Editorial

Epigenetics of asthma—the field continues to evolve

Deepa Rastogi

Children's National Hospital, George Washington University School of Medicine and Health Sciences, Washington, DC, USA

Correspondence to: Deepa Rastogi, MBBS, MS. Children's National Hospital, George Washington University School of Medicine and Health Sciences, 111 Michigan Ave NW, Washington, DC 20010, USA. Email: drastogi@childrensnational.org.

Comment on: Zhang T, Huang P, Qiu C. Progresses in epigenetic studies of asthma from the perspective of high-throughput analysis technologies: a narrative review. Ann Transl Med 2022;10:493.

Submitted Oct 11, 2022. Accepted for publication Oct 21, 2022.

doi: 10.21037/atm-22-5022

View this article at: https://dx.doi.org/10.21037/atm-22-5022

The rise of multifactorial diseases, that affect almost all organs of the body, have brought the interaction of genes and environment to the forefront (1). Progress in the field of genomics over the past two decades has improved access to deep sequencing that can be done at lower costs in shorter periods of time and can reveal extensive details regarding cellular function (2). While the analysis of genetic footprint via genome-wide association studies has identified a role of genetic susceptibility in multifactorial diseases (3), analysis of transcriptomic or genome-wide gene expression analysis has highlighted the importance of post-transcriptional modification of the genetic footprint in disease (4).

Dr. Conrad Waddington was the pioneer scientist who defined the field of epigenetics, coining the term as an explanation for variation in cellular programming in the setting of the same genetic footprint (5). Epigenetics has now evolved as a major area of research interest for multifactorial diseases, as a potential mechanism to explain the gene by environment interactions as well as inter-individual differences in cellular functioning (1). Biological mechanisms associated with epigenetic influences include DNA methylation, histone modification, including acetylation and methylation, chromatin remodeling and non-coding RNA (6).

The high disease burden of asthma across the lifespan and its intricate association with environmental exposures makes it a prime disease for investigation of the role of epigenetics in disease pathobiology (7). There are several studies that have investigated the contribution of epigenetics in asthma. In this journal, Zhang *et al.* summarize these studies in a narrative review (6). The authors are to be commended for the breadth of epigenetic mechanisms that they discuss in their review, with frequent inclusion of the downstream effects of the epigenetic marks on gene expression and function. Although the review includes studies conducted over two decades (August 2001 to August 2021), they emphasize analysis of those using high-throughput analysis, including epigenome-wide association studies (EWAS), chromatin immunoprecipitation with sequencing (CHIP-seq), and micro-RNA sequencing and delve into explaining these mechanisms in detail. They also discuss the importance of co-expression analysis using newer analytic tools. Their approach of classifying epigenetic marks as pre- and post-transcriptional also allow for a better understanding of the role of epigenetics in asthma (6).

While the review has many strengths, it is limited in its discussion of the biological relevance of the genes that have been identified to be influenced by epigenetic mechanisms in the context of asthma. A narrative review with the breadth as the current one is a prime approach to inform the reader of the relationship between the different genes, particularly between those identified in the studies included in the review. It is also important to elucidate any overlapping or redundant pathways that may be the target of epigenetic influences, since redundancy increases the likelihood of that pathway being relevant for the biological process. While the review addresses the differences between studies conducted among children and adults, it would have benefitted with inclusion of potential differences by race and/or ethnicity since there is clear evidence of the impact of differences in the genome on its modification by epigenetic mechanisms.

Notwithstanding these limitations, the review is an

important contribution to the field of the pathobiology of asthma. The field of oncology has incorporated investigation of the epigenetic footprint in phenotyping the patients and thereby incorporating it in endotyping of disease for precision medicine (8). This review by Zhang *et al.* highlights the breadth of investigation of epigenetics in asthma and identifies key genes that can be pursued for further investigation as biomarkers for asthma. Overlap of differential epigenetic marks with genomic footprint, as have been elucidated in EWAS studies, will further define the role of ancestry in asthma disease onset and burden (6,9). Incorporation of quantification of epigenetic marks on these genes and their downstream effects on cellular function will support their use as "biomarkers" for asthma (6,7).

Acknowledgments

Funding: This work was funded by National Institutes of Health, Bethesda, US (No. HL141849).

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Translational Medicine*. The article did not undergo external peer review.

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5022/coif). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Brookes E, Shi Y. Diverse epigenetic mechanisms of human disease. Annu Rev Genet 2014;48:237-68.
2. Lavelle TA, Feng X, Keisler M, et al. Cost-effectiveness of exome and genome sequencing for children with rare and undiagnosed conditions. Genet Med 2022;24:2415-7.
3. Raby BA. Asthma severity, nature or nurture: genetic determinants. Curr Opin Pediatr 2019;31:340-8.
4. Khodadadian A, Darzi S, Haghi-Daredeh S, et al. Genomics and Transcriptomics: The Powerful Technologies in Precision Medicine. Int J Gen Med 2020;13:627-40.
5. Noble D. Conrad Waddington and the origin of epigenetics. J Exp Biol 2015;218:816-8.
6. Zhang T, Huang P, Qiu C. Progresses in epigenetic studies of asthma from the perspective of high-throughput analysis technologies: a narrative review. Ann Transl Med 2022;10:493.
7. Sharma S, Yang IV, Schwartz DA. Epigenetic regulation of immune function in asthma. J Allergy Clin Immunol 2022;150:259-65.
8. Feng S, De Carvalho DD. Clinical advances in targeting epigenetics for cancer therapy. FEBS J 2022;289:1214-39.
9. Herrera-Luis E, Li A, Mak ACY, et al. Epigenome-wide association study of lung function in Latino children and youth with asthma. Clin Epigenetics 2022;14:9.

Cite this article as: Rastogi D. Epigenetics of asthma—the field continues to evolve. Ann Transl Med 2022;10(22):1190. doi: 10.21037/atm-22-5022

