Features of the bronchial bacterial microbiome associated with atopy, asthma, and responsiveness to inhaled corticosteroid treatment

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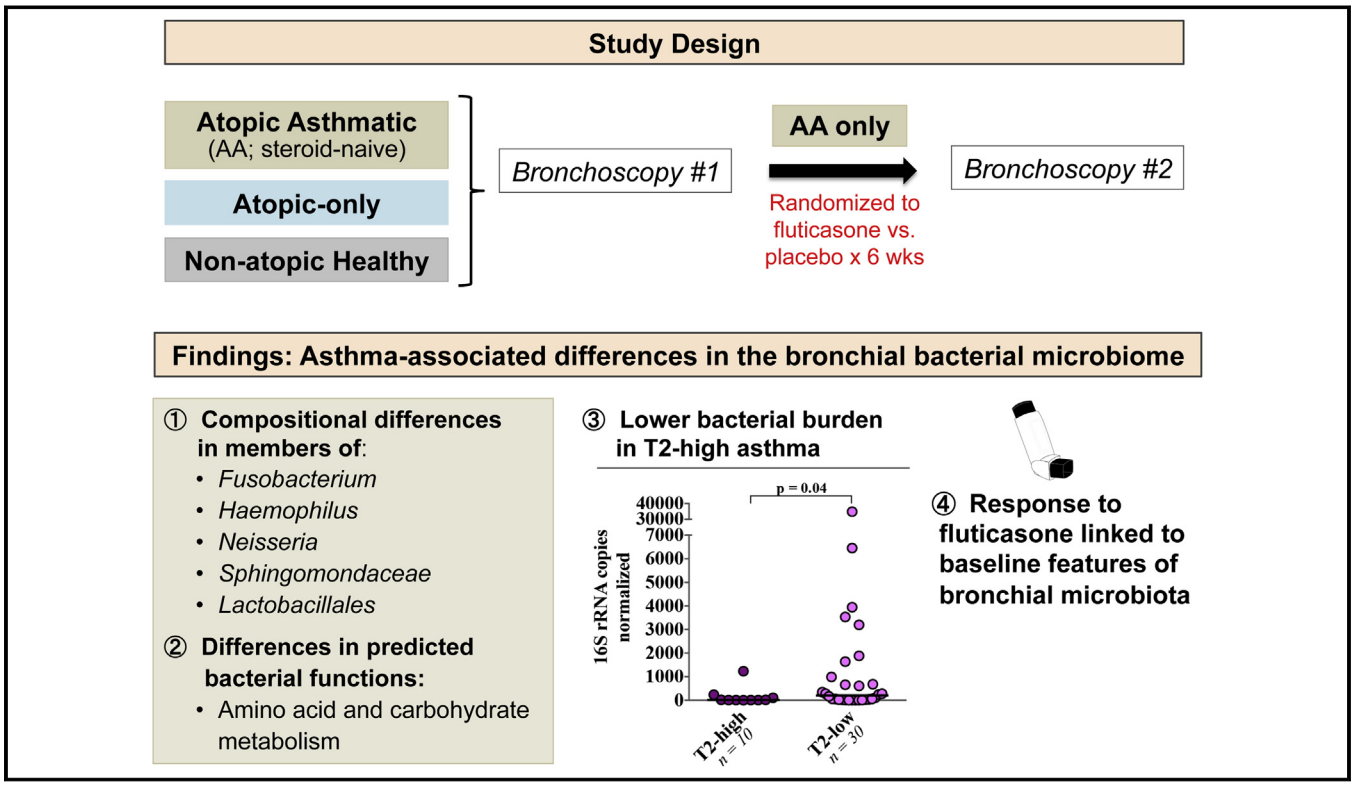
GRAPHICAL ABSTRACT



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Background: Compositional differences in the bronchial bacterial microbiota have been associated with asthma, but it remains unclear whether the findings are attributable to asthma, to aeroallergen sensitization, or to inhaled corticosteroid treatment.

Objectives: We sought to compare the bronchial bacterial microbiota in adults with steroid-naive atopic asthma, subjects with atopy but no asthma, and nonatopic healthy control subjects and to determine relationships of the bronchial microbiota to phenotypic features of asthma.

Methods: Bacterial communities in protected bronchial brushings from 42 atopic asthmatic subjects, 21 subjects with atopy but no asthma, and 21 healthy control subjects were profiled by using 16S rRNA gene sequencing. Bacterial composition and community-level functions inferred from sequence profiles were analyzed for between-group differences. Associations with clinical and inflammatory variables were examined, including markers of type 2–related inflammation and change in airway hyperresponsiveness after 6 weeks of fluticasone treatment.

Results: The bronchial microbiome differed significantly among the 3 groups. Asthmatic subjects were uniquely enriched in members of the *Haemophilus*, *Neisseria*, *Fusobacterium*, and *Porphyromonas* species and the Sphingomonodaceae family and depleted in members of the Mogibacteriaceae family and Lactobacillales order. Asthma-associated differences in predicted bacterial functions included involvement of amino acid and short-chain fatty acid metabolism pathways. Subjects with type 2–high asthma harbored significantly lower bronchial bacterial burden. Distinct changes in specific microbiota members were seen after fluticasone treatment. Steroid responsiveness was linked to differences in baseline compositional and functional features of the bacterial microbiome.

Conclusion: Even in subjects with mild steroid-naive asthma, differences in the bronchial microbiome are associated with immunologic and clinical features of the disease. The specific differences identified suggest possible microbiome targets for future approaches to asthma treatment or prevention. (J Allergy Clin Immunol 2017;140:63-75.)

Key words: *Asthma, atopy, microbiome, corticosteroids, 16S ribosomal RNA, bacteria, T_H2 inflammation, three-gene mean, metabolic pathways, short-chain fatty acids*

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Recent culture-independent studies have documented that the composition of commensal lower respiratory tract bacteria (microbiota) differs between asthmatic and healthy adults.[1-6] Additionally, phenotypic features of asthma, such as measures of airway hyperresponsiveness, asthma control, and transcriptional response to steroids, correlate with patterns of bronchial microbiota composition.[4,5] Although different studies have reported asthma-associated enrichment (higher relative abundance) of different taxa (ie, bacteria-derived 16S ribosomal RNA gene sequences that exhibit an operator-defined level of sequence homology [typically 97%]), enrichment in members of the phylum Proteobacteria is a repeating signature. Asthmatic subjects in most previous studies were treated with inhaled corticosteroids (ICSs), casting some uncertainty on whether the findings reflect the effects of ICS treatment or of asthma itself. Similarly, many asthmatic patients are atopic,[7,8] raising the question of whether asthma-associated differences in respiratory microbiota are

Disclosure of potential conflict of interest: S. V. Lynch has received grants from the National Institutes of Health (NIH)/National Institute of Allergy and Infectious Disease (NIAID; AI113916, AI089473-01, and AI097172), Janssen, the Broad Foundation, the Sloan Foundation, Pfizer, the NIH/National Institute of Child Health and Human Development (HD082147-01), the NIH/National Heart, Lung, and Blood Institute (NHLBI; HL098107 and HL098964), and the NIH/National Institute of Diabetes and Digestive and Kidney Diseases (DK104664); has a patent Stan449-PRV REDUCTIVE PRODRUG CANCER CHEMOTHERA issued, a patent Combination antibiotic and antibody therapy for the treatment of *Pseudomonas aeruginosa* infection with royalties paid, a patent provisional filing for use of *Lactobacillus sakei* and other lactic acid bacteria as a therapeutic strategy for chronic rhinosinusitis issued, a patent provisional filing for claims associated with use of PhyloChip as a diagnostic and prognostic clinical tool issued, and a patent Bacterial Therapeutic Consortium for induction of Immune Tolerance pending. S. Nariya has received a grant from the NHLBI and the National Institute of Allergy and Infectious Disease (NIAID). N. R. Bhakta has received a grant from the NIH/NHLBI and has received personal fees from Roche/Genentech. M. Castro has received personal fees from Boston Scientific, Holaira, Genentech, Teva, GlaxoSmithKline, Boehringer Ingelheim, Elsevier, and Neostem; has received grants from Amgen, Teva, Novartis, GlaxoSmithKline, Sanofi-Aventis, Vectura, Boehringer Ingelheim, MedImmune, Invion, and Pfizer; and owns stock in Sparo. A.-.M. Dyer has received a grant from the NHLBI. E. Israel has received personal fees from AstraZeneca, Novartis, Philips Respironics, Regeneron Pharmaceuticals, Campbell, Campbell, Edwards & Conroy, Crammer, Bishop & O'Brien, Fox Rothschild, Ryan Deluca LLP, TEVA Specialty Pharmaceuticals, UpToDate, Cowen & Co, Bird Rock Bio, Nuvelution Pharmaceuticals, and Vitaeris; has received a grant from Genentech and Sanofi; has received nonfinancial support from Boehringer Ingelheim, GlaxoSmithKline, Merck, Sunovion, and TEVA; and has received other compensation from Novartis, Research in Real Life, and TEVA Specialty Pharmaceuticals. R. J. Martin has received a grant from MedImmune; has received personal fees from Teva, AstraZeneca, and Genentech; and has received travel support from the Respiratory Effectiveness Group. D. T. Mauger has received a grant from the NHLBI and has received nonfinancial support from GlaxoSmithKline, Merck, Boehringer Ingelheim, Teva, and Sunovion. S. R. Rosenberg has received grants from AstraZeneca and Boehringer Ingelheim. T. Sharp-King has received a grant from the NHLBI and has received personal fees from Pearl Therapeutics and Insmed. S. R. White has received grants from the NIAID (U19-AI-095230) and AstraZeneca and has received personal fees from Marathon Pharmaceuticals. P. G. Woodruff has received personal fees from Genentech, Johnson & Johnson, Roche, and Neostem and has a patent pending related to asthma biomarkers with Genentech. P. C. Avila has received grants from the NIH/NHLBI, Genentech, AstraZeneca, and Novartis. L. C. Denlinger has received a grant from the NIH/NHLBI and has received personal fees from Novartis and GlaxoSmithKline. S. C. Lazarus has received a grant from the NIH/NHLBI and has received personal fees from Respiratory Disease Young Investigators' Research Forum. N. Lugogo has received a grant from the NIH. W. C. Moore has received a grant from the NHLBI. S. P. Peters has received a grant from the NIH/NHLBI. C. A. Sorkness has received grants from the NHLBI and the NIAID. M. E. Wechsler has received personal fees from Sepracor/Sunovion, Asthmatx/BSCI, Merck, Regeneron, MedImmune, Ambitbio, Vectura, Sanofi, Teva, Mylan, AstraZeneca, Genentech, Meda, Theravance, Novartis, Boehringer Ingelheim, GlaxoSmithKline, Tunitas, and Gliacure. S. E. Wenzel has received grants from Sanofi, Genentech, AstraZeneca, GlaxoSmithKline, and Boehringer Ingelheim and has received personal fees from AstraZeneca, Aerocrine, GlaxoSmithKline, Actelion, and Boehringer Ingelheim. H. A. Boushey has received grants from the NIH/NHBI and the NIH/NIAID and has received personal fees from the McGraw-Hill Companies. Y. J. Huang has received grants from the NHLBI (K23HL105572) and the Michigan Institute of Health and Clinical Research, has received travel and lodging compensation from the NIH, and has received payment for lectures from the American Academy of Allergy, Asthma & Immunology; the Massachusetts Institute of Technology; the European Respiratory Society; the Microbiome R&D Business Forum; and the European Academy of Allergy, Asthma, and Clinical Immunology. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication March 21, 2016; revised August 2, 2016; accepted for publication August 12, 2016.

Available online November 10, 2016.

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0091-6749/$36.00

http://dx.doi.org/10.1016/j.jaci.2016.08.055