GENOME WATCH

A new piece in the microbiome puzzle

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This month's Genome Watch discusses the detailed analysis of the human 'archaeome' from various body sites and highlights how current sequencing methods underestimate archaeal diversity and abundance.

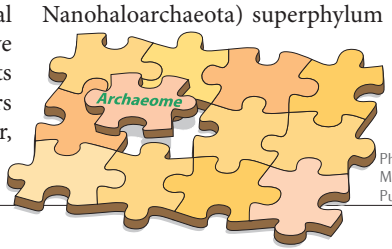
The human microbiome is inextricably linked with our health as well as disease states and conditions. The bacterial component of the human microbiota has been the main focal point of study owing to its abundance, although studies of viruses, fungi and microscopic eukaryotes and archaea are increasing. Archaea specifically are reported to occur in most individuals and may represent in excess of 10% of the anaerobic microorganisms in the large intestine. Methanoarchaea are hypothesized to be 'keystone species' in metabolic processes in the gut. In addition, associations between the presence of certain archaea and conditions such as irritable bowel disease have been noted. Despite this importance, only limited research has focused on the role of archaea, possibly due to the absence of known archaeal pathogens or the poor recovery of archaeal species in microbiome studies.

In their recent paper, Koskinen et al.[1] report that specific archaeal communities are associated with different sites in the human body. Previously, studies of archaea in humans have typically been limited to what is recovered from 'universal' 16S rRNA profiling, designed to target broad ranges of bacteria and some archaea. Koskinen et al. demonstrate that the universal primers are inefficient in recovering archaea from the human microbiome. The universal primers only detected a single archaeal operational taxonomic unit (OTU) in a human stool sample, whereas archaeal 16S rRNA-specific primers detected higher numbers and more diverse archaeal OTUs. A study of the gut archaeome of five great ape species[2] reported similar results when comparing the same universal primers against archaeal-specific primers. Moreover, Raymann et al. reported a progressive reduction in archaeal diversity between more distantly related apes and humans[2], a finding that was also previously described for the bacterial component of the human microbiome. These data further suggest that archaeal diversity and prevalence in humans may have been underestimated to date.

To accurately assess the archaeal component of the gastrointestinal tract (GIT), nose, lung and skin microbiome, Koskinen et al. analysed the sequences resulting from amplification with archaeal-specific primers. Conventional analysis with the Mothur and Qiime software packages produced 400–600 archaeal OTUs. In contrast, application of the more stringent DADA2 software detected only 10–20 OTUs. DADA2 (REF. 3) differs from traditional OTU clustering by modelling and correcting Illumina amplicon errors and then using the corrected sequences to detect ribosomal sequence variants. Using this approach, the authors discovered a biogeographical landscape, with the skin and GIT being characterized by distinct archaeal phyla and the nose sharing phyla with both these communities. Notably, a similar distribution of bacterial communities was reported by the Human Microbiome Project[4]. Furthermore, spatial distributions of archaea have been reported in several other environments, often linked to microclimate, including elevation on Mount Fuji[5] and oil pollution in Sundarbans mangroves[6].

The optimized approach used by Koskinen et al. identified the presence of archaeal species that were not previously thought to be associated with humans. For example, Woesearcheota, a member of the DPANN (Diapherotrites, Parvarchaeota, Aenigmarchaeota, Nanoarchaeota and Nanohaloarchaeota) superphylum typically associated with soil, was found in the lung environment. The *Methanobacterium* genus, also a member of the DPANN superphylum that is typically associated with anaerobic digesters, was identified in biopsies of the ileum and left colon. These observations suggest that archaea may contribute to the human microbiome in currently unknown ways.

In summary, studies using tailored approaches to specifically study archaea have uncovered the vast diversity and abundance of archaea in the human microbiota and discovered previously unseen similarities between archaea and bacteria, including distinct biogeographical communities and higher diversity in more evolutionarily ancient apes compared with humans. Future studies using unbiased shotgun metagenomic or specific archaea-targeting methods are important to elucidate the role of archaea in the human microbiome and additional similarities or differences with the bacterial component of the human microbiome.



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Competing interests statement
The authors declare no competing interests.