Results The results show precise expression levels for each of the 60 markers in the assay in each individual cell in the sample, maintaining spatial information about each cell. Dozens of immune cell subtypes were identified and quantified based on protein expression profiles. Spatial analysis of the samples reveals quantifiable heterogeneity of immune cell infiltration within the tumor samples, demonstrating the utility of the ChipCytometry platform for in-depth immune profiling in clinical samples.

Conclusions The ChipCytometry platform enables simultaneous detection of multiple protein markers on a single tissue section for deep immune cell profiling in the tumor microenvironment. Combined with the single-cell spatial information, such data sets provide an opportunity for the discovery of new complex multiplexed biomarker signatures to inform therapeutic development.

Disclosure Information T.D. Campbell: A. Employment (full or part-time); Significant; Canopy Biosciences. N. Stanislawski: A. Employment (full or part-time); Significant; Canopy Biosciences. J. Brooks: A. Employment (full or part-time); Significant; Canopy Biosciences.

Background While Immune checkpoint inhibitors (ICIs) are revolutionizing the management of many advanced cancers, several studies have reported that the gut microbiota composition may have an impact on ICI response. Antibiotics have been shown to alter the efficacy of immunotherapies, but other commonly used comedications known to interact with the microbiota might also impact the clinical benefit of those treatments. Clinical studies revealed that patients treated with ICI could be stratified into responder (R) or non-responder (NR) according to their microbiota composition. In a total of 635 patients with advanced cancer treated with anti-PD-1, anti-PD-L1 or anti-CTLA-4 between 2015 and 2017 in Bordeaux, M. Kostine et al. described an association between the baseline use of co-medications, including proton pump inhibitors (PPIs), and a significantly shortened overall survival.1 Our results revealed that omeprazole treatment resulted in a decrease of bacteria associated with a healthy gut and an expansion of oral bacteria and environmental pathobionts, consistent with published studies.2, 3 Notably, omeprazole administration led to a striking reduction in Lachnospiraceae spp., which are enriched in the ‘microbiotype’ of ICI-responders.4 Multi-omics integration of the gut microbiome and transcriptional data sets using weighted gene co-expression network analysis (WGCNA) identified omeprazole-induced transcriptional modules in the colon significantly associated with depletion or enrichment of specific microbiota components. From this integration, we will reconstruct the bacterial and host metabolic networks towards identifying metabolic signals linked to impaired anti-tumor immunity.

Conclusions Collectively, our results present the impact of PPI on microbiome changes in tumor-bearing individuals and unravel potential mechanisms for intervention aimed at enhancing the anti-tumoral immune responses elicited by immunotherapies.

REFERENCES