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**Michelle Trenkman, Ph.D.**

Senior Editor

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Dear Michelle,

Please consider our manuscript entitled “*Longitudinal profiling of the microbiome at four body sites reveals core stability and individualized dynamics during health and disease*” by Zhou *et.al.* as a research article for publication at *Nature*.

This is the first study to systematically examine microbiome-host interaction at four body sites in a cohort with extensive multi-omics and clinical phenotyping. Importantly, we follow the cohort for up to six years (over 3000 total microbiome samplings!). We discover:

- 1) The stability of the human microbiome varies among individuals and body sites.
- 2) The existence of highly individualized core microbial species that are more stable over time as well as those that vary.
- 3) Under periods of illness (*e.g.*, respiratory viral infection) and stress systemic changes occur across all four body sites and interesting microbial correlations are revealed.
- 4) At each of the four body sites, systematic interactions between the host and bacteria can be detected. These include important microbial interaction with lipids, and other molecules and clinical markers such as cytokines.
- 5) Individuals with insulin resistance have lower microbiome stability, a more diversified skin microbiome, and significantly altered host-microbiome interactions at several of the body sites (stool and skin), but not as much as others.

Overall, we believe that our discoveries will be of wide interest to Nature's readership.

In addition, we like to underline the cohort's full consent to the release of their data to the public. Consequently, our data, analysis methods, and conclusions serve as a valuable resource for many other investigations. The raw data and analysis are available on our data portal: <https://med.stanford.edu/ipop.html>. You have our assurance that all authors approved the submitted manuscript and disclosed any conflicts of interest. The paper will not be sent elsewhere for peer review until Nature's editorial office has made a final decision. We hope that you enjoy the manuscript as much as we do.

Sincerely,

Michael P. Snyder, Ph.D.

Stanford B. Ascherman Professor and Chair, Department of Genetics  
Director, Center for Genomics and Personalized Medicine