Correspondence

Reply

To the Editor:

In our recent report we studied associations between early-life exposure to individual bacterial genera of the indoor microbiota and the development of asthma.[1] In a correspondence to this report, Fu et al[2] compliment our novel approach, but question some of the statistical choices made and ask for a new sensitivity analysis.

The vast richness of indoor dust microbiota highlights the need for data reduction. Therefore, instead of testing all potential genera against asthma, we used a 2-step approach. First, we performed a principal coordinate analysis to summarize the relative abundance weighted phylogenetic variance of all bacterial data available and then identified those 2 axes that were associated with asthma. In the second step, we identified bacterial genera using correlation analyses with these 2 axes. In this second step, we favored biological criterion over statistical criteria, which can naturally be questioned. We used a fairly relaxed criteria in the correlation analyses ($r > |0.4|$), but reduced the data to avoid multiple testing by omitting microbes with low population-level relative abundance, an approach that has been used previously by others.[3] This reduction is based on the assumption that environmental microbes with low abundance are biologically less likely to result in sufficient exposure to cause health effects.

In response to the correspondence by Fu et al,[2] we repeated the principal coordinate analysis–based approach. The second step of our analyses was performed without the mean relative abundance–based restriction, that is, including all 658 genera detected in the samples. In this sensitivity analysis, we identified 4 additional genera with mean abundance between 0.03 and 0.08 (Cellulomonas, Phycicoccus, unidentified genera within the C111 family (U.), and Cellvibrio) that were found to be inversely associated ($P < .1$) with the development of asthma, but not independently of each other.

In our original study, we also explored the possibility to create a sum variable of the 12 protective bacterial genera that we identified. Adding these 4 additional genera into the original sum variable did not change the sum variable's protective association with asthma, but the new variable explained slightly more of the association between bacterial richness and asthma than the original sum variable (82% vs 77% [calculated with the estimates from Table E4; explanation percentage (61%) that was mentioned in the text was unfortunately incorrect], respectively). Fu et al[2] also request for the names of the original 12 genera. They are listed in Fig E3 in the article's Online Repository at www.jacionline.org,[1] but we repeat them here: Sphingomonas, Janthinobacterium, Brevibacterium, other genus (O.) within the Dermabacteraceae family, Nocardioides, Nocardioidaceae U., Microbacteriaceae U., Microbacteriaceae O., Salinibacterium, Micrococcaceae U., Mycobacterium, and Chitinophagaceae U.

We thank Fu et al[2] for their insightful comments. We clearly need larger studies and new methodological work, when the aim is to identify individual, potentially very rare taxa that are strongly associated with asthma. An alternative strategy is to search for common characteristics across taxa. This strategy is supported by our earlier[4] and this current study, both of which concluded that communities of selected bacteria are more strongly linked to asthma protection than individual bacterial taxa.

Anne M. Karvonen, PhD[a]
Pirkka V. Kirjavainen, PhD[a,b]
Martin Täubel, PhD[a]
Juha Pekkanen, MD[a,c]

From [a]the Department of Health Security, Finnish Institute for Health and Welfare and [b]the Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland; and [c]the Department of Public Health, University of Helsinki, Helsinki, Finland. E-mail: anne.karvonen@thl.fi.

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Karvonen AM, Kirjavainen PV, Täubel M, Jayaprakash B, Adams RI, Sordillo JE, et al. Indoor bacterial microbiota and development of asthma by 10.5 years of age. J Allergy Clin Immunol 2019;144:1402-10.
2. Fu X, Yuan Q, Li Y, SunY. A novel strategy to identify asthma-associated microbial clusters. J Allergy Clin Immunol 2020;145:XXX-XXX.
3. Birzele LT, Depner M, Ege MJ, Engel M, Kublik S, Beranu C, et al. Environmental and mucosal microbiota and their role in childhood asthma. Allergy 2017;72:109-19.
4. Kirjavainen PV, Karvonen AM, Adams RI, Täubel M, Roponen M, Tuoresmäki P, et al. Farm-like indoor microbiota in non-farm homes protects children from asthma development. Nat Med 2019;25:1089-95.

https://doi.org/10.1016/j.jaci.2020.01.008