Results Combination of HLA peptidomics with 16S rDNA sequencing of 17 melanoma metastasis derived from 9 different patients, lead us to the unbiased identification of an intracellular bacterial peptide repertoire presented on HLA-I and HLA-II molecules. We were able to validate these results by co-culturing the bacterial species identified by 16S sequencing with the patient derived melanoma cells, further validating the peptide's presentation by preforming HLA peptidomics on the infected cells. Importantly, we were able to identify common bacterial peptides from different metastases of the same patient as well as from different patients. Some of the common bacterial peptides, as well as others, were able to elicit an immune response by the autologous tumor infiltrating lymphocytes (TILs), suggesting potential therapeutic implications of these peptides.

Conclusions The insights gathered through this study elucidate the effect of intra-tumor bacteria on the immune response and so, may lead to the development of novel clinical applications.

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PRECISION MICROBIOME MAPPING IDENTIFIES A MICROBIOME SIGNATURE PREDICTIVE OF IMMUNE CHECKPOINT INHIBITOR RESPONSE ACROSS MULTIPLE RESEARCH STUDY COHORTS

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Background The gut microbiome of cancer patients appears to be associated with response to Immune Checkpoint Inhibitor (ICIs) treatment.^{1–4} However, the bacteria linked to response differ between published studies.

Methods Longitudinal stool samples were collected from 69 patients with advanced melanoma receiving approved ICIs in the Cambridge (UK) MELRESIST study. Pretreatment samples were analysed by Microbiotica, using shotgun metagenomic sequencing. Microbiotica's sequencing platform comprises the world's leading Reference Genome Database and advanced Microbiome Bioinformatics to give the most comprehensive and precise mapping of the gut microbiome. This has enabled

us to identify gut bacteria associated with ICI response missed using public reference genomes. Published microbiome studies in advanced melanoma,^{1–3} renal cell carcinoma (RCC) and non-small cell lung cancer (NSCLC)⁴ were reanalysed with the same platform.

Results Analysis of the MELRESIST samples showed an overall change in the microbiome composition between advanced melanoma patients and a panel of healthy donor samples, but not between patients who subsequently responded or did not respond to ICIs. However, we did identify a discrete microbiome signature which correlated with response. This signature predicted response with an accuracy of 93% in the MELRESIST cohort, but was less predictive in the published melanoma cohorts.^{1–3} Therefore, we developed a bioinformatic analytical model, incorporating an interactive random forest model and the MELRESIST dataset, to identify a microbiome signature which was consistent across all published melanoma studies. This model was validated three times by accurately predicting the outcome of an independent cohort. A final microbiome signature was defined using the validated model on MELRESIST and the three published melanoma cohorts. This was very accurate at predicting response in all four studies combined (91%), or individually (82–100%). This signature was also predictive of response in a NSCLC study and to a lesser extent in RCC. The core of this signature is nine bacteria significantly increased in abundance in responders.

Conclusions Analysis of the MELRESIST study samples, precision microbiome profiling by the Microbiotica Platform and a validated bioinformatic analysis, have enabled us to identify a unique microbiome signature predictive of response to ICI therapy in four independent melanoma studies. This removes the challenge to the field of different bacteria apparently being associated with response in different studies, and could represent a new microbiome biomarker with clinical application. Nine core bacteria may be driving response and hold potential for co-therapy with ICIs.

Ethics Approval The study was approved by Newcastle & North Tyneside 2 Research Ethics Committee, approval number 11/NE/0312.

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LATE ANTIBIOTIC ADMINISTRATION DURING DURVALUMAB TREATMENT MAY BE ASSOCIATED WITH CLINICAL BENEFIT

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Background Early concurrent antibiotic usage in patients receiving immune checkpoint inhibitors (ICIs) is linked to