MICROBIOTA
Improve treatment responses by manipulating the composition and status of the microbiota

CONTEXT

It is increasingly clear that the human microbiota contributes to cancer incidence in many direct and indirect ways. Microbes have been shown to influence cancer initiation and/or development via diverse mechanisms including the induction of DNA damage, modulation of inflammation and alteration of the metabolic equilibria. Studies have also shown that microbiota can affect the host response to cancer therapies, although the mechanisms underlying this relationship (particularly outside the gut) remain relatively poorly understood.

There is an opportunity to expand on preclinical and clinical studies that have shown an association between microbiota and treatment response to further understand the behaviour, composition and status of the human flora, and identify and validate ways in which microbiota can be exploited to maximise the efficacy of cancer therapy in individual cancer patients.

OPPORTUNITIES AND BARRIERS

Microbiology and cancer biology must combine productively and creatively if we are to understand further the mechanistic basis of the relationship between cancer therapy and host microbiota. This challenge is likely to involve multidisciplinary teams with expertise in microbiology, physiology, pharmacology, synthetic biology, and perhaps theoretical modelling to uncover and exploit links between the microbiota and its response to treatment.

This Grand Challenge calls for bold approaches that build on our current knowledge base in new and unexpected ways. Examples of the types of questions that could be addressed in this challenge include (but are not limited to):

- Can we develop preclinical systems that accurately model the mechanistic settings in which microbiota can be used to drive or modulate clinically valuable therapies?

- Can we develop methods to manipulate the composition and status of the microbiota based on further insights into the mechanisms mediating therapeutic response?

- Can drugs be synthesised, modified, or enhanced by the human flora that are more efficacious than current cancer therapies?

- Can we learn to use microbiota as therapeutic agents or modulators for cancers outside the gut, skin, or other easily accessible tissues?

VISION AND IMPACT

This Grand Challenge seeks to expand our mechanistic understanding of how the presence and status of human microbiota influences the response to cancer therapy. It is hoped that funding of this scale will inspire teams to propose ambitious and novel approaches that will provide new insights into how the microbiota can be manipulated, and that this knowledge can be translated into clinical interventions for individual patients.