channels respectively, when the cells were dialyzed with a K-glutamate-rich pipette solution containing 100nM or less than 1 nM free Ca^{2+}. When the cells were dialyzed in a bath solution contain-

ing TEA (10mM) with K-glutamate-rich pipette solutions having higher than 300nM of free Ca^{2+} concentration, a different type of conductance was observed. The TEA-insensitive, Ca^{2+}-activated conductance was highly K^+ selective over Na^+ or Cs^+, but it had an equal permeability of K^+ and Rb^+. In inside-out macro-patches, a TEA-insensitive Rb^+ conductance was maximally activated by 1 μM of free Ca^{2+} concentration in the fluid bathing the cytosolic surface of the patch. In outside-out macro-patches, quinine (1 mM) and Ba^{2+} (1 mM) inhibited the TEA-insensitive, Ca^{2+} (1 μM) -activated Rb^+ conductance. The conductance was also blocked by clotrimazole (100nM), but not by *d*-tubocurarine (100μM).

These results provide evidence for Ca^{2+}-activated K^+ channels, distinct from the Maxi-K^+ channels, in bovine parotid acinar cells. The K^+ channels reported here may be responsible for muscarinically stimulated salivary secretion driven by HCO_3^- transport in ruminant parotid acinar cells. Furthermore, electrophysiological properties of the Ca^{2+}-activated K^+ channels in bovine parotid acinar cells are strikingly similar to those of the cloned SK4/IK1 channels in heterologous expression system.

Functional analysis of SSeCKS, a bacterial lipopolysaccharide-responsive protein, in endothelial cells

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Endothelial cells play major roles in inflammation responses. They increase permeability and pinocytotic activity in response to bacterial products and proinflammatry cytokines. Recently, we reported that bacterial lipopolysaccharide (LPS) induces the expression of SSeCKS (src suppressed C kinase substrate) in endothelial cells of several organs in mice. In this study, I investigated the physiological role of SSeCKS using a murine endothelial cell line (IBE cell). When IBE cells were transfected with SSeCKS cDNA, their structure changed dramatically to result in cell flattering and lamellipodia structures with temporal loss of F-actin stress fibers. In these cells, immunoreactive signals of ectopically expressed SSeCKS were present throughout the cytoplasm, particularly being rich in perinuclear regions and colocalized with membranous F-actin at the cell membrane of lamellipodia structures. Since lamellipodia closure and actin dynamics are known to be associated with pinocytosis, I examined the relation of SSeCKS to pinocytotic activity of IBE cells by measuring uptake of Texas-Red-conjugated dextran. Overexpression of SSeCKS caused a 3.5-fold increase in the pinocytotic activity. Immunocytochemical examination revealed that SSeCKS colocalized with transport vesicles in IBE cells and also in pinocytotic vesicles of sinusoidal endothelial cell of the liver. All these results suggest that SSeCKS promotes pinocytosis in endothelial cells by altering F-actin cytoskeletal architecture associated with pinocytotic vesicles.