Special Lecture

Personalized Medicine in Asthma

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Asthma is a complex disease affecting over 300 million individuals in the developed world. Ninety percent of all asthma cases, including asthma in adults, have its origins in childhood. Asthma is the leading chronic disease cause of hospitalizations and school absences in children. It has been estimated that 20% of the subjects with asthma contribute 80% of the economic costs of asthma. Notably, it has also been estimated that as many as one-half of asthmatic patients do not respond to treatment with ?2-agonists, leukotriene antagonists, or ICS. A number of guidelines directed at the medical management of asthma have been developed. Each of these has in common the "step-wise" care of asthma, beginning with as needed short-acting β-agonists, with the sequential steps of inhaled corticosteroids (ICS), then low and high dose ICS + long-acting β-agonists (LABA), respectively. Each change in therapy is accompanied by a period of observation for clinical response, leading to significant lags in optimal care. While therapeutic delays related to step care therapy are undesirable, broad-based empiric implementation of ICS + LABA (i.e. higher step therapy) does not significantly improve therapeutic outcomes, but significantly increases costs. Overall, strict adherence to the guidelines is lacking, with physicians generally reluctant to change medications. Recently, several biologics have been approved for therapy of severe asthma. However, these medications are expensive with potential for systemic side effects. Overall, the ability to immediately match a given patient with the appropriate asthma therapy has direct implications for minimizing morbidity and maximizing clinical outcomes.

Personalized medicine in asthma broadly applied would seek to define factors that would enhance primary disease prevention, secondary disease progression, or tertiary disease treatment. Much progress has been made in precision therapeutics for asthma. For instance, the biologics for severe asthma have unique biomarkers based on their targeted pathway, such as IgE for omalizumab, periostin for lebrikiuzmab, and eosinophils for mepolizumab. Additionally, many genes have been identified that influence more traditional classes of treatment response in asthma, such as beta-agonists, inhaled corticosteroid, and leukotriene

modifiers. These studies have been conducted using traditional pharmacogenetic studies focusing on genotype, as well as pharmacogenomic studies using gene expression and other 'omic technologies. Newer approaches, including integrative pharmacogenomics and systems biology approaches have combined data types to enhance potential prediction of therapeutic response, as well as the potential for novel therapeutic targets. Nonetheless, personalized therapeutics for asthma remains in its infancy, and additional studies and approaches are needed.