Trivial, interesting, or overselling? The microbiome and 'what it means to be human'

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Abstract

Discussions of microbiome research increasingly refer to the microbiome's impact on 'what it means to be human'. These claims are rarely carefully explained or justified. Given the increasing importance of microbiome research across the life sciences, philosophy and the public sphere, it is worth exercising more care in these discussions. This paper offers a guide for doing so. There are many different ways to interpret the details of ambiguous claims about the microbiome and 'what it means to be human'. I discuss some possible interpretations, and show how the resulting claims can range from trivial, to suggestive of interesting research, to controversial and overhyped. I recommend greater caution and clarity in ongoing discussions of microbiome research and its implications.

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1. Introduction: overselling the microbiome

Microbiome research analyzes the microbial communities living in host organisms or other environments. A problematic trend in scientific and media discussions of the field has been 'overselling the microbiome' (Eisen 2018) by overinflating claims about the human microbiome's causal role in various health and disease states (see also Cani 2018, Hooks et al. 2019). A related critical discussion targets the idea that whole microbiomes can even be causal entities in the first place (Lynch et al. 2019, 2020, Gomez-Lavin 2019, Lean 2019).

This paper turns a critical eye to a different sort of overselling the microbiome. This sort is more conceptual than empirical, but still problematic. To see the issue, consider the following claims:

> "The study of the microbiome… is beginning to call into question what it means to be 'human.'"
> — (Wischmeyer et al. 2016)

> "To fully understand what it means to be human, we need to embrace, explore and explain what microbes mean to us."
> — Gordon, quoted in (Nerlich and Hellsten 2009)

> "[The microbiome] has enormous implications for the sense of self."
> — Insel, quoted in (Smith 2015)

> "Growing understanding of the microbiome is changing what it means to be human."
> — (Redford et al. 2012)

> "The human microbiota is a fundamental component of what it means to be human."
> — (Relman 2015)

This sample is representative of dozens of similar claims being made in the microbiome literature and in philosophical and science media discussions. Most of these claims are made

in a single sentence without further development or defense, often as a catchy opening line (exceptions include Gligorov et al. 2013, Rees et al. 2018a, Ironstone 2019). These claims (and others) share a common theme, which I'll summarize as follows:

> **The microbiome-humanity claim:** The microbiome profoundly affects what it means to be human.

At face value, microbiome-humanity claims appear to be getting at something important, signaling the magnitude of the field's impact. The problem with these claims is that they are ambiguous. The phrase 'what it means to be human' could refer to myriad different ideas (see Section 2), and there are a range of different ways to characterize 'the microbiome' (see Section 3).[1] Ambiguous claims like this are hard to take very seriously, let alone engage with productively. Without further clarification, they (perhaps counterintuitively) lack substance precisely because of the rich range of things they might refer to. Given the scientific importance of microbiome research and its increasing focus in philosophical discussions (O'Malley and Parke 2020), these discussions would benefit from less ambiguity and more clarity. People should stop making microbiome-humanity claims, and should instead address the underlying concerns with more conceptual rigor. This paper offers some guidance for doing so.

Why is this sort of conceptual clarity important? Let's look back in recent history to another case where impactful scientific discoveries sparked a profusion of similar claims. Especially in the early days of genomics research, it was common to hear sweeping statements about the

[1] 'Profoundly affects' is also ambiguous: it suggests some sort of causal relationship without specifying the details. The nature and validity of causal claims about microbiomes is an important issue, but it is not my focus here (see Lynch et al. 2019, 2020, Attah et al. 2020, Klassen 2020, Oftedal 2020, Schneider 2020b).

human genome. Consider a claim like ‘the human genome profoundly affects who we are’. At a first pass this sounds important and true. But this ambiguous claim could be intended, and interpreted, in various ways. Someone saying this might really have in mind something trivial: ‘the human genome [namely, some coding regions of it] affects who we are [namely, some aspects of our phenotypes]’. This is true, but it is a boring claim. Of course coding regions of the genome affect our phenotypes. On the other hand, someone might have a more particular claim in mind: ‘The human genome [a specific portion of it, to be determined] affects who we are [in the sense of where we are on the introvert/extrovert spectrum]’. This postulated causal relationship sounds like grounds for a potentially interesting, if tricky, research question. And here is yet another version of the claim: ‘The human genome [in its entirety] affects [i.e., determines] who we are [every aspect of our phenotypes and personalities]’. This claim, unlike the previous two versions, is extremely strong and—as we now know, despite having heard such claims in the past—patently false. The lesson here is that, depending on how we fill in the blanks, an attention-grabbing but ambiguous claim can actually turn out to be trivial, interesting, or overhyped and problematic.

Let’s see how microbiome-humanity claims fare once we fill in the blanks. First, a note about terminology: while most microbiome-humanity claims refer to the microbiome’s impact on ‘what it means to be human’, they occasionally invoke the human ‘self’ (e.g., Kundu et al. 2017, Rees et al. 2018a). There is no clear difference in how most people use these terms in this context, and some use them interchangeably (e.g., Rees et al. 2018a, Ironstone 2019). For consistency’s sake, I will stick to ‘what it means to be human’ here.

2. What does 'what it means to be human' mean?

The phrase 'what it means to be human' covers a vast range of issues, calling to mind many important ideas. Because of this, that phrase is ambiguous: in and of itself (without further explanation) it does not clearly communicate much at all. Its possible interpretations span the subject matter of biology, psychology, anthropology, philosophy, the social sciences and humanities. These interpretations range from characterizing the human genome (Pääbo 2001), to uniquely human cognition (MacLean 2016), to human nature (Downes and Machery 2013), to how we tie our identity and sense of self to social groups (Stets and Burke 2000)—and that is merely a sample. My aim here is not to survey all of these interpretations, nor is it to endorse any particular understanding of 'what it means to be human'.

Rather, I will draw attention to nine particular issues that claims about the microbiome affecting 'what it means to be human' appear to be really concerned with: our bodies' material composition, genetic composition, and development and ongoing functioning; our individuality; our immune systems; our brains, behaviors and mental states; what is special about us humans; agency or free will; and personal identity. These draw primarily on recent microbiome discussions in biology and philosophy of biology; other disciplines might well have further aspects of 'what it means to be human' to add to this list. Thus, these nine are a sample and a starting point for filling in the blanks, and clarifying the conceptual landscape of microbiome-humanity claims.

Three straightforward aspects of 'what it means to be human' concern the microbiome's role in the form and functioning of our bodies. First of all, the microbiome affects our bodies' material composition, in the most basic sense of what we are 'made of'. At some point in the

past we thought that all of the cells in our bodies were *Homo sapiens* cells. We now know that many of them are actually microbes, living in our guts, on our skin, and virtually everywhere else. Some estimates point to 10 times as many microbial cells as human cells in our bodies (Backhed 2005, Cani 2018); others put that ratio closer to 1:1 (Sender et al. 2016). In any case, a substantial proportion of 'our' cells are microbes.

The same point can be made about genes. At some point we thought that all of the genes in our bodies were human genes; we now know that a lot of them are microbial. Our resident microbes' genomes are part of our bodies' total genetic makeup, even though they are not part of the chromosomes we acquired from our parents at fertilization. Some microbiome-humanity claims have this interpretation in mind: "[The microbiome] has enormous implications for the sense of self. We are, at least from the standpoint of DNA, more microbial than human" (Insel, quoted in Smith 2015).

Our resident microbes can be thought of as a 'second hereditary system' (Pradeu 2011, Gilbert et al. 2012): we acquire them through both vertical and horizontal transmission, from our parent(s) during and after birth, and from our environments. A third way to think about microbial impacts on 'what it means to be human' involves our inherited microbes' pivotal roles, alongside our inherited genes, in the development and ongoing functioning of our bodies. Microbes, especially bacteria, appear to be crucial not only for the functioning of their animal hosts' digestion and other bodily systems, but also the very development of key body parts, including various organs, tissues and immune systems (Pradeu 2011, Gilbert 2019).

These three empirical insights about how microbes affect the form and functioning of our bodies are important in themselves. They are also foundational for a range of further, less strictly biological concerns about microbiome impacts on aspects of 'what it means to be human'.

One of these further substantial issues is individuality. Our relationships with microbes influence how we think about the boundaries separating us from the rest of the world, or about what sorts of cohesive biological units we are. Microbiome insights might motivate us to re-examine our views on what sorts of individuals we are, when combined with a view about how to identify and differentiate individuals. Relevant criteria here include evolutionary, physiological, or immunological mechanisms (Pradeu 2016a). Some discussions surrounding microbiome-humanity claims have this sense of 'what it means to be human' in mind, among others (e.g., Ma et al. 2018).

Individuality is a hot topic of debate in philosophy of biology (Clarke 2010, Bouchard and Huneman 2013, Pradeu 2016a, 2016b), and developing a clear individuality-based interpretation of microbiome-humanity claims would require significant further nuance. The division between evolutionary and physiological individuality in a helpful starting point. We could ask: do we plus our microbes together constitute a single unit of selection, or evolutionary individual? This is debated. Some say that we need to rethink individuality, including evolutionary individuality, in light of the microbiome (Gilbert et al. 2012). Others argue against the plausibility of entire microbiomes co-evolving with their hosts (Douglas and Werren 2016). On the other hand, we could ask a different question, about physiological individuality: do we plus our microbes together constitute a single living agent, united by properties and functions such as a cohesive metabolic cycle or division of labor in service of

a unified whole (see Godfrey-Smith 2009)? While an affirmative answer would need further justification, the fact that we are physiologically unified with at least some of our microbes is at face value more plausible than the evolutionary individuality claim, especially in light of our increasing knowledge of the microbiome's critical role in our bodies' development and ongoing functioning (see Pradeu 2011, Gilbert et al. 2012).

Another aspect of 'what it means to be human' zooms in on microbes' role in the development and functioning of our immune systems. Though the details are still unfolding, this role is clearly important (Thaiss et al. 2016). In light of this, Tobias Rees and colleagues (2018a) argue that we need to rethink 'the human self'. In particular, what we consider to be a key aspect of keeping 'self' in and 'non-self' out (our immune system) is actually mediated by something that we consider to be paradigm non-self (other species, specifically microbes). Here, in contrast to other instances of microbiome-humanity claims (in Rees et al. 2018a and elsewhere), the meaning of 'self' is reasonably straightforward: 'self' is whatever the immune system keeps in, 'non-self' is whatever it keeps out (Pradeu 2011, Morar and Bohannan 2019, Schneider 2020a). But it is quite easy to slide from this restricted sense of 'self' to much looser senses (e.g., Tauber 2012, Rees et al. 2018a).

Yet another aspect of 'what it means to be human' regards our brains, behaviors and mental states. We have known for a long time that microscopic creatures can affect their hosts' behaviors. Famous examples include the rabies virus and *Dicrocoelium dendriticum*, the parasitic flatworm that takes over ants' brains (Carney 1969). Recent work suggests that our own resident microbes influence our brain development, neurotransmitters, behaviors, moods and psychiatric states via the gut-brain axis, a line of communication involving the central nervous system (Sampson and Mazmanian 2015, Hooks et al. 2018, Johnson and Foster

2018, Valles-Colomer et al. 2019). The microbiome-humanity concern here seems to be that if our brains and cognitive states are not genuinely under 'our' control, then we need to rethink who we are (Rees et al. 2018a, Ironstone 2019; see also Schneider and Winslow 2014).

Some discussions suggest that the microbiome should affect our sense of what is special about us humans (Gligorov et al. 2013). This could be thought of in terms of how exactly we understand the criteria for human species identity (see Newman 2017 for interesting discussion of how scientific advances can affect this understanding on genetic and developmental grounds). Or, it could be thought of along the lines of our status in the living world, viewed through an anthropocentric lens, as especially complex beings made of a body and a mind (Rees et al. 2018a). In either case, this take on 'what it means to be human' underlines the idea that humans are center-stage only if our microbes share the spotlight[2] (Schneider and Winslow 2014, p. 221). In other words, we would not be who we are if it were not for our microbes. So discussions of 'who we are as humans', however understood, are remiss if they do not bring our microbes into the picture. The challenge is to show precisely what this means and why it matters, above and beyond pointing to the first three biological insights discussed above, namely the facts of microbial contribution to our bodies' cellular and genetic makeup, development, and ongoing functioning.

Another more philosophical concern is our agency or free will. This regards the extent to which we have genuine control over our own actions. Some authors go so far as to claim that in light of the microbiome, "'we' are not what we imagined ourselves to be… We are not autonomous individuals" (Ironstone 2019, p. 331). These claims build on microbiome

[2] Thanks to Maureen O'Malley for this point.

findings pertaining primarily to several biological aspects of 'what it means to be human' discussed above: microbial influence on our bodies' material and genetic composition, development and ongoing functioning, and especially our brains and behaviors. The concern is that if our microbes at least partially control some of our cognitive states, then perhaps our agency or free will is an illusion. Again, the challenge is to show why this deeper philosophical concern follows from empirical findings about microbes playing some presumed causal role in a limited set of cognitive states. As far as I am aware, nobody has carefully filled in this inference.

The last sense of 'what it means to be human' on our list regards personal identity: our beliefs about our physical or psychological identity as persons over time. This could be thought of in terms of our first-person experience of self-identity or self-conception (Gligorov et al. 2013), or in terms of generic third-person criteria for distinguishing the continuity of persons over time (this philosophical debate goes back centuries; for an overview see Olson 2019). A version of the microbiome-humanity claim focusing just on physical personal identity over time might just collapse into issues discussed earlier, about our bodies' material or genetic composition. But at least some discussions surrounding microbiome-humanity claims have in mind the broader philosophical spectrum of ideas about personal identity (Gligorov et al. 2013, Ma et al. 2018).

3. What does 'the microbiome' mean?

'What it means to be human' is not the only ambiguous part of microbiome-humanity claims. There are also different ways to fill in the blanks on the 'microbiome' side. As we will see

below, different microbiome characterizations can affect the scope and coherence of microbiome-humanity claims.

Returning to the five representative microbiome-humanity claims from Section 1, some appear to have in mind microbiome research as a whole: all of our study and understanding of the microbiome. But perhaps what these authors really have in mind are particular findings, insights or trends in microbiome research. If so, then identifying the relevant findings, insights or trends could help make microbiome-humanity claims more concrete and plausible. In contrast, some other representative claims apparently have in mind the microbiome itself affecting what it means to be human. In this case, we can ask: 'the microbiome' on what characterization?

Recent collaborative work by biologists and philosophers highlights a whole range of ways to conceptualize and characterize microbiomes. Nicolae Morar and Brendan Bohannan (2019) identify five different ways in which people conceptualize the human microbiome as an entity in relation to its host. The first three are conceptualizing the microbiome (1) as one of our many *organs*, (2) in terms of our *self/non-self* discrimination mechanisms, or (3) as our cohabitants in an *ecosystem*. The other two are conceptualizing us plus our microbes as (4) a functionally or evolutionarily integrated *superorganism*, or (5) a *holobiont*, which is closely related to the superorganism concept but often emphasizes the inclusive genetic profile (hologenome) and relaxes membership criteria.

Kate Lynch and colleagues (2019) discuss four ways to characterize microbiomes as bases for causal claims about health and disease: (1) *compositionally*, in terms of constituent microbial taxa and their relative proportions; (2) *functionally*, in terms of metabolic and other

biochemical pathways; (3) *outcome-oriented*, where the microbiome's state is characterized in terms of the host state; and (4) in terms of a *causal core*, where 'the microbiome' does not refer to all of a host's microbiota, but instead to some core group of microbes (distinguished compositionally, functionally, or both) thought to play a causal role in a host state of interest.

Together these accounts give us nine ways to characterize microbiomes, which are combined in all sorts of ways in the literature. Not all of these nine options will affect the meaning of microbiome-humanity claims. But some of them will. For example, many discussions of holobionts take for granted that holobionts are units of selection (e.g., Rosenberg and Zilber-Rosenberg 2018, Morar and Bohannan 2019, but cf. Skillings 2016, Doolittle and Booth 2017). So, if someone adopts a holobiont microbiome concept, especially in its 'hologenome' version, she is typically taking a stand on who we are as individuals in a specifically evolutionary sense. On the other hand, if someone uses the term 'the microbiome' as shorthand for a causal core (Lynch et al. 2019), she has in mind a particular functional or taxonomic subset of our microbes. In this case, assuming the referent of the causal core characterization is made explicit, any further claim she makes about 'microbiome' effects should be easier to assess empirically because it refers to something more specific than literally all of our microbes (Surana and Kasper 2017, Lynch et al. 2019). Finally, if someone endorses a superorganism microbiome concept (Morar and Bohannan 2019) it does not make sense to worry that, in light of findings about the gut-brain axis, our brains and behaviors might not be fully under 'our' control. This is because 'our', in this case, just refers to a composite entity of a host plus its microbes. On the other hand, if we regard the microbiome as our cohabitants in a host-microbe ecosystem, these concerns are at least coherent.

Stepping back, we have three ways to interpret the 'microbiome' part of microbiome-humanity claims: in reference to all of microbiome research, particular insights or findings in microbiome research, or the microbiome itself (on one or more of at least nine possible understandings). Combined with the nine aspects 'what it means to be human' discussed in Section 2, this apparently leaves us with 27 different ways to fill in the blanks of microbiome-humanity claims, represented as follows:

(1) 'The microbiome'	**…profoundly affects …**	**(2) 'what it means to be human'**
(1a) All of microbiome research		(2a) Our bodies' material composition
(1b) Particular insights or findings		(2b) Our bodies' genetic composition
(1c) The microbiome itself		(2c) Our bodies' development and functioning
		(2d) Individuality
		(2e) Our immune systems
		(2f) Our brains, behaviors and mental states
		(2g) What is special about us humans
		(2h) Agency or free will
		(2i) Personal identity

Of course, there are way more than 27 options, because there will be variations on each version. Each of (1a–c) and (2a–i) represent a family of interpretations, rather than a single clearly specified idea. In the vast majority of cases where someone has made a microbiome-humanity claim in writing, it is unclear which of these interpretations they have in mind, and some authors appear to be making a number of these different claims all at once (Rees et al. 2018a, Ironstone 2019).

4. Microbiome-humanity claims: trivial, interesting, or overselling?

Recall the appealing but ambiguous genomics claim example from Section 1. The same issues hold for microbiome-humanity claims. To see how, we can use the framework from Section 3 to fill in the blanks in three examples.

As a first example, someone might have in mind that *(1b) particular findings quantifying the microbes living in and on our bodies affect (2a) our understanding of our bodies' material composition*. Of all possible interpretations of the microbiome-humanity claim, this one is the most superficial: its justification requires no conceptual work. Assuming you understand and accept the empirical insight about microbial cell counts, it is tautological to say that this affects our understanding of the material composition of our bodies.

However, the finding that microbes constitute a significant proportion of our bodies is, in itself, far from trivial. It is the basis for substantial further concerns, including at least a few discussed above: the nature of individuality, personal identity, agency and free will, and what is special about us humans. What is missing from most present discussions of microbiome-humanity claims is a clear chain of reasoning linking the insight about the material composition of our bodies to these further, more philosophical concerns.

A second, different specific claim would be that *(1c) the microbiome itself affects (2f) our brains, behaviors and mental states*. This version of the claim is not at all trivial; it refers to a fascinating set of open research questions (Sampson and Mazmanian 2015, Johnson and Foster 2018, Hooks et al. 2019). Of course, in order to specify a clear and interesting research question, we need to fill in the details and point to a more particular aspect of our brains, behaviors or mental states, such as memory (Magnusson et al. 2015) or depression (Valles-Colomer et al. 2019).

A third, again quite different claim would be that *(1c) the very existence of all these inevitable microbes living in and on us affects (2i) our agency or free will*. This claim is neither trivial nor suggestive of a clear empirical research question. And it is not immediately

plausible philosophically. The concepts of agency and free will are complicated, controversial, and themselves open to different interpretations (Bayne 2017, Schlosser 2019). Such an argument would need to clarify the precise notion of agency or free will at stake, and justify why that notion is undermined by the fact that a lot of our body is microbial. Some authors have this interpretation of the microbiome-humanity claim in mind, among others (Rees et al. 2018a, Ironstone 2019). But barring further detailed justificatory work, this version of the microbiome-humanity claim is overselling the microbiome.

These three examples illustrate how microbiome-humanity claims, which might have appeared to be relatively innocuous hype at the outset, could be filled in and interpreted in many ways. When someone says 'the microbiome profoundly affects what it means to be human', she might actually be saying something trivial, or suggesting an interesting line of research, or conceptually overselling the microbiome.

5. Conclusion

We should resist the temptation to make attention-grabbing but ultimately uninterpretable statements about the microbiome and 'what it means to be human' or 'the self'. A few authors have set a good example for this, avoiding ambiguous microbiome-humanity claims and instead developing positions about microbiome effects on our understanding of particular issues such as individuality (e.g., Pradeu 2011, Gilbert et al. 2012, McShane 2014).

Debates about the microbiome's impact increasingly span the life sciences, humanities and social sciences. This cross-disciplinarity underlines the need for clear communication (Parke et al. 2018, Rees et al. 2018b). Furthermore, unlike some other issues at the interface of

science and philosophy which are largely internal to academia, this one has real implications for public understanding of science. Imaginations can really run wild with big ambiguous claims about 'what it means to be human', and this can undermine clear translation of scientific findings into the public sphere. The things we are learning every day about microbes and how they affect aspects of our physical and perhaps even mental lives are fascinating enough. They do not need overselling.

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