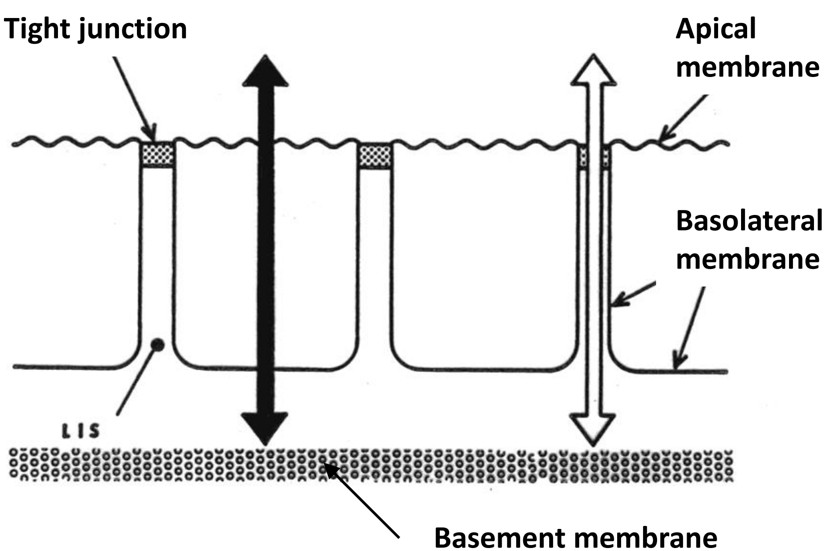
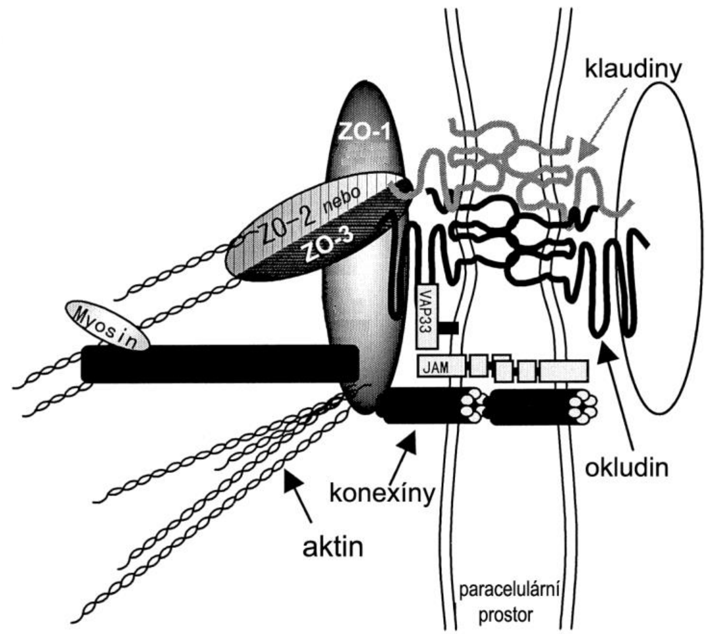
# Model of the epithelium and its principal compartments




Transcellular flux

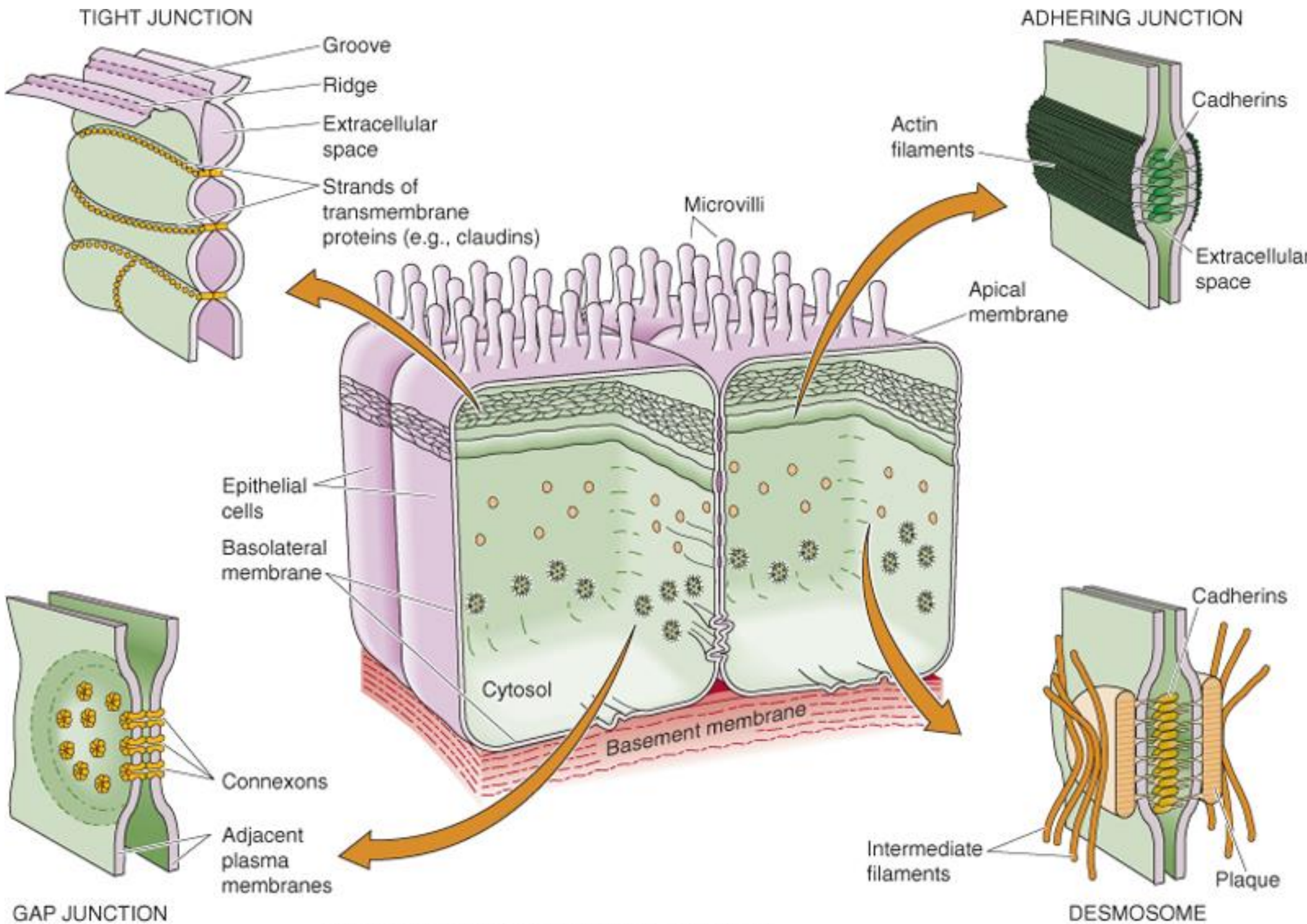
Paracellular flux

**LIS** - Lateral intercellular space



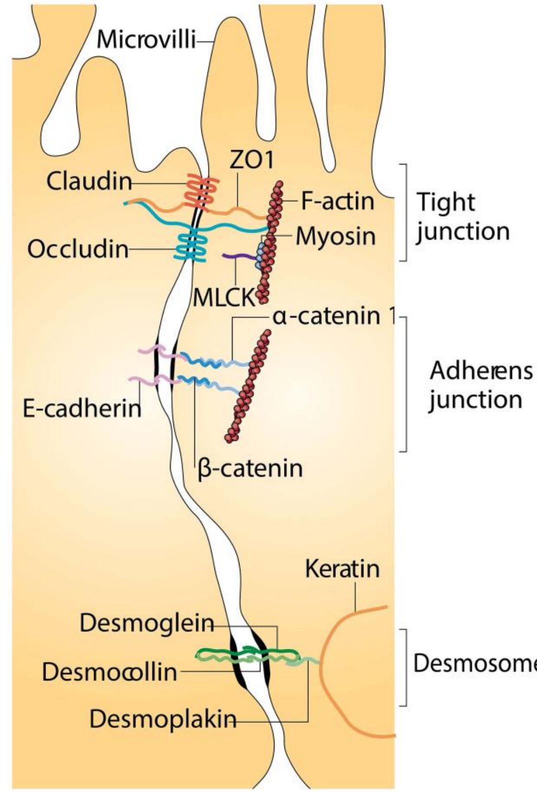

**Tight junction**

# Epithelial cell and its junction complexes

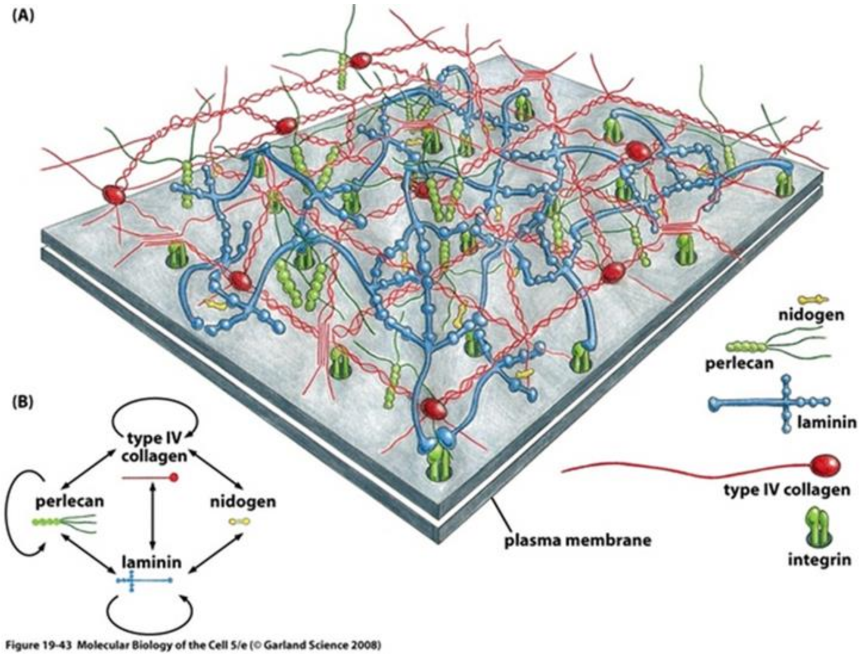



Boron & Boulpaep: Medical Physiology, 2nd Edition.

## Epithelial cell and its junction complexes

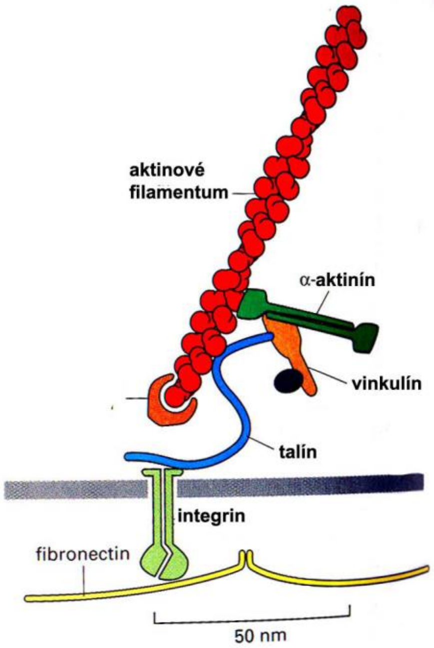


# Interaction of epithelial cells with basement membrane




Principal proteins of the basement membrane

Epithelial cell is attached to the basement membrane via integrins (heterodimer receptors)



# Transport of solutes across epithelium

$$J_i = (1-\sigma_\iota).C_i.J_V + P_i.(\Delta c_i + z_i.F/\Delta\varphi.C_i) + J_i^{akt}$$

**„solvent drag“**

**electrodiffusion**

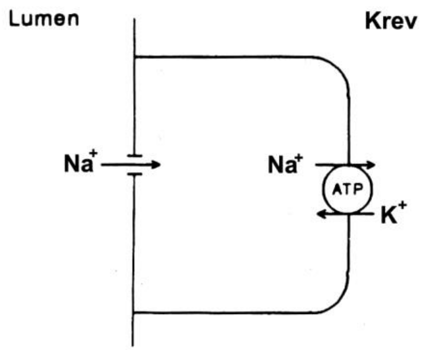
**active transport**

$J_i$ Flux of transported molecule/ion
$\sigma_t$ Staverman reflection coefficient
$C_i$ Intraepithelial concentration of the solute i
$J_V$ Volume flow
$P_i$ Permeability coefficient
$\Delta c_i$ Concentration difference mucosa-serosa
$z_i$ Valency
$F$ Faraday number
$\Delta\varphi$ Transepithelial voltage

## NaCl transport in renal proximal tubule

| | Ji | | | |
|---|---|---|---|---|
| Na | 100 % | 29 % | 32 % | 38 % |
| Cl | 100 % | 49 % | 51 % | 0 % |

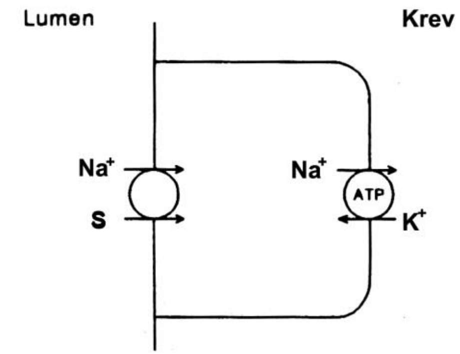
# Transport of solutes

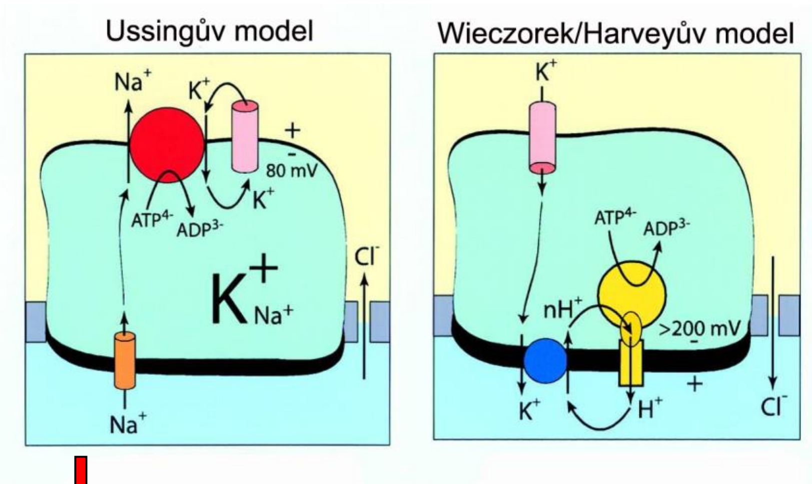


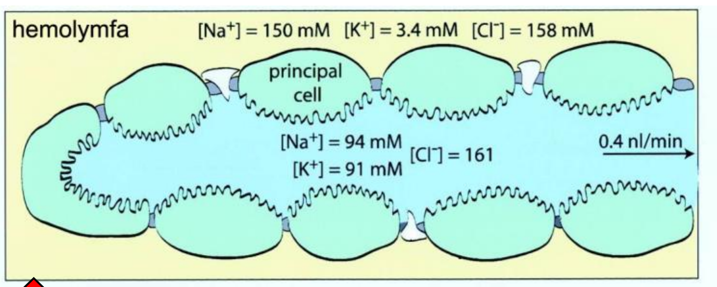

active transport

primary

secondary



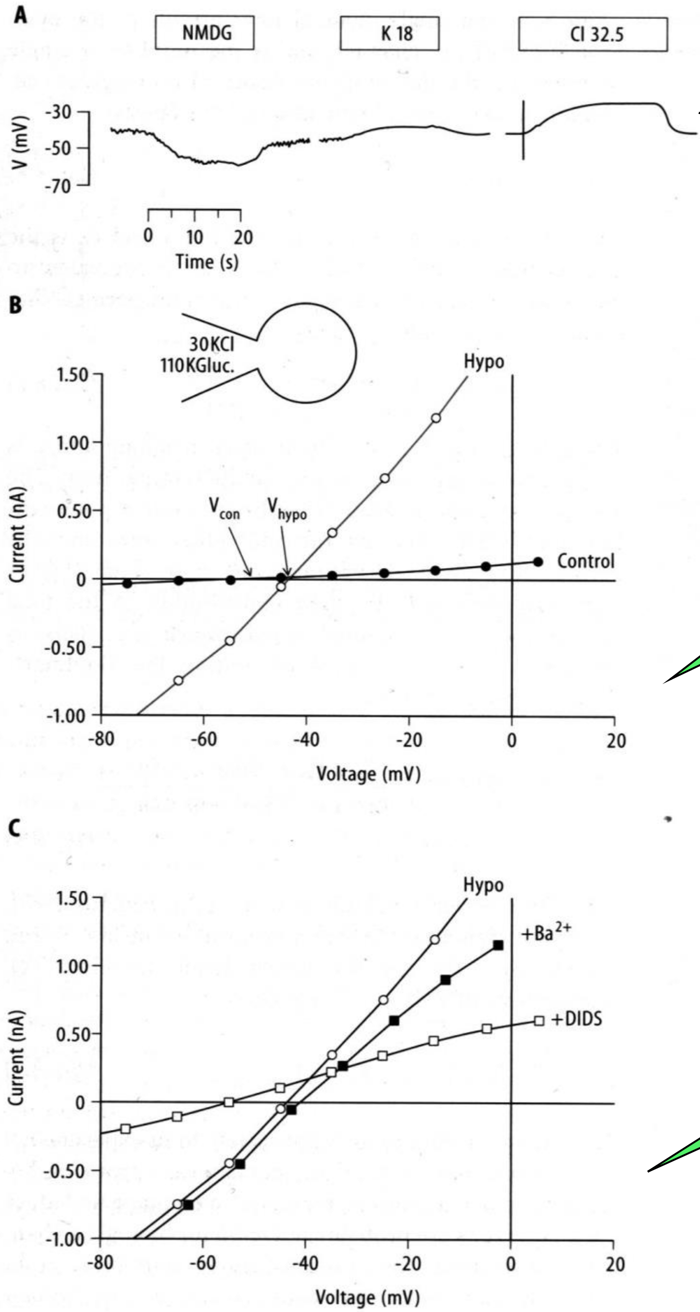




Malpighian tubule (Insects)

Frog skin, urinary bladder, colon, renal collecting tubule, etc.

# Conductance of epithelial cells

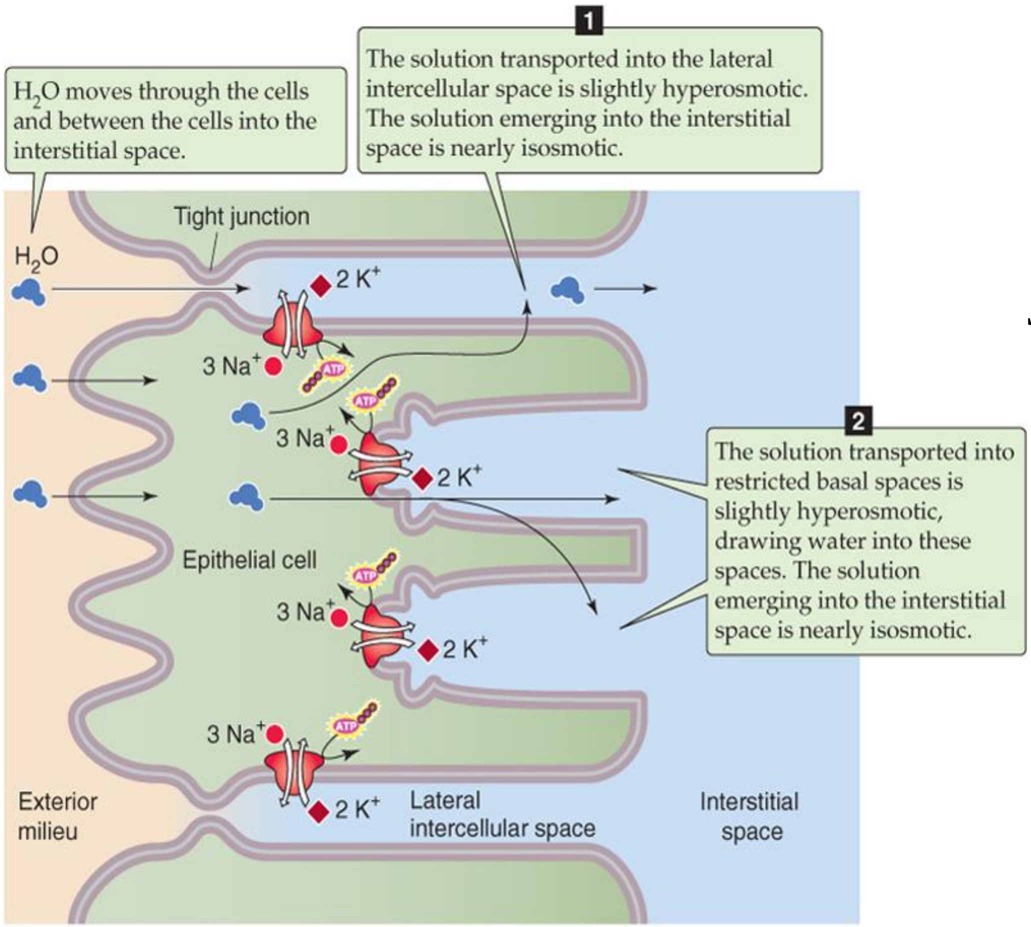



**Ion conductances of plasma membrane, membrane potencials**

**Effect of hypotonic stress on membrane conductance**

**Barium and DIDS sensitive conductance is induced by hypotonic stress**

# Transport of solutes and water

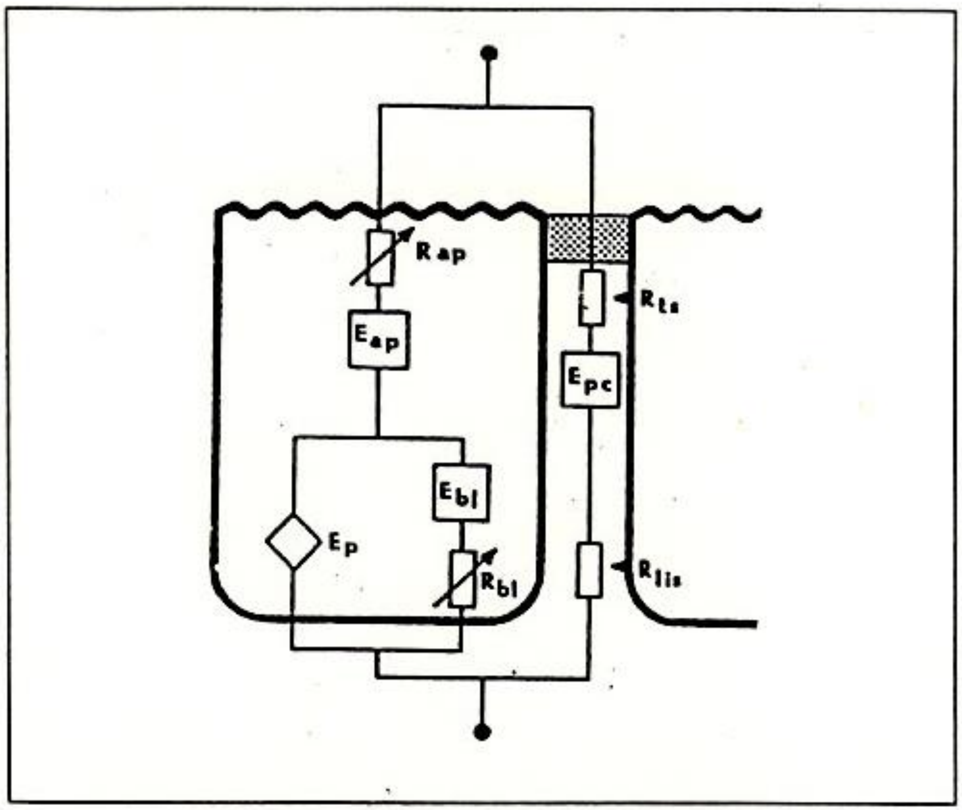





$$J_V = L_P(\Delta p - R.T.\Delta c_1 - \sigma_\iota . R.T.\Delta c_2)$$

- $J_V$ Volume flow
- $L_P$ Hydraulic conductivity
- $\Delta p$ Hydrostatic pressure difference
- $R$ Gas constant
- $T$ Absolute temperature
- $\Delta c_1$ Concentration difference mucosa-serosa
- $\Delta c_2$ Concentration difference mucosa-serosa
- $\sigma_t$ Staverman reflection coefficient

## Equivalent electrical circuit for the epithelium




**Rap** = parallel resistance (1/conductance) for individual ion species that move across the apical membrane

**Eap** = parallel electromotive forces equal to Nernst equilibrium potentials of individual ion species that move across the apical membrane

**Rbl, Ebl** = the same for the basolateral membrane

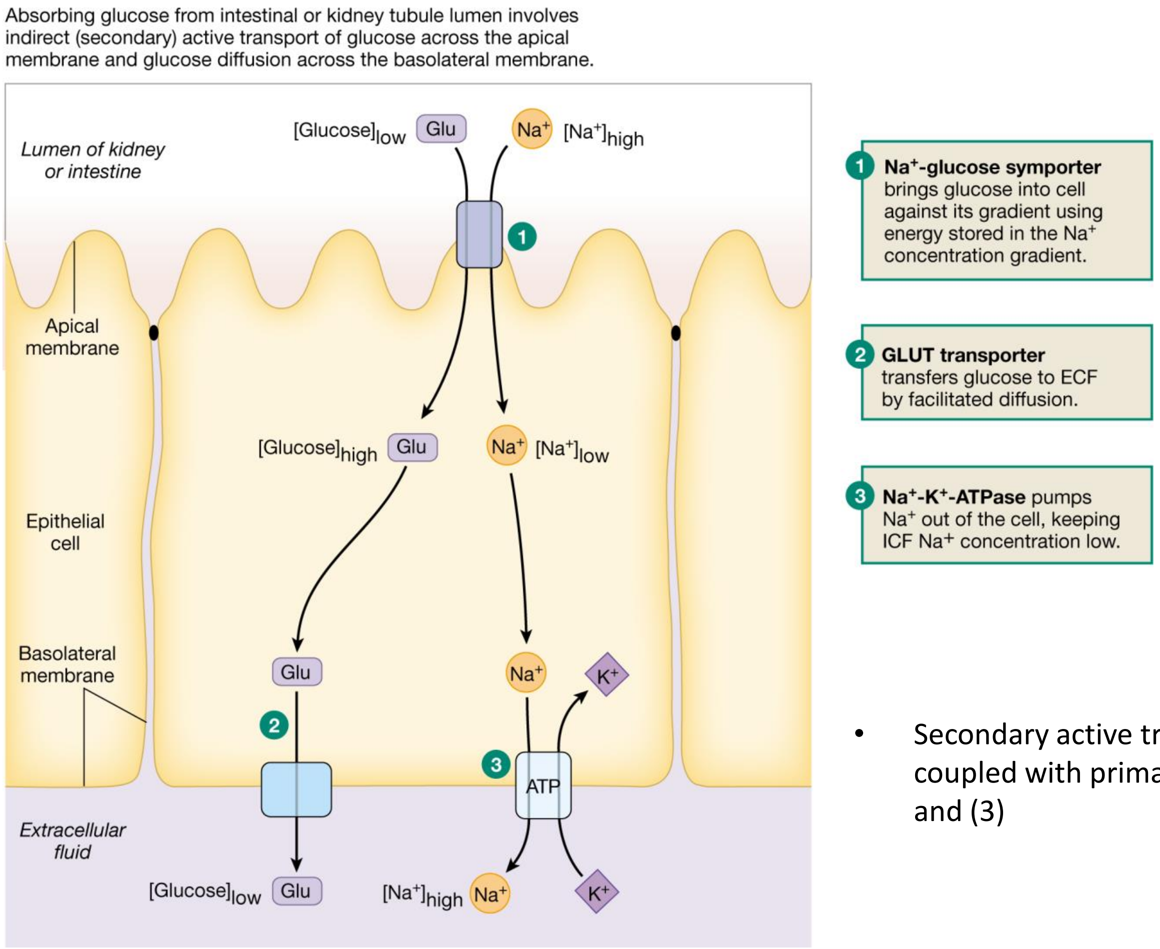
**Ep** = electromotive force of the electrogenic ion pump of the basolateral membrane (Na,K-ATPasa)

**Rts** = resistance of the tight junction

**Epc** = electromotive force corresponding to the diffusion potential of the tight junction

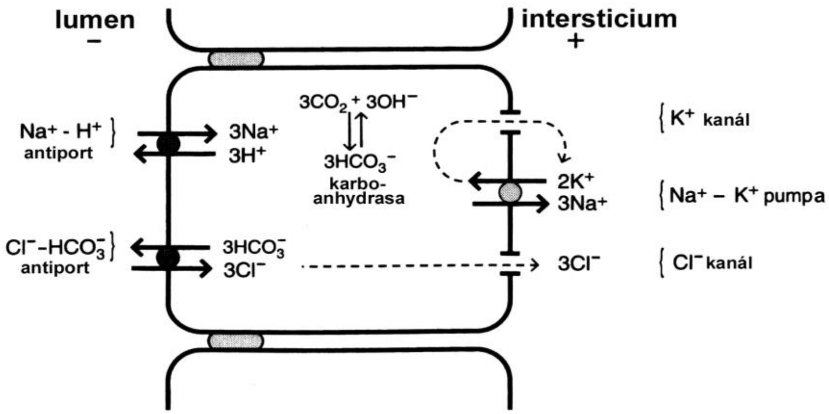
**Rlis** = resistance of the lateral intercellular space

# Coupling of apical and basolateral transport

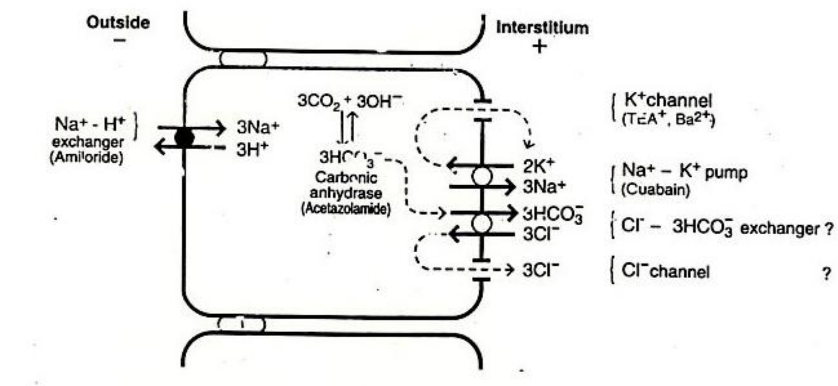



- Secondary active transport has to be coupled with primary active transport (1) and (3)

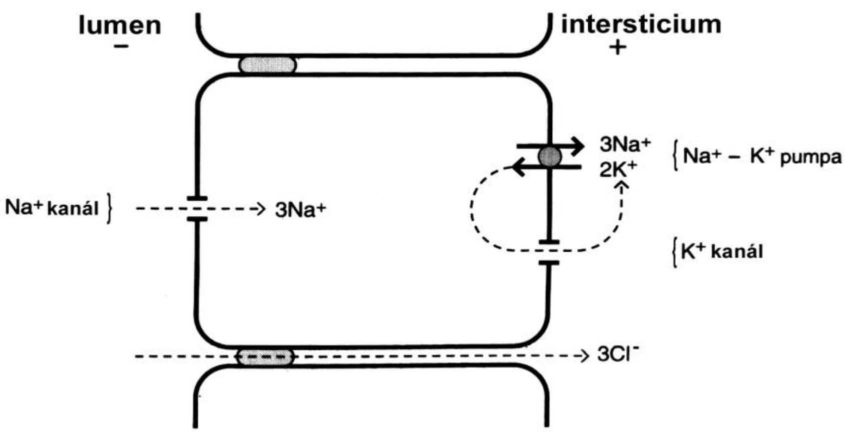
# Mechanisms of NaCl ($NaHCO_3$) absorption



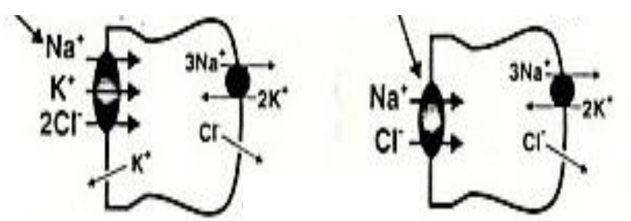

*Transcellular NaCl transport*




*Transcellular NaHCO3 transport*



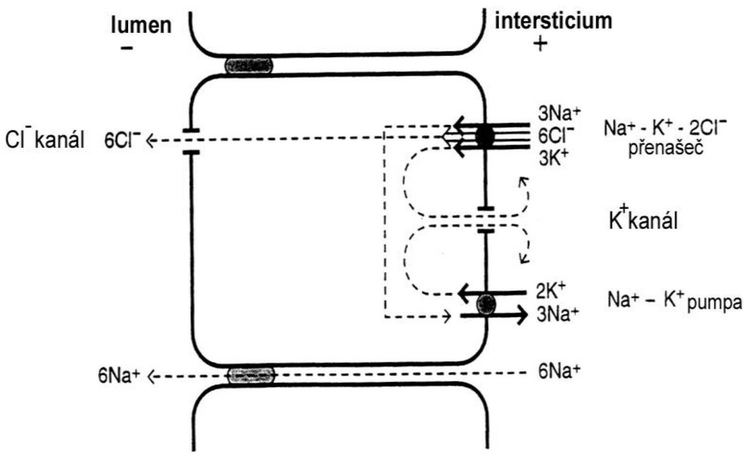

*Transcellular transport of Na+ and paracellular transport of Cl-*



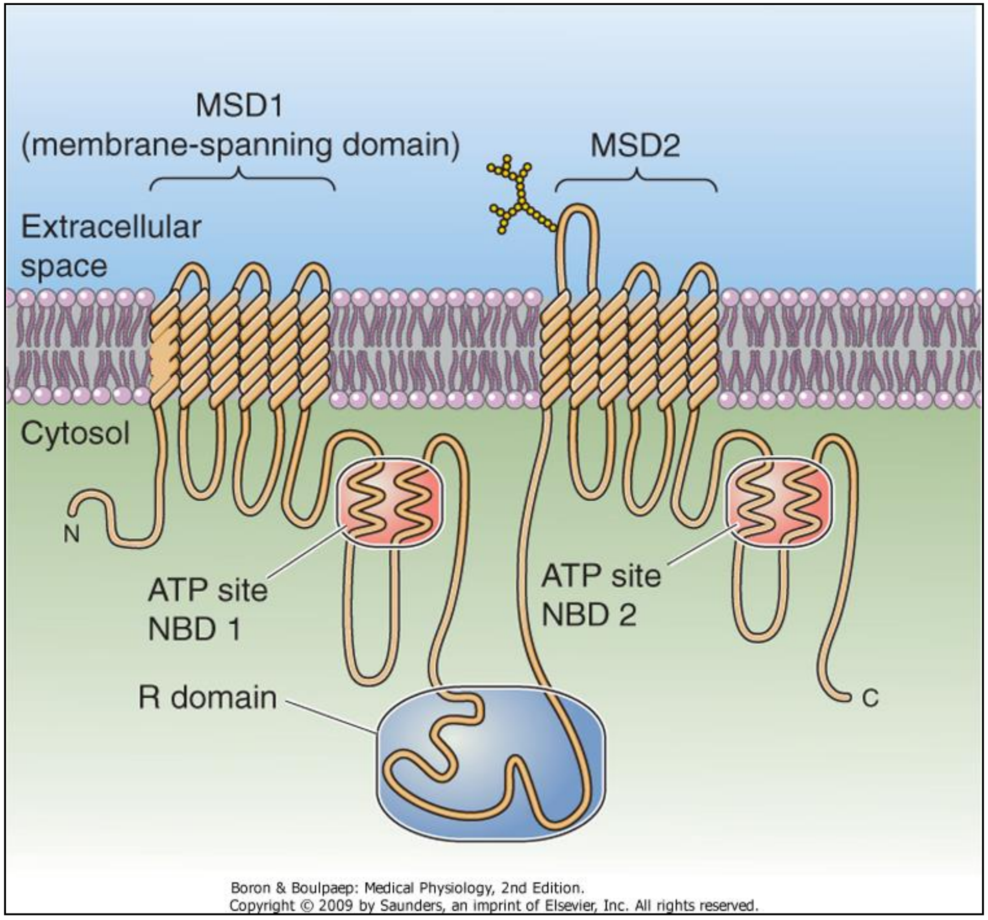

*Transcellular NaCl transport*

# NaCl and water secretion

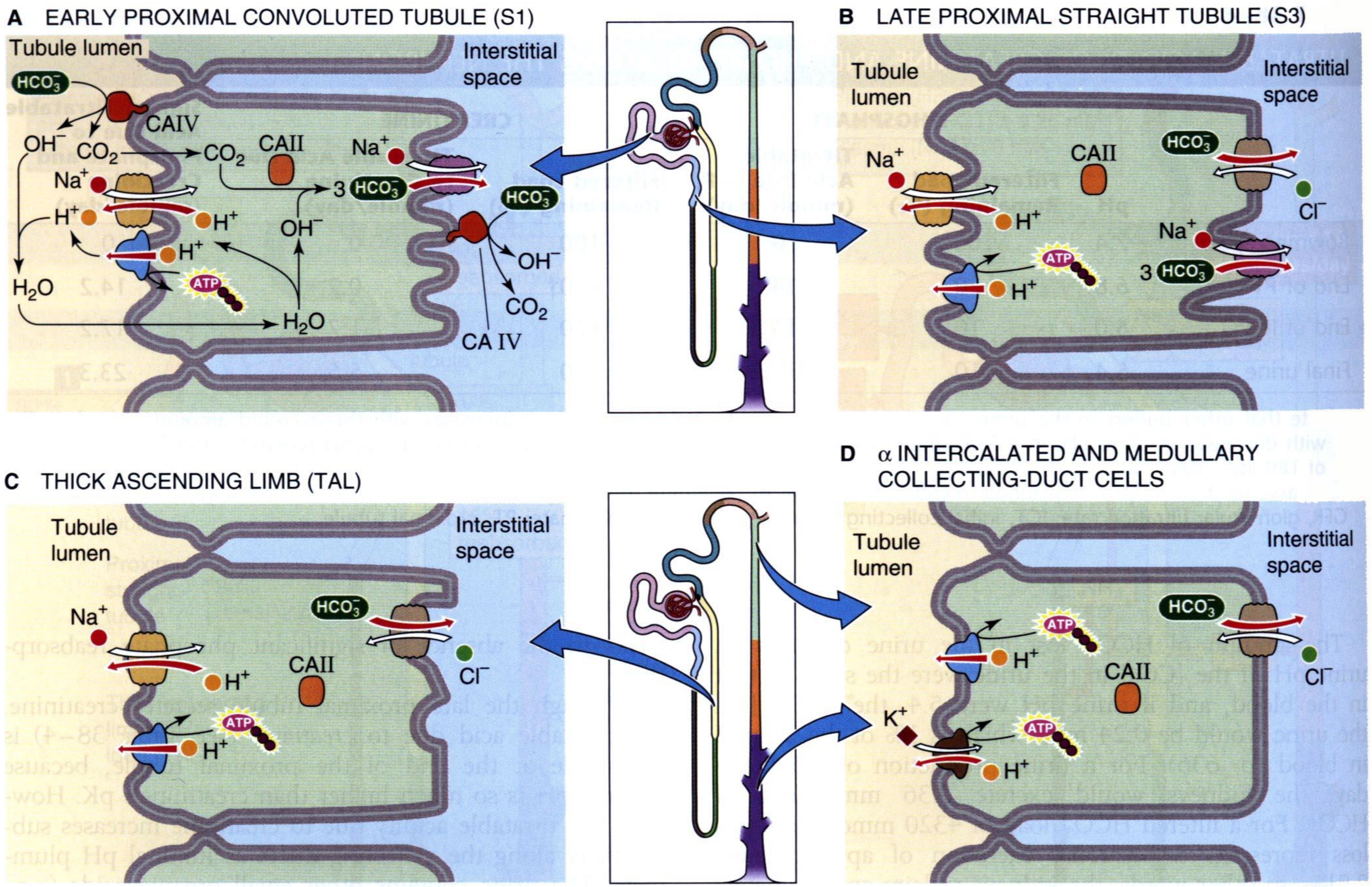
Transcellular transport of Cl- via NKCC cotransporter on the basolateral membrane and chloride channel CFTR on the apical membrane. The negative charges that move across the cell from the interstitium to lumen generate a lumen-negative voltage that can drive passive Na+ secretion across the paracellular pathway (tight junctions). The driving force is the secondary active transport of Cl- across the basolateral membrane.



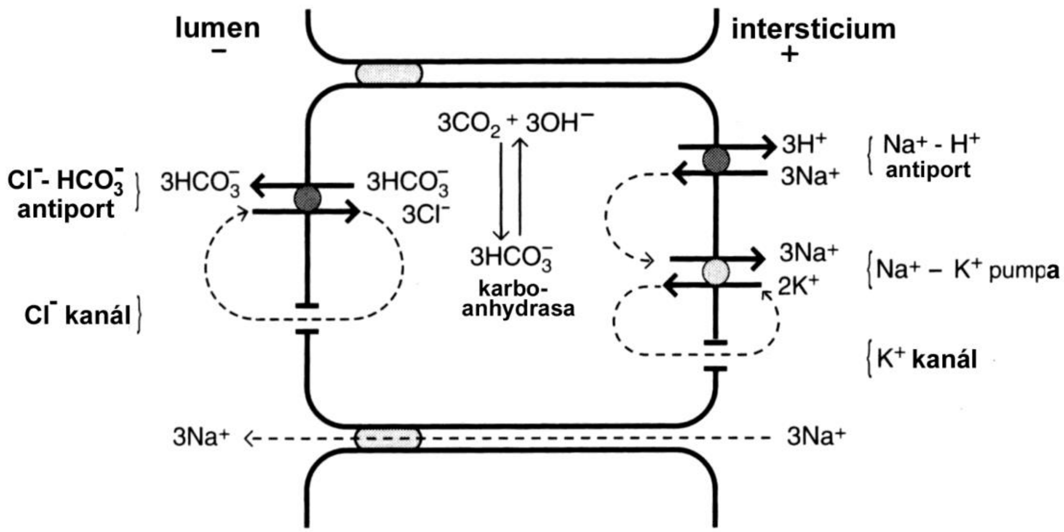

**CFTR**



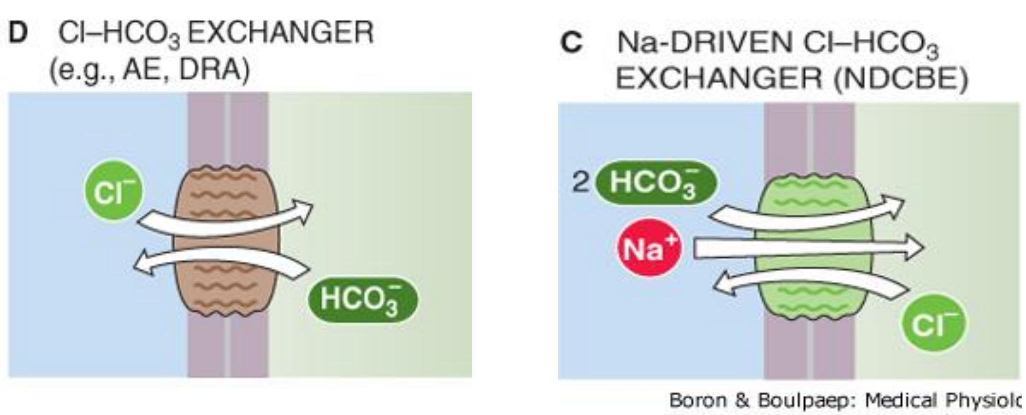
# Acid-base transport – luminal acidification



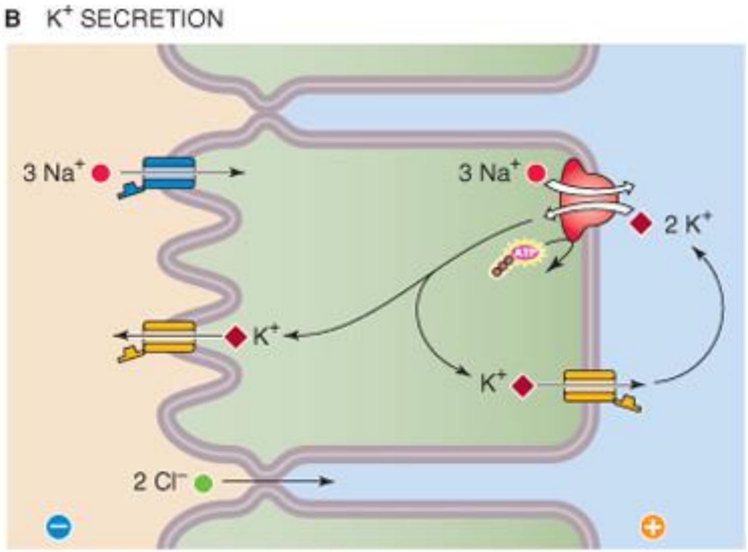
# Acid-base transport – luminal alkalinization



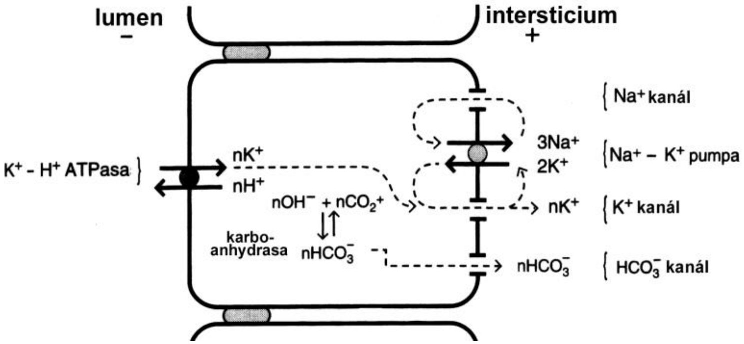

***Exchangers***



# Potassium transport

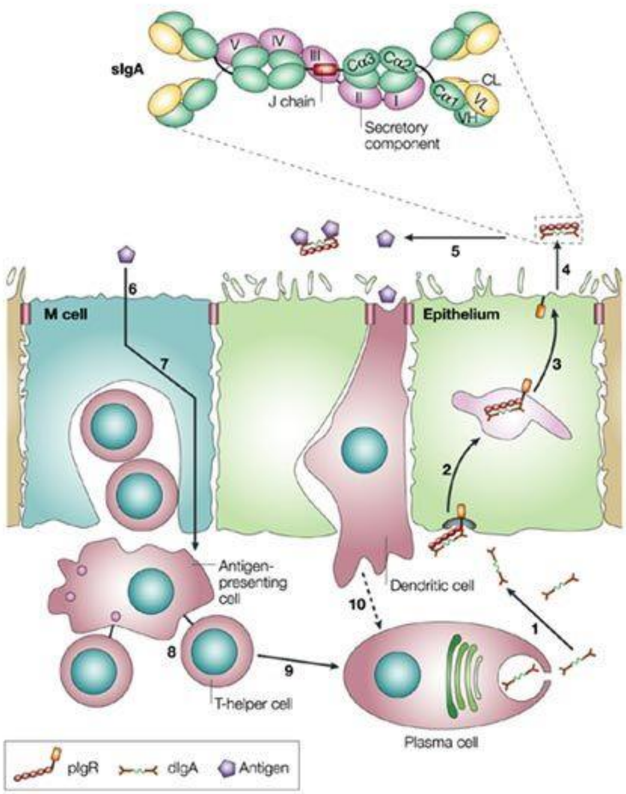



Transcellular secretion: K+ is taken up by Na-K pump across the basolateral membrane to be secreted across the apical membrane via potassium channels.




1. Paracellular absorption trough tight junctions.
2. Transcellular primarily active absorption driven by H-K-pump.

# Immunoglobulin transport across polarized epithelial cells

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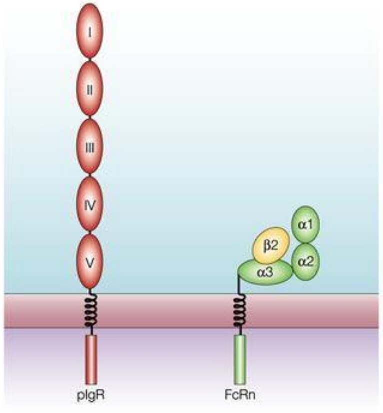
- Receptor mediated transcytosis
- Transport of IgA and IgG is mediated through the polymeric immunoglobulin receptor pIgR
- pIgR is proteolytically cleaved in the cell or at the apical surface
- The cleaved extracellular domain of the receptor = secretory component (SC)
- Transport of IgG is mediated through FcRn receptor

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# Control of epithelial transport

1. **Cell control – „**crosstalk“ between apical and basolateral membrane – protection against the increasing concentration of osmolytes in the cytoplasm
2. **Tissue control** – e.g.. enteric nervous system,
3. **Organism control** – e.g. hormones calcitriol, aldosterone, vasopressin

**Hormone regulatory pathways** – endocrine, paracrine, autocrine, intracrine

**Nervous regulatory pathways** – symphatetic, parasymphatetic and enteric nervous systems

**Immune regulatory pathways –** mucosal immune system