



Sexual Dimorphism in the Gut Microbiome: Microgenderome or Microsexome?

TO THE EDITOR: An emerging concept of “microgenderome” has been recently evoked by Yoon and Kim¹ in their comprehensive review on the role of sex hormones and gender in the gut microbiota. However, does this term really reflect sexual dimorphism in the microbiome or is it rather a misnomer? Should not the term “microsexome” be used instead? To the best of our knowledge, that renaming was originally proposed by Spencer Stubbs (unpublished communication). It is important to emphasize the differences between sex- and gender-related influences on the gut microbiota. Indeed, the term “microgenderome” has been coined to describe sex differences in bidirectional interactions between the microbiota, hormones, immunity and disease susceptibility.^{2,3} However, as recently stated by Vemuri et al,⁴ since gender is a social construct, and sex is a biological construct, the term “microgenderome” may not accurately reflect most of the factors driving the binary male or female differences in the microbiota determined by biological sex rather than gender.⁴

While gender is defined as the range of characteristics pertaining to and differentiating between masculinity and femininity, these characteristics include behaviors, sex-based social structures (ie, gender roles), or gender identity. However, in basic research, “gender” is commonly used to refer to the biological sex of animals. It should be emphasized that the main reason for that inconsistency and ambiguity of nomenclature is the interchangeable use of the terms “sex” and “gender” in basic science, which has been uncritically extrapolated into translational research and also human studies.⁵

Importantly, we cannot exclude that gender (not only sex) can also have impact on the microbiome. For example, gender norms and roles may influence factors such as diet, physical activity, antimicrobial exposure, and psychiatric comorbidity. Moreover, a large

body of evidence shows that the gut microbiota in return may affect behaviors and social functions confirming close interactions within the brain-gut-microbiota axis.^{6,7}

The term “microsexome” should be used preferentially in the context of the mainstream microbiome research addressing the characteristics related to biological sex and/or sex hormones. The sex bias present in numerous diseases is not entirely a host-intrinsic factor, since it may also be significantly reinforced by the commensal microbiota, as in the case of disorders of gut-brain interaction.^{2,8-10} Unravelling fundamental processes regulating sexual dimorphism in the host-microbiome bidirectional interactions should allow us to tailor prevention and treatment strategies in a sex-dependent manner as a step towards personalized medicine.

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