PRESS RELEASE

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International researchers develop practical recommendations to strengthen cancer microbiome research

Singapore, 25 March 2026 – An international team led by researchers from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) and A*STAR Genome Institute of Singapore (A*STAR GIS), has published a new paper in *Nature Cancer* highlighting the importance of greater care, consistency, and rigour in studies reporting microbes in human tumours.

In recent years, advances in DNA sequencing have enabled researchers to detect traces of bacterial, fungal, and viral genetic material in diverse samples. Some studies have reported microbes even in sites traditionally considered microbe-free, such as the brain or the placenta, and findings on microbes in tumours from diverse organs have generated interest in how tumour-associated microbes could influence cancer growth, spread, or response to treatment. However, the researchers caution that interpreting such signals can be complex. Tumour tissues from diverse organs typically contain extremely low amounts of microbial material or none, making them especially vulnerable to contamination introduced during surgery, sample handling, storage, laboratory processing, or sequencing. Limitations in data analysis and reference databases can further complicate interpretation, leading to microbial signals that may not reflect true biological presence.

“Finding microbial DNA in tumours is like finding a needle in a haystack,” said Associate Professor Niranjan Nagarajan, Department of Biochemistry and Infectious Diseases Translational Research Programme (TRP), NUS Medicine, a lead author of this report. “If appropriate checks and additional validation are not built into the analysis, it becomes very difficult to distinguish genuine microbial signals from background noise.” Associate Professor Nagarajan is also Associate Director, AI and Compute, and Senior Group Leader, Laboratory of Metagenomic Technologies and Microbial Systems at A*STAR GIS.

The team reviewed current practices across the rapidly growing field of cancer microbiome research and identified recurring methodological challenges, including insufficient use of negative controls, heavy reliance on bioinformatic analysis alone, and limited validation using independent or complementary methods. They drew parallels with early challenges in ancient DNA research, where the adoption of stringent standards helped mature that field into a reliable scientific discipline.

Importantly, the researchers stress that their report does not question the role of cancer-associated microbes in general. Microorganisms are already known to contribute to certain cancers, particularly in tissues exposed to abundant microbes, such as the gastrointestinal tract. Rather, the paper encourages careful evaluation of claims of diverse tumour-resident microbiomes in low-biomass tissues, especially where supporting evidence is limited.

To help the field move forward, the researchers propose a practical checklist of best practices covering the entire research pipeline—from sample collection and handling, to sequencing, data analysis, and biological validation. A more detailed explanation can be found below, in Annexe A.

These recommendations emphasise preventing contamination, incorporating appropriate controls, validating findings with multiple independent approaches, and being transparent about data limitations. This work reflects an international collaboration involving scientists from Singapore, the United States, the Netherlands, Denmark, and Australia, bringing together expertise in genomics, computational biology, microbiome science, pathology, and immunology.

“When researchers work with very small signals, even minor background noise can influence the outcome,” said Dr Chia Minghao, Senior Scientist at A*STAR GIS, and co-author of the study. “By putting stronger safeguards in place and confirming results through multiple approaches, the scientific community can improve reproducibility and ensure that future discoveries about microbes and cancer rest on solid foundations.”

Microbes associated with tumours could provide important insights into cancer biology and inform future diagnostics or therapies. At the same time, inconclusive or weakly supported findings can slow progress. By encouraging higher and more consistent standards across the field, the researchers hope to strengthen confidence in cancer microbiome research and support future findings that are reliable, reproducible, and clinically relevant.

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ANNEXE A

List of proposed best practices

1. Prevent contamination during sample collection
- Tumour samples should be collected and handled using strict aseptic techniques to minimise the introduction of microbial DNA during surgery or tissue harvesting.
- Environmental sampling controls should be collected alongside tumour samples to identify microbes that may originate from the surrounding environment rather than the tissue itself.
- Whenever possible, researchers should analyse matched normal tissue samples collected at the same time as the tumour to help distinguish real signals from contamination.

2. Maintain clean handling and storage procedures
- Tissue samples should be handled and stored under controlled laboratory conditions, ideally separated from areas where DNA amplification takes place to reduce contamination risk.
- Handling and storage controls, including blank samples or environmental swabs, should be processed and sequenced to detect contamination introduced during these stages.
- For formalin-fixed paraffin-embedded (FFPE) tissues, blank paraffin blocks should be processed and sequenced as additional controls.

3. Use strict laboratory and sequencing controls
- Samples should be processed in clean laboratory environments that minimise nucleic acid contamination.
- Key findings should ideally be replicated in independent laboratories, or validated using different DNA extraction or library preparation kits.
- Blank controls and reagent controls should be included in every sequencing run to identify contamination originating from laboratory reagents or sequencing batches.

4. Ensure sequencing quality and transparency
- Sequencing libraries should be quantified before sequencing to help identify potential contamination signals.
- Measures such as dual indexing or avoiding multiplexing should be used to reduce sequencing artefacts such as barcode hopping.
- Detailed metadata about sample collection, processing centres, and sequencing batches should be reported so potential technical biases can be assessed.

5. Apply conservative and transparent bioinformatic analysis
- Microbial classification should be performed using high-quality reference databases, including complete human genome references, to reduce false microbial assignments.
- Researchers should examine the genomic distribution and alignment quality of microbial reads to confirm that detected microbes show biologically plausible patterns.
- Computational methods should be used to identify and remove likely contaminant species, especially in low-biomass samples.

6. Validate findings using independent experimental methods
- Sequencing results should be confirmed using targeted laboratory techniques, such as PCR, fluorescence in situ hybridisation (FISH), or immunohistochemistry.
- Spatial imaging methods should demonstrate that microbes are actually present within or near tumour cells, rather than appearing at tissue edges where contamination is more likely.
- Evidence should also be sought for viable or metabolically active microbes, for example through RNA detection or culture-based methods.

7. Provide transparent reporting and multiple lines of evidence
- Researchers should clearly acknowledge limitations and describe steps taken to detect or prevent contamination.
- Strong claims of tumour-resident microbes should rely on multiple independent lines of evidence, rather than a single sequencing signal.

Please refer to their published study for the checklist and the reasoning behind those items:
https://www.nature.com/articles/s43018-026-01121-6

About National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research, and entrepreneurship, with a focus on Asian perspectives and expertise. We have 15 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established our NUS Overseas Colleges programme in more than 15 cities around the world.

Our multidisciplinary and real-world approach to education, research, and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 30 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

For more information on NUS, please visit www.nus.edu.sg.

About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven, and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,0000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus in innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher World University Rankings 2026 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2025).

For more information about NUS Medicine, please visit https://medicine.nus.edu.sg/