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164 Identification of Biomarkers in Allergy and Asthma: Effects of Glucocorticosteroids on Cell Surface and Soluble Factors

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The clinical manifestations of asthma are thought to result from the effects of environmental factors superimposed on genetic predispositions. Corticosteroids are efficacious in asthma but are associated with both perceived and real side effects that limit their clinical usefulness. A better understanding of the response to corticosteroids will spearhead the development of beneficial drugs with fewer side effects. Biomarker discovery at SurroMed includes a wide range of assays to phenotype subjects with different disease subclasses and treatment regimens. The differential phenotyping tools include cytometry assays to analyze different cell types, immunoassays to quantitate soluble factors, and mass spectrometry to characterize proteins and small organic molecules. This phenotyping panel has been used to characterize biomarkers in a group of subjects with allergy and asthma undergoing a short course of glucocorticosteroid treatment. Cell surface markers and soluble factors have been analyzed from approximately 80 subjects from the following patient cohorts: 1) mild asthmatic, allergic (positive methacholine challenge and a positive skin prick test to one or more tested allergens) 2) non-asthmatic, allergic (negative methacholine challenge and a positive skin prick test to one or more tested allergens) 3) non-asthmatic, non-allergic (negative

methacholine challenge and a negative skin prick test). Blood samples were analyzed both before and after a three day course of glucocorticosteroids or placebo taken twice a day. A new microvolume laser scanning cytometry (MLSC) platform developed at SurroMed (SurroScan™) allows for the identification, characterization and enumeration of over 200 unique populations of cells, including subsets of lymphocytes, monocytes, neutrophils, eosinophils and NK cells from less than 2 ml of blood. In MLSC, a suspension of whole blood is incubated with a cocktail of fluorescently labeled antibodies specific for the relevant cell surface antigens, loaded onto capillary arrays and imaged with a confocal laser scanning microscope. In the current study a panel of 64 three-color assays was applied and both absolute cell counts of each population and level of antigen expression of each marker was analyzed. A significant increase in total numbers, and subpopulations of B cells, neutrophils, and monocytes was observed in the glucocorticosteroid treated group compared to placebo. A significant decrease in eosinophils was also observed post-treatment. Furthermore, differences in cell surface expression levels were detected, including significant decreases in the levels of HLA DP, DQ, and DR on both monocyte s and B cells following glucocorticosteroid treatment. The immunoassay panel includes detection of over 60 soluble factors by ELISA, including immunoglobulin subtypes, cytokines, chemokines and soluble receptors. These data are still being analyzed; differences between the different subject cohorts and treatment regimens have been identified. It is hoped that this kind of phenotyping data will lead to a better understanding of the targets involved in glucocorticosteroid therapy for allergy and asthma and, in turn, to better treatment regimens.

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