

Challenges in studying the microbiome

Although the microbiome is an exciting and rapidly emerging area, there are a number of important challenges faced by researchers. Applicants should consider these carefully when designing experiments and ensure these have been recognised and minimised as far as possible:

Correlation vs causation - The literature to date has been dominated by associative studies. These often show that people with disease X have different microbiomes to people without disease X, but the challenge lies in distinguishing which of these differences are (a) simply secondary to the disease state itself; (b) those which are secondary effects related to the risk factors that contribute to disease X (though not mediating the risk factor effect on disease) (c) those which are actually causal for disease. The first two are interesting phenomenological discoveries, but only the third has clinical potential.

Functionality - Whilst a list of what organisms make up a microbiome is potentially useful and biologically important as a frame of reference, there is a need to understand their functionality; how human diet and lifestyles (including stress and medications) impact on microbial communities, and how any changes (links between underlying mechanisms and development of disease) then affect the health of the host. Given the metabolic interdependence of some bacteria, an understanding of the interactions among microbes may prove to be important when considering relationship with disease.

In addition, a key issue is the determination of the role and importance of both abundant organisms and also rarer species.

Microbiome diversity - Healthy humans carry a remarkable diversity of organisms. Each person has a relatively different microbiome, reinforcing the notion that there is no single "healthy" microbiome profile and that each host has a unique biological relationship with its microbiota. An additional complication is the fact that differences in the microbiome exist across age, cultures and geography.

Sampling - sampling strategies (storage, timing, frequency and location/site) may be critical in studies trying to prove a link between changes in the microbiome and the development of disease.

- Rapid isolation and the appropriate storage of biological samples is important to ensure their quality and integrity
- Temporal colonisation and the fact that exposure changes with time is a significant research challenge
- The body harbours a number of unique habitats each with its own distinct microbial populations making it extremely difficult to determine how many discrete microbiomes occupy a bodily site. The use of faecal samples, for example, will not provide an accurate picture of the molecular interactions within the microbial ecosystems occupying specific niches in the gut.

Animal experiments – there may be issues of generalisability due to variable factors such as genetic background, how the animals are maintained, sterility of the environment, diet etc.

Data deluge - next generation 'omics' technologies are now well established and able to describe the microbiome at a detailed genetic and functional (transcriptomic, proteomic and metabolic) level. In turn this has led to the generation of vast data sets. Therefore, there is a need to ensure that adequate expertise and infrastructure is in place to meet the challenge of collecting, storing and analysing the data generated as well as a robust and reliable context or framework for interpreting the data.

References

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