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### **“Ion transport in bronchial epithelia under mucous metaplasia conditions”**

Mucous cell metaplasia, consisting of a marked increase in the number of mucus-producing goblet cells, is driven by the Th-2 cytokines IL-13 and IL-4. In short-circuit current recordings, human bronchial epithelial cells treated with IL-4 for 72 hrs show increased calcium- and cAMP-activated chloride/bicarbonate secretion. The upregulation of the calcium-dependent component is consistent with a strong expression of TMEM16A protein, which occurs in non-ciliated MUC5AC-positive cells. A large percentage of these cells also express the anion exchanger SLC26A4 (pendrin). The cAMP-dependent component is instead mediated by CFTR. However, CFTR expression does not appear to be increased by IL-4. Therefore, upregulation of CFTR function may occur through other mechanisms such as increased driving force for anion secretion. In fact, microarray analysis reveals that IL-4 increases the expression of several genes coding for ion channels and transporters. Interestingly, analysis of the ion composition of the apical surface fluid reveals enhanced bicarbonate concentration in epithelia treated with IL-4. Mucin release, elicited by purinergic stimulation and detected with fluorescent nano-beads, requires the presence of bicarbonate in the basolateral solution and is defective in cells derived from cystic fibrosis patients. In conclusion, Th-2 cytokines induce a profound change in expression and function in multiple ion channels and transporters that results in enhanced bicarbonate transport ability. This change may be required to favor release and expansion of mucus.

**Wednesday, May 4<sup>th</sup>, 2016 at 3:00 PM**

**Room 1034**

**McIntyre Medical Sciences Building, 3655 Promenade Sir William Osler**

*Refreshments will be served before the seminar.*

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