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A Cell Culture Model for Alveolar Epithelial Transport

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Background

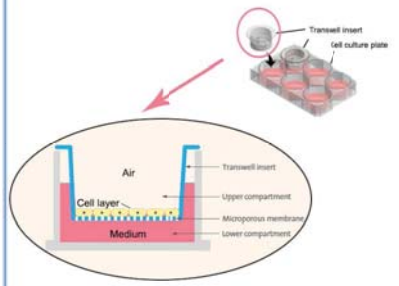
Human lungs are lined throughout by a thin layer of liquid whose depth is tightly regulated by a balance between secretion and absorption of water and ions[1]. Vectorial transport of Na+ and Cl- between the apical (air-facing) and basolateral (blood-facing) surfaces establishes an osmotic pressure gradient that results in net water movement from the alveolar to interstitial spaces. Aquaporins (AQPs), epithelial Na^+ channels (ENaCs), cystic fibrosis transmembrane conductance regulator (CFTR) and Na^+-K^+-ATPase are transport-related proteins. They play important roles in Na^+, Cl^- and water transport[2,3]. Studies on the ion and water transport are crucial to uncover the contributions of different channels under both normal and pathological conditions.

Objectives

- Establish a cell culture model system using H441 and A549 cell lines with alveolar epithelial-like phenotype[4]
- Characterise the ion and water transport profile under this model.

Methods

1. Cell culture model



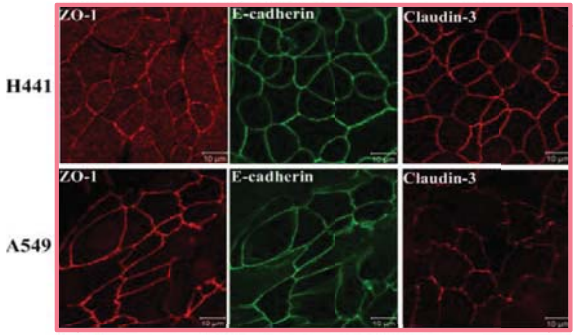
2. Trans-epithelial resistance (TEER) and potential difference (TEPD) were measured using a voltohmmeter

3. Cell phenotype was characterized by determining gene and protein expression

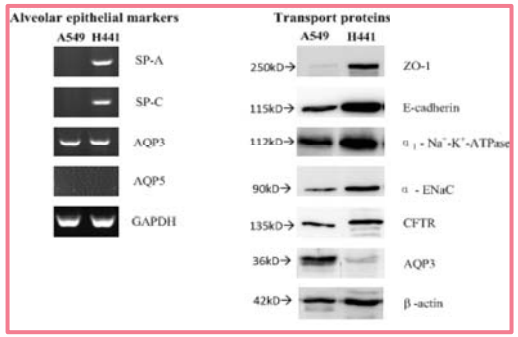
4. Contributions of different pathways to ion transport were determined by using inhibitors and agonists.

Results

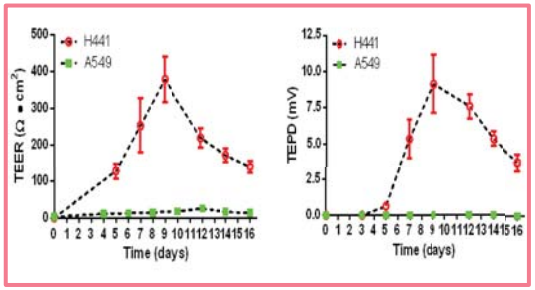
1. Tight monolayer formation under air-liquid culture system.



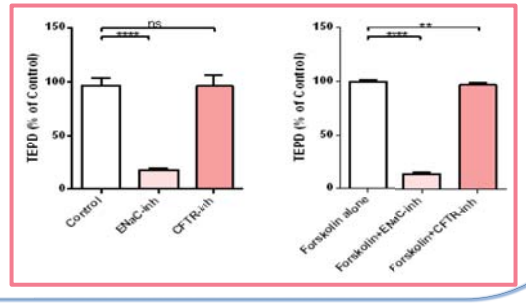
2. H441 cells exhibit phenotype similar to primary alveolar epithelial cells.



3. H441 but not A549 cells develop high TEER and TEPD.



4. ENaC activity is the major contributor to TEPD under baseline and stimulation.



Summary

- H441 cells exhibit phenotype and ion transport properties similar to alveolar type 2 cells in vitro[5].
- Na^+ absorption from apical surface by ENaC under baseline and stimulation.
- Absence of CFTR contribution to TEPD indicates Cl- transport is primarily from paracellular pathway.
- Results similar to Shelley Fong's mathematical model (see adjacent poster).

Future Work

- Ion and water transport will be studied in an Ussing chamber
- Contributions of paracellular and transcellular pathways will be determined by two-path impedance measurements

References

(1) **Matthay MA, et al.** *Physiol Rev* 2002 Jul;82(3):569-600.

(2) **Dobbs LG, et al.** *Respir Physiol Neurobiol.* 2007 Dec 15;159(3):283-300.

(3) **Hollenhorst Mi, et al.** *J Biomed Biotechnol.* 2011;2011:174306.

(4) **Brown SG, et al.** *Am J Physiol Lung Cell Mol Physiol.* 2008 May;294(5):L942-54.

(5) **Bove PF, et al.** *The Journal of Biological Chemistry* 2010 Nov 5;285(45):34939-49.

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