Research team diagnoses asthma with nasal brush test

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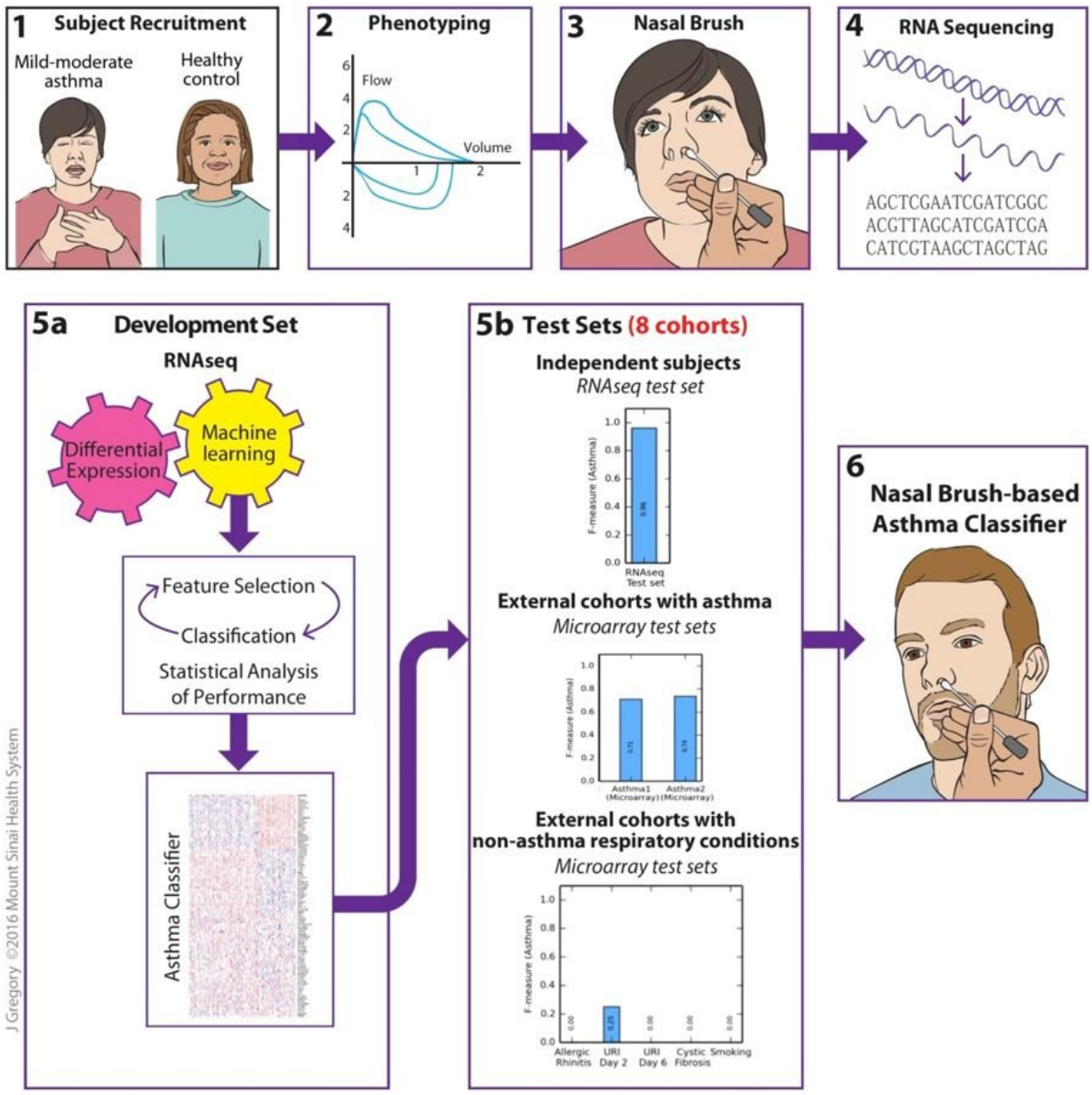

Study flow for the identification of a nasal brush-based classifier of asthma by machine learning analysis of RNAseq data. One hundred and ninety subjects with mild/moderate asthma and controls without asthma were recruited for phenotyping, nasal brushing, and RNA sequencing of nasal brushings. The RNAseq data generated were then a priori split into development and test sets. The development set was used for differential expression analysis and machine learning (involving feature selection, classification, and statistical analyses of classification performance) to identify an asthma classifier that can classify asthma from no asthma as accurately as possible. The asthma classifier was then evaluated on eight test sets, including (1) the RNAseq test set of independent subjects with and without asthma, (2) two external test sets of subjects with and without asthma with nasal gene expression profiled by microarray, and (3) five external test sets of subjects with non-asthma respiratory conditions (allergic rhinitis, upper respiratory infection, cystic fibrosis, and smoking) and nasal gene expression profiled by microarray. Figure drawn by Jill Gregory, Mount Sinai Health System, licensed under CC-BY-ND. Credit: Jill Gregory, Mount Sinai Health System, licensed under CC-BY-ND

Mount Sinai researchers have identified a genetic biomarker of asthma that can be tested for using a simple nasal brush and basic follow-up data analysis. This inexpensive diagnostic test can accurately identify mild to moderate asthma and differentiate it from other respiratory conditions such as allergic rhinitis, smoking, upper respiratory infection, and cystic fibrosis. The research team, led by a collaboration of clinical and computational scientists in the Department of Genetics and Genomic Sciences, the Icahn Institute for Genomics and Multiscale Biology, and the Department of Pediatrics at the Icahn School of Medicine at Mount Sinai, published their results in June 2018 in *Scientific Reports*.

"Mild to moderate asthma can be difficult to diagnose because symptoms change over time and can be complicated by other respiratory conditions," said Dr. Supinda Bunyavanich, physician and researcher at the Icahn School of Medicine. "Our nasal brush test takes seconds to

collect—for time-strapped clinicians, particularly primary care providers at the frontlines of asthma diagnosis, this could greatly improve patient outcomes through early and accurate diagnosis."

Currently, pulmonary function testing (PFT) is the most reliable diagnostic tool for asthma. However, access to the equipment and expertise needed to perform these tests is not always prevalent in primary care settings where asthma is frequently diagnosed and treated. It is also difficult to differentiate between asthma and other respiratory diseases using PFT alone, while the nasal brush and subsequent analysis for this asthma biomarker provides a binary result of asthma or not asthma.

Data scientists leading the study applied machine learning algorithms to the genetic (RNA) data acquired from nasal brushes of patients with and without asthma. This robust data collection, and machine learning analysis identified a 90-gene biomarker indicative of asthma status. "One of the most exciting components of this study is demonstrating the power of machine learning when applied to biomedical data," said Dr. Gaurav Pandey, who led data science efforts to develop the biomarker. "Collaborations between computational scientists and biomedical researchers and clinicians are advancing medicine at an inspiring pace—we have the power of insights we didn't have many of in the past and that opens a window to an entirely new world of diagnostic tools and treatments"

Similar genetic biomarker tests are currently being used in other disease areas, including MammaPrint and Oncotype DX, both used for certain types of breast cancer prognosis. In fact, the Oncotype DX tool was used in the largest clinical trial of personalized breast cancer prognosis ever conducted, demonstrating that mammography testing is unnecessary to diagnose breast cancer in a large fraction of breast cancer patients. The positive clinical impact biomarker tests such as this have shown indicate

great potential for further diagnostic tools based on biomarkers.

Dr. Bunyavanich says the next step to bringing this test into clinical practice is a study in a larger population of patients. "With prospective validation in large cohorts, our asthma biomarker could lead to the development of a minimally invasive test to aid asthma diagnosis at clinical frontlines where time and resources often preclude pulmonary function testing."

Asthma affects 10 percent of children and adults in the United States. When undiagnosed, it can lead to restricted activity, emergency room visits, and hospitalizations. "We're hopeful that further studies can help bring this test into primary care settings, transforming the ease and accuracy of diagnosing asthma and our ability as doctors to appropriately treat our patients," said Dr. Bunyavanich.

More information: Gaurav Pandey et al, A Nasal Brush-based Classifier of Asthma Identified by Machine Learning Analysis of Nasal RNA Sequence Data, *Scientific Reports* (2018). DOI: 10.1038/s41598-018-27189-4

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