

## Dopamine Transport Across Respiratory Epithelium

N. V. Chemuturi<sup>1</sup>, P. J. Hayden<sup>2</sup>, M. Klausner<sup>2</sup>, and M. D. Donovan<sup>1</sup>

<sup>1</sup>University of Iowa, <sup>2</sup>MatTek Corporation

**PURPOSE:** To investigate the active and passive transport pathways of dopamine in a human tracheobronchial cell culture (EpiAirway™) as a model for nasal drug transport.

**METHODS:** Transport studies across the tracheobronchial cell cultures were carried out using Sweetana-Grass diffusion cells. The transport was followed in the apical to basolateral (a-b) and basolateral to apical (b-a) direction as a function of dopamine concentration. Studies using a specific DAT inhibitor, GBR 12935; an OCT inhibitor, quinidine; and an OCT-2 inhibitor, amantadine, were also conducted to study the role of these transporters in dopamine flux across the cell culture. The presence of DAT and OCT-2 in the cell cultures was confirmed using immunohistochemistry.

### RESULTS:

Flux of dopamine in the tracheobronchial culture showed non-linear dependence on concentration in the b-a direction while being linearly dependent on concentration in the a-b direction. The  $V_{max}$  for b-a flux was determined to be  $3.5 \mu\text{g}/\text{cm}^2/\text{min}$ , and the  $K_m$  was approximately 2 mM. Flux decreased in the b-a direction by ~35% and increased in the b-a direction by ~500% in the presence of the DAT inhibitor, GBR12935, resulting nearly equal flux values in both directions. In the presence of amantadine, an OCT-2 inhibitor, the transport of dopamine was absent in both a-b and b-a directions. Immunohistochemistry studies showed that DAT was present on the basolateral surface while OCT-2 was present predominantly on the apical surface.

### CONCLUSIONS:

The decrease in dopamine transport in the presence of both DAT and OCT inhibitors confirms the presence of both transporters in respiratory cells. This demonstrates that active transport processes play a key role in drug absorption across the respiratory epithelium similar to other epithelial sites.