Cystic fibrosis epithelial cell and bacterial binding

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TO THE EDITOR: The recently published article entitled “Sugar administration is an effective adjunctive therapy in the treatment of Pseudomonas aeruginosa pneumonia” by Bucior et al. (1) describes the administration of a mix of simple sugars mannose, fucose, and galactose in a cellular model of bacterial adhesion and a murine model of acute pneumonia and lung injury. The authors report that when the sugars are used in combination, rather than administered as a single sugar, the mixture competitively inhibited adhesion of nonmucoid and mucoid P. aeruginosa to bronchial epithelial cells and reduced bacterial lung colonization and lung injury.

However, the authors did not cite or mention the posttranslational process of sialylation. The sialylation defects associated with posttranslational modification and presentation of putative asialo-GM1 binding sites in cystic fibrosis (CF) epithelial cells should be considered, for better understanding the cellular mechanisms of this potential adjunctive therapeutic approach. One possible explanation for the efficacy of multiple, rather than single sugar solutions is that there are multiple glycosylated moieties that need to be competitively blocked to decrease bacterial binding.

Our previous work and that of others have described the findings of altered sialylation in CF epithelial cells that express the ΔF508 CFTR mutation. These changes occur during posttranslational modification of glycoproteins and glycolipids and may be one major factor contributing to colonization with Pseudomonas and Staphylococcus species in the CF airway (2, 3). Our studies identified that an increased in membrane associated asialo-GM1 putative bacterial receptors may in part account for increased binding of Pseudomonas pilus to the epithelial cell membrane in CF. In studies of specific binding of Pseudomonas to asialo GM1, exogenous asialo GM1 was reported to competitively inhibit Pseudomonal binding to epithelial cells (4). The strategy of exogenous competitive binding to CF epithelial cell surface glycosylated putative bacterial binding sites is one that holds promise in future therapeutic development.

In developing new therapeutic strategies such as adjunctive therapy to standard antibiotics by blocking the initial binding between the bacteria and glycoproteins and glycolipids, correcting underlying sialylation defects associated with mutant CFTR is an important consideration.

REFERENCES


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