Fluid transport in epithetlial alveolar cells (**Alveolar Epithelial Fluid Transport in Lung Injury**

Hans G. Folkesson)

* Active Na and Cl transport participates in regulating alveolar edema resolution
* Starling forces (differences in hydrostatic and protein osmotic pressures) were believed to account for removal of excess air space fluid but experiments were done on dog (low rate of active ion and fluid transport) at room temperature

Human lung

* Highly branched hollow tubes ending blindly in alveoli, conducting airways (cartilaginous trachea, bronchi, membranous bronchioles) occupying first 16 airway generations
* Alveoli approx. 143m2 and airways approx. 1.4m2 lined by continuous epithelium
* Distal airway epithelium composed of polarized epithelial cells, transport na+ and cl-
* Include ciliated Clara cells and nonciliated cuboidal cells
* Alveoli composed of thin alveolar epithelium covering 99% of air space surface area in lung, containing thin squamous type I cells (95% of alveolar surface) and cuboidal type II cells
* Apposition of alveolar epiethlium and vascular epithelium assists in exchanging ases, tight barrier to liquid movement/protein movement and keeps the alveoli dry

Epithelial cells of alveoli

* Tight junction critical for barrier function
* Connects adjacent epithelial cells near apical surfaces, maintaining apical and basolateral cell polarity
* Originally believed tight junctions were rigid structures, physically restricting passage of larger molecules, however it is regulated by cytoskeletal proteins and intracellular Ca2+ concs
* Studies of protein flux across endothelial-epithelial barrier suggests 92% of albumin flux resistance is due to epithelium

Model for transepithelial fluid movement

* Active salt transport drives osmotic water transport
* Na+ transport inhibitors reduce rate of fluid absorption in lungs
* Changes in protein osmotic pressures/hydrostatic pressures cannot cause removal of fluid from distal air spaces
* Isosmolar fluid absorption occurred in spite of rising alveolar protein concentration and protein oncotic pressure

Electrolyte and fluid transport across the mature

alveolar epithelium

GEORGES Saumon

* Mature alveolar epithelial cells has active ion and fluid transport, and transport by passive forces possibly much less important
* Alveolar epithelium separated by gas phase by aq layer containing surfactant – reduces surface tension of fluid at air-surface interface
* Type 1 cells – 35-50% large (5000-7000um^2, flat, thin, possibly from proliferated type 2 cells) and type 2 cells (100-200um^2, cuboidal, found in alveolar ‘corners, secretes surfactant); type 3 cells (brush cells) found in rat alveoli
* METHOD: fills lung with fluid, determine rate of clearance of solute or water from alveoli
  + LIMITATIONS – the molecular species studied must travel across the barriers (epithelial and endothelial), may accumulate in interstitial fluid, perfusion may be unevenly distributed, epithelial transport may differ from one site to antoher, hard to determine which cell type responsible for active transport
  + In vivo models used as closer to normal physiological conditions (bronchial perfusion, lymphatic drainage are maintained), ion transport inhibitors can also cause cardiac effects
  + Amphibian lungs simple shape can be used in using chambers, but interspecies difference in Cl- secretion of Na+ absorption

Passive transport

* Tight barrier b/w gas + blood, more resistance to hydrophilic solute movement than contiguous endoythelium
* Cell pepbrane forms barrier, imperable to polar solutes
* Epithetlial perability to hydrophilic solutes – solutes escaped from alveoli proportional to free solution diffusion coefficient – nonselective leakage **other studies conclude permeability restricted depending on solute size**, as if water filled channels of finite size exended across epithelium 🡪 98.7% of total pore population are small pores (0.5nm type) allowing for small solute permeability
* Large pores are fewer in number (~100nm radius), which is why alumin is detectable in alveolar lining layer
* Ions are actively transported adds to rate of unidirectional transepithelial transport – passive permeability estimated by inhibiting active transport with drugs
  + In rats passive Na+ permeability is 7\*10-7 cm/s, Cl- permeability is 1\*10^8mc/s assuming exchange SA of 5000cm/s
  + Resistance of 18000 ohm cm^2 in rat lung, suggesting alveolar epithelium is tight epithelia

Resorption of alveoliar fluid

* Hydrostatic and oncotic pressure differences operating across the alveolus-airway barrier
* Cleared by lymphatic pumping and circulation
* High permeability edema 0 fluid leaks from microvessels and fills peribronchovascular cuffs and alveoli, and has a higher protein content, so oncotic pressures are noy different, however it resulves (**how?)**
* Matthay et al, sheep lung lobes with autologous serum, protein concs increased and water still removed, fluid absorption continued even with unfavourable pressure difference, maybe there is active transport by epithelium lining the alveolus-airway barrier (defs found in foetal lungs 17 103) – fluid absorption enhanced by epinephrine and slowed by amiloride (a Na+ transporter in epithelia)
* Fluid absorption (apical to basolateral side) follows Na+ transport – Na\_ absorped at apical membrane, pumped out of basolateral membrane by NAKATPase so Na+ chem potential lower inside the cell (passive in, active out), and for K+, active out of apical, passive in for basolateral, then recycled