Human oral microbiome cannot predict Pleistocene starch dietary level, and dietary glucose consumption is not essential for brain growth

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Fellows Yates et al. (1) find amylase-binding bacteria in Late Pleistocene Neandertals and *Homo sapiens* dental calculus and project a starch-rich diet early and throughout human evolution and an essential role for starch in brain expansion. We recently argued for the need to use more paleobiological-type evidence to reconstruct past trophic levels (2), so welcome the evidence they present as a valuable contribution.

While groundbreaking in many respects, we fail to see how Fellows Yates et al.'s results support some of their critical conclusions concerning the role of high starch consumption in *Homo* evolution. Our main contention is with the attempt to tie a "core" Late-Terminal Pleistocene microbiome with regular high-starch consumption over the previous two million years of *Homo* evolution. We also question their assertion that high starch consumption was a necessary condition for brain expansion.

A switch from fruit-sourced sucrose to starch consumption must have started 7 to 5 Ma with hominins' appearance (3). The early evolution of the genus *Homo*, at least from 2.0 Ma, is more conspicuously associated with archaeological evidence for the addition of scavenging and carnivory to the hominins' suit of behaviors (4).

For argument's sake, we accept that AMY1 multicopy copy numbers indicate adaptation to starch consumption (but see ref. 3). In that case, however, one cannot ignore the (so far) uncontested conclusion that the appearance of more than two copies of AMY1 in the *Homo* genome postdates the split with Neandertals 765 to 550 ka (5). This means that saliva-sourced α-amylase substrate would have been limited in pre-*H. sapiens Homo* species to the same level as in the "noncore" chimpanzee, which also has two copies of AMY1.

Moreover, even if α-amylase–dependent bacteria were present in early *Homo*, the authors do not supply any evidence for a minimum level of starch consumption that would have maintained the "core microbiome" throughout human evolution. On the contrary, the authors find high consistency of oral microbiome in present-day *Homo*, "regardless of . . . diet." This nonassociation with diet may mean that the core microbiome could have also been maintained with a low-starch consumption.

Regarding their claim for the obligatory association of high starch with brain expansion, we will mention that circumpolar native groups have been living for generations with large brains on a negligible supply of carbohydrates, and epileptic children grow a perfect-size brain on a very low-carbohydrate ketogenic diet (6). Humans can generate glucose both from protein and triglycerides in a process called gluconeogenesis to the tune of more than 35% of their daily energetic requirements (7), far exceeding the brain's requirements, typically only 20% of the daily energy needs. Additionally, fat-sourced ketones can substitute a large part of glucose as brain fuel. Humans are exceptionally adapted to synthesizing ketones from fats (2). Ketones are the default source of energy in babies (8).

Thus, while arguably *Homo* species did consume starch throughout their evolution (9), we do not find support in the present findings for regular high-starch consumption or the necessity for high-starch diets for the expansion of the human brain.

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