# An Exclusive Interview With...

**Mike Romanos**
Co-founder and CEO
**Microbiotica**

Mike Romanos is a molecular biologist/entrepreneur and Chief Executive of Microbiotica which he co-founded with Trevor Lawley and Gordon Dougan FRS out of the Sanger Institute. He has 30 years' experience in the biopharma industry and previously co-founded Crescendo Biologics which he led as CEO and CSO, developing a leading antibody fragment discovery platform and pipeline in oncology and inflammation. Prior to that he held global VP roles in GlaxoSmithKline R&D over 10 years, during which time he formed and led international divisions of up to 300 scientists which helped shape the company's discovery platforms and development pipelines across therapeutic areas and modalities (including NCEs, biologics, antibodies, vaccines and gene therapy).

Mike is highly experienced in biotech translation and commercialisation, currently serving as a Trustee of the life-sciences charity LifeArc, and previously as Translational Adviser in Biomedicine at Imperial College, Venture Partner in UK Innovation and Science Seed Fund, and member of the MRC's Developmental Pathway Funding Scheme for translational research.

Mike's early work included research in virology and in yeast genetics and biotechnology. He holds a degree in Natural Sciences from Cambridge University, a PhD in Molecular Virology from Imperial College, and is a Fellow of the Royal Society of Biology.

MICROBIOME MOVEMENT
DRUG DEVELOPMENT

# Live Bacterial Therapeutics as an emerging modality and the move to Precision Medicine in the microbiome

**What do you think have been the most exciting developments within the microbiome space in the last year?**

The microbiome represents a paradigm shift in biomedicine that affects how we think about health and disease and presents new modalities for therapeutic intervention. It is remarkable to consider our co-evolved microbiome as a major part of our physiology and representing our closest interaction with the external environment. The promise in biomedicine has been latent for more than 10 years, but in the last year successful translation has become very tangible. There are three areas I have been very excited about:

1. The three late-stage clinical successes with donor-derived bacterial products for C. difficile from Seres, Rebiotix and Finch have fired up the whole field. These should lead to the first approved live bacterial therapies. The Seres and Finch products validate therapeutic intervention and engraftment of microbiota by oral delivery and this has also been demonstrated by Seres in Ulcerative Colitis. In my view the next necessary stage is the development of fully-defined products which represent true live pharmaceuticals. The precedence is in place for those too, with recent clinical validation of oral delivery and engraftment of such products in several trials.
2. The breadth of therapeutic applications is beginning to unfold with clinical data such as that from SER-287 in Ulcerative Colitis and faecal microbiota transplant (FMT) studies validating the role of gut bacteria in response to Immune Checkpoint Inhibitors in cancer.
3. I have been amazed by the number of new studies showing links between the microbiome and disease mechanism or therapy. In some cases they are clinical associations (such as the reliable prediction of liver cirrhosis from microbiome profile), in other cases they are mechanistic (e.g. the role of the gut and gut bacteria in the origins of Parkinson's Disease). The links in immunology, metabolism and CNS are becoming more extensive and clearer, and show that the modern medicine cannot ignore the microbiome dimension.

We are at an exciting point where these advances herald the arrival of live bacterial products as a new modality with cross-therapeutic application, as well as other modalities, such as phage therapy, microbiota-derived bioactives, and the microbiome as a biomarker of health, disease and drug-response.

**What is unique about Microbiotica's approach and how are you using it to develop breakthrough medicines and biomarkers?**

Microbiotica excels in rigorous identification of bacteria driving clinical outcomes as the starting point for therapeutics, biomarkers and novel targets. It is well known that animal models and in vitro screens have their limitations in drug discovery. We believe that in the microbiome particularly we should be mechanism-agnostic and see what the biology in patients is telling us. That way we can identify new mechanisms that have been pre-validated in patients and develop truly transformative therapies.

To do this is not simple. It requires (a) high-quality large patient data sets and samples, (b) the ability to identify and isolate the majority of the gut bacteria, and (c) bioinformatic tools including machine learning to associate groups of bacteria ("bacterial signatures") to patient phenotype.

Microbiotica has leading tools in these areas that we believe allow an



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unprecedented level of precision in analysing gut bacteria that enable the identification of bacterial signatures missed by others. The science is based on over a decade of investment at the Wellcome Sanger Institute, led by Trevor Lawley (Microbiotica's CSO), who addressed key barriers to translation, including the first design of defined bacterial therapeutics, mass isolation of gut bacteria, and comprehensive analysis of gut bacteria based on expanded reference genome collections.

These capabilities have attracted top quality collaborators, such as Genentech, Cancer Research UK, University of Cambridge and University of Adelaide, with clinical datasets and samples to feed the pipeline. We believe that armed with our platform and these clinical datasets we can make unique discoveries of bacterial signatures linked to biology that form the basis for highly differentiated defined live bacterial therapeutics and biomarkers.

**What has Microbiotica achieved in the last year and how is Microbiotica applying these capabilities and what are the next goals for Microbiotica?**

In the last year the company has made great strides. First we kept the operation running right through the pandemic while moving to our new facility in Chesterford Research Park, so we can now house all our scientists in the same building for the first time. Second we have significantly expanded and strengthened our executive team. Third and more importantly we have made great progress toward the clinic in our lead programs, both in Ulcerative Colitis, in Immuno-Oncology and in our collaboration with Genentech. A key new strategic collaboration for us is with Cancer Research UK and Cambridge University Hospitals, which we signed in 2020 and which supports a major landmark clinical study in multiple cancers (MITRE). This gives us a great long-term position in Immuno-oncology.

> "The microbiome represents a paradigm shift in biomedicine that affects how we think about health and disease"

**How are your programs and products differentiated from others in the field?**

We believe our programs are differentiated in that they use a precision medicine approach – they start with patient datasets and strong validation from the clinic, to which we add class-leading microbiome profiling. Out of this come products paired with highly predictive biomarkers to which we add mechanism.

It's worth noting that we always identify multiple bacteria with differing mechanisms by this approach. As a result our products comprise consortia of bacteria from each of the major three phyla all derived from clinical data. In the case of our Immuno-oncology program we have identified, we believe, the first universal signature of checkpoint inhibitor drug response in melanoma and lung cancer patients. The bacterial signature is so predictive that it has potential as a companion diagnostic and it gives us high confidence as we head to the clinic.

**What progress have you made in your lead programs and what are your aims in the next 12 months?**

In Ulcerative Colitis we started by analysing the excellent FMT study conducted by Sam Costello at the University of Adelaide. Applying our technology, we undertook a unique analysis of this study, isolating and banking all the bacterial species from the donors and identifying at the strain level bacteria engrafted in patients linked to remission. During 2020, we showed that our product (MB310) is efficacious in a mouse model of IBD and that the individual bacteria had multiple therapeutic mechanisms demonstrated in cellular assays, including innate and adaptive immune-modulation and potent healing of damaged gut epithelium. We feel this has great promise to address the multiple pathologies of this disease and are very excited to take it into the clinic.

In Immuno-oncology we feel we have made remarkable progress using a similar clinic-first approach but this time based on melanoma patients receiving checkpoint inhibitor therapy. We based this on our completed MELRESIST study, identified a bacterial signature 91% predictive of drug response, then showed the signature was also predictive in an additional three data sets from around the world, and also in lung cancer. From this signature we have identified nine bacteria that are most raised in abundance in responders and have shown them to be therapeutic preclinically, and having mechanisms profoundly stimulating cytotoxic T cell killing of tumours. The predictivity of the signatures gives us confidence for clinical efficacy of the product MB097, and also for the potential of a companion diagnostic for drug therapy.

We are very excited to take these programs to the clinic and have a laser-like focus on completing process development and manufacture ready for clinical trials in 2022.

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Initially built out of 10 years' investment in the Wellcome Sanger Institute and based in Cambridge UK, Microbiotica identifies gut bacteria linked to patient phenotype with unprecedented precision in order to develop validated live bacterial therapeutics and biomarkers based on clinical datasets. The company is in development with best-in-class live bacterial therapeutics for immuno-oncology and ulcerative colitis, and has partnerships with Genentech, Cancer Research UK, University of Cambridge and University of Adelaide.

**www.microbiotica.com**