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Micronoma™

Precision medicine through the cancer microbiome

With its Oncobiota platform, Micronoma is pioneering the analysis of the cancer microbiome for early cancer detection and creating tools for personalized cancer treatment.

Along with a unique genome, we all carry a unique constellation of microbiota called the microbiome. Our microbiome not only plays a key part in our everyday health, but also in serious diseases, including cancer. Over the past five years, extensive research has suggested that there are close links between cancer and the microbiome, with many microbes living within or around tumor tissue—the cancer microbiome—influencing, in some cases, how the immune system and/or therapeutics interact with the tumor.

Micronoma is the first company to use the cancer microbiome for the early detection of cancer through the development of its Oncobiota platform, which is also perfectly placed to expand to other applications such as the identification of the tissue origin of metastatic tumors, guidance toward treatment selection, and monitoring of treatment efficacy and resistance. Rather than looking for the presence or absence of individual microbial species, some of which are known to cause cancer—for example, human papillomavirus (HPV) and cervical cancer, or *Helicobacter pylori* and stomach cancer—Oncobiota takes a community-level perspective and analyzes the overall compositional balance of circulating microbiota as a biomarker of cancer presence, origin, and likely prognosis.

Oncobiota grew out of the academic work of Greg Poore, Micronoma's co-founder and Chief Analytics Officer, in the renowned lab of Rob Knight at the University of California San Diego, United States. In a landmark study published in *Nature* in 2020[1], Poore and colleagues used machine learning methods to analyze whole genome and RNA sequencing cancer microbiome data for 33 different cancer types from 10,000 treatment-naive patients (18,116 samples), thereby generating diagnostic classifiers capable of distinguishing between healthy and tumor tissue, but also between cancer types and different stages of the same cancer type. A strength of this approach is that it can remain agnostic as to whether the cancer microbiome actually drives cancer or simply reflects the presence of cancer, either of which may apply in any given case.

Detecting early

The patent-pending Oncobiota platform uses minimally invasive liquid biopsies—small plasma samples—that enable the evaluation of suspect lesions that are otherwise hard to reach. While it is possible to use plasma samples to detect cell-free-circulating DNA derived from tumors (ctDNA) in late-stage cancers (stages III and IV), traditional ctDNA-based analyses lack the sensitivity required for small tumors. In contrast, the Oncobiota platform can detect cell-free microbial DNA (cf-mbDNA) associated with even small, early-stage cancers using as little as 400 microliters of plasma from a standard blood draw.

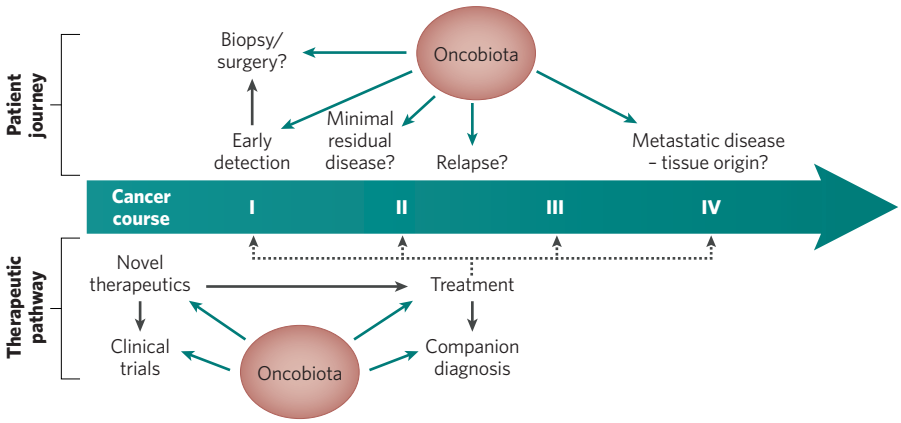

Fig. 1 | Oncobiota and the future of cancer diagnosis and treatment. Oncobiota from Micronoma provides a powerful tool for diagnosing and monitoring cancer patients, and has the potential to make a big impact on the development and use of cancer therapies.

Initially, Micronoma is focusing on early detection of cancers that are not just prevalent but also difficult to detect and highly deadly—cancers for which early detection will have the biggest impact on saving lives and reducing health care costs. To this end, Micronoma is exploring diagnostics for lung, liver, pancreatic, and ovarian cancers, which are typically detected late and consequently have poor five-year survival rates.

Currently, the most developed diagnostic is for lung cancer. Over the past year, Micronoma has collated data from 1,200 plasma samples comprising the major histological subtypes of lung cancer including hundreds of stages I and II cancers, as well as samples of benign pulmonary nodules, to identify the discriminant microbiome signatures of early-stage disease. Micronoma is now working to finalize the validation of this diagnostic tool.

Micronoma's diagnostic tests are not intended for screening in healthy people to pick out the rare cancer cases because that could generate lots of stressful and costly false positives. In the case of lung cancer, the diagnostic would be used when a suspect nodule has been identified through low-dose computerized tomography (CT) scans or chest X-rays, and the physician needs to decide whether the nodule is malignant or benign, and whether invasive biopsy or immediate surgical resection are justified. By identifying cancer-specific cf-mbDNA signatures derived from minimally invasive blood samples, Oncobiota can be used as an alternative to traditional biopsy-based longitudinal genomic profiling of tumors. Biopsies are often hindered by dangerously or difficultly located tumors and yields that are too low for representative tissue analysis. Moving forward, Micronoma plans to expand the applications of the Oncobiota platform beyond diagnostics and early detection into support for treatment decisions.

Looking ahead

Future applications of Oncobiota include identifying cf-mbDNA signatures of residual disease post-surgery or potential relapses of the disease, and for patients detected at stage IV, the tissue origin of metastatic tumors. Oncobiota will also be applied to stratifying patient populations for clinical trials based on cancer type/stage identified through cf-mbDNA signatures, as well as pharmacomicrobiomic signatures that point to microbiome-drug interactions that can be used to guide treatment decisions and offer companion diagnostic assays. In the long-term, Micronoma's vision is to use the cf-mbDNA signatures identified by Oncobiota to develop novel anticancer therapeutics that precisely modulate the cancer microbiome in ways that are damaging to tumors and slow down or halt cancer growth (Fig. 1).

Micronoma, rooted in a solid science base, is dedicated to fully exploring the possibilities opened up by the new understanding of the cancer microbiome, and welcomes discussions with investors and strategic partners interested in this journey.

1. Poore, G.D. et al. *Nature* **579**, 567–574 (2020).

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