

## MRC guidance for applicants submitting proposals relating to the microbiome

This is an important emerging area and the Medical Research Council is keen to support robust studies which clearly distinguish between correlation and causation by focusing on the elucidation of the role of the microbiome in disease aetiology – including biological mechanisms, the interplay between microbe/microbe and microbe/host, and the influence of intrinsic and extrinsic factors.

In particular, there is a need for well-controlled, rigorous studies which:

- Employ a stable background (whether in mice or humans) for whatever is measured
- Control for the influence of host genetics on the architecture of the microbiome
- Have robust health outcomes
- Undertake measurements in a meaningful way with appropriate power
- Design interventions which will inform disease mechanism

Parallel studies including approaches in rodent model systems may be required to establish causal capability and to uncover exact mechanisms leading to disease.

### Minimum requirements when submitting a proposal

- Evidence that the trait or disease in question is important and there is sufficient preliminary evidence for the involvement of the microbiome
- Given the large amount of research activity on this topic internationally, a concise description of why the study is unique and filling a niche
- Multidisciplinary approach from the outset to provide well-constructed proposals (e.g. linking clinicians with a knowledge of the disease, epidemiologists and population health scientists with microbiologists - including expertise in microbial ecology, immunologists, modellers, statisticians and bioinformaticians)
- Evidence that you are aware of the challenges in studying the microbiome and have minimised these as far as possible
- Robust experimental design to cope with inter-subject variability and minimise sampling issues
- Clear rationale for the utilisation of a particular cohort and the inclusion of sufficient information to justify its suitability for the proposed study
- Availability of/access to appropriate samples in sufficient numbers
- Appropriate expertise is in place for data handling, data/statistical analyses
- Clear delineation of work flow, time frame and potential translation for multi-faceted or phased applications

### Other considerations:

Boards will scrutinise very carefully the funding requests for the collection of new samples as to value for money, and competitiveness in terms of timing, and will favour studies using existing cohorts, collections and data-sets. However, it is recognised that new sample collection will be necessary when existing cohorts either do not offer suitable samples or do not have a sufficient number of samples available. Applicants wishing to establish a new cohort or longitudinal study to include the monitoring of the microbiota in relation to health and disease, or to include additional sample collection for existing cohorts and biobanks should discuss their proposals with the appropriate MRC Programme Manager in the first instance.

Applications from national/international groupings should specifically address the issue of overlap with other relevant national/international collaborations to ensure minimal duplication of effort.

It is expected that applicants will utilise existing infrastructure for sequencing, metabolomics etc. (such as MRC's high-throughput sequencing hubs, MRC-NIHR National Phenome Centre) rather than request additional equipment for the proposed work.