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METAGENOMICS AT THE INTERFACE OF DIAGNOSTICS AND SURVEILLANCE: A NEAR-TERM PERSPECTIVE

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INTRODUCTION

The global landscape of infectious diseases is undergoing rapid and profound change. Increased human mobility, climate-driven shifts in vector ecology, intensified human-animal-environment interactions, and geopolitical instability have collectively amplified the risk of emerging and re-emerging infectious diseases. At the same time, public health systems are increasingly confronted with pathogens that are unexpected, genetically diverse, or poorly represented in existing diagnostic panels. These developments highlight the growing limitations of exclusively targeted diagnostic approaches and underscore the need for broader, more adaptive tools.

In this context, metagenomic sequencing has emerged as a transformative technology. By enabling unbiased detection and genomic characterization of pathogens directly from clinical, environmental, or animal samples, metagenomics offers capabilities that extend far beyond conventional diagnostics. While historically confined to research and outbreak investigations, metagenomics is now approaching a level of maturity that warrants serious consideration for integration into routine diagnostics and risk-oriented surveillance frameworks.

METAGENOMICS AND DISEASES WITH INCREASED RISK

Diseases with increased epidemic or pandemic potential, particularly zoonotic and vector-borne infections, pose unique diagnostic and surveillance challenges. These pathogens often circulate at low levels, exhibit substantial genetic diversity, and may evade detection by assays designed for known targets. In such scenarios, metagenomic sequencing provides a critical advantage by enabling the detection of both expected and unexpected agents without prior assumptions.

Metagenomics is especially valuable for early-phase outbreak detection, investigation of unexplained clinical syndromes, and identification of novel or divergent pathogens. It also facilitates the detection of co-infections and mixed microbial communities, which may influence disease severity or transmission dynamics. Importantly, the genomic information generated through metagenomic analysis supports downstream applications such as phylogenetic reconstruction, source attribution, and monitoring of viral evolution capabilities that are essential for informed public health decision-making.

From a biosafety and biosecurity perspective, metagenomics also strengthens preparedness against deliberate or accidental biological events. The ability to rapidly characterize unknown biological agents enhances situational awareness and supports timely risk assessment in complex or ambiguous scenarios.

THE ROLE OF METAGENOMICS IN ROUTINE DIAGNOSTICS

Despite its clear strengths, metagenomics has not yet replaced targeted diagnostics in routine laboratory settings. Targeted PCR-based assays remain indispensable due to their superior sensitivity, speed, and cost-effectiveness for known pathogens and high-throughput screening applications. However, metagenomics should not be viewed as a competing approach, but rather as a complementary one.

A realistic near-term vision involves tiered diagnostic strategies, in which targeted assays serve as the first-line tools, while metagenomic sequencing is applied selectively, when routine diagnostics fail, when unusual epidemiological patterns emerge, or when genomic resolution is required. Such hybrid approaches maximize diagnostic yield while maintaining operational feasibility and cost control.

Recent advances are accelerating the transition of metagenomics toward routine use. Improvements in sample preparation, host nucleic acid depletion, sequencing chemistry, and bioinformatic automation are steadily enhancing analytical sensitivity and reducing turnaround times. At the same time, declining sequencing costs and increased computational capacity are making metagenomic workflows more accessible to public health laboratories.

ONE HEALTH AND INTEGRATED SURVEILLANCE

One of the most significant strengths of metagenomics lies in its applicability across the human-animal-environment interface. Many high-risk pathogens circulate silently in wildlife or vectors long before they cause detectable human disease. Integrating metagenomic surveillance across these domains enables earlier detection of spillover events and provides insights into ecological drivers of emergence.

By generating comparable genomic data from diverse sample types, metagenomics supports integrated One Health surveillance frameworks and facilitates data sharing across sectors. This is particularly important in regions where pathogen diversity is high but genomic data remains scarce. Expanding metagenomic surveillance in such settings can help close existing knowledge gaps and improve global preparedness.

CHALLENGES AND FUTURE DIRECTIONS

For metagenomics to be fully integrated into routine diagnostics and surveillance, several challenges must be addressed. Standardization of laboratory workflows, validation criteria, and data interpretation frameworks is essential to ensure reproducibility and comparability across laboratories. Clear guidance is also needed on result reporting, including thresholds for diagnostic significance and strategies to distinguish true pathogens from contaminants or background flora.

Capacity building remains a critical priority. Investments in training, infrastructure, and interdisciplinary collaboration are required to ensure that metagenomic data can be generated, interpreted, and acted upon effectively. Importantly, ethical and data governance considerations must be addressed, particularly with respect to data sharing and the handling of sensitive genomic information.

CONCLUSION

Metagenomic sequencing is no longer a distant prospect but a rapidly maturing technology with tangible relevance for routine diagnostics and high-risk disease surveillance. While targeted assays will continue to form the backbone of diagnostic testing, metagenomics offers unparalleled breadth and genomic resolution, enabling detection and characterization of pathogens that would otherwise remain undetectable.

The near future of diagnostics will be defined not by the replacement of existing methods, but by their intelligent integration. By combining targeted testing with selective metagenomic analysis, public health systems can enhance preparedness, improve outbreak response, and strengthen biosafety and biosecurity in an increasingly complex global health landscape.