International Advance Journal of Engineering, Science and Management (IAJESM)
ISSN -2393-8048, January-June 2019, Submitted in April 2019, iajesm2014@gmail.com

Metagenomic Approaches in Systems Microbiology

Shilpa Deshpande Kaistha[12]*, Pramila Devi Umrao, Vineet Kumar, Jitendra Kumar
[1]Department of Microbiology, Institute of Biosciences & Biotechnology, Chhatrapati Shahu Ji Maharaj University, Kanpur 208016, UP, India. Email: shilpakaistha@csjmu.ac.in

Abstract

Metagenomic approaches have revolutionized our understanding of microbial communities in various ecosystems. These techniques involve the sequencing and analysis of DNA directly extracted from environmental samples, allowing for the study of microbial diversity and function without the need for cultivation. Systems microbiology is an interdisciplinary field that aims to understand the behavior and interactions of microorganisms at the systems level. Metagenomic approaches have been used to explore the interactions and dynamics of microbial communities in complex environments to identify key players and metabolic pathways involved in ecosystem processes. Metagenomics has also been used to study microbial adaptation to environmental stresses and to investigate the functional potential of unculturable microorganisms. This book chapter highlights recent advances in metagenomic approaches in systems microbiology and their applications in understanding the ecology and function of microbial communities.

Keywords: Systems Microbiology, Metagenomics, uncultured organisms, microbial diversity

1. Introduction

Systems microbiology is an interdisciplinary field that aims to understand the behavior and interactions of microorganisms at the systems level (Kitano et al., 2002). Leroy Hood's definition of systems biology as "the science of discovering, modeling, understanding and ultimately managing at the molecular level the dynamic relationships between the molecules that define living organisms" (Hood 2004). Metagenomics offers to expand the definition by extending it to communities within ecosystems (Alivasatos et al., 2015).

It is a relatively new field that has emerged from the need to understand the complex interactions that occur between microorganisms and their environment, as well as the role that these interactions play in shaping the function and stability of microbial communities. Systems microbiology combines the principles and techniques of microbiology, genetics, biochemistry, physics, and engineering to study microbial communities in their natural environments (Collins and Greenberg, 2016).

The field of systems microbiology has grown rapidly in recent years due to advances in high-throughput sequencing and computational techniques, which have made it possible to study microbial communities at a systems level. Prior to the development of these techniques, microbiologists had to rely on culture-based methods to study microorganisms, which were limited by the fact that only a small fraction of microorganisms can be cultured in the laboratory Alivasatos et al., 2015)(. This approach therefore only provided a partial view of the microbial communities in natural environments. To study microbial communities at a systems level, systems microbiologists use a range of experimental and computational tools (Collins and Greenberg, 2016). These include metagenomics, transcriptomics, proteomics, metabolomics, and mathematical modeling. By combining data from these different approaches, systems microbiologists can gain insights into the structure and function of microbial communities, as well as the underlying mechanisms that govern their behavior.

2. Metagenomic Approaches

Metagenomics is a rapidly evolving field that allows researchers to study the genetic material of entire microbial communities without the need for culturing individual organisms (Handelsman, 2004; Risenfield et al., 2004). Metagenomics has been applied to a wide range of environments, including soil, water, and the human gut, and has provided insights into the structure, function, and diversity of microbial communities (Tringe et al., 2005).

Commonly used techniques in metagenomics are briefly reviewed below:

DNA extraction: The first step in metagenomics is to extract DNA from the environmental sample (Zhou et al., 2018). This can be challenging since the DNA from the target organisms may be mixed with DNA from other organisms or from the environment itself. Different extraction methods can be used depending on the type of sample and the desired downstream applications.

Shotgun sequencing: Shotgun sequencing is a high-throughput sequencing method that involves randomly fragmenting the extracted DNA and sequencing the resulting fragments (Kultima et al., 2019; Sharon et al., 2011). This approach generates a large number of short reads that can be assembled to reconstruct the genomes of individual organisms present in the sample. This technique is particularly useful for studying complex microbial communities, where individual organisms cannot be cultured and identified by traditional methods.

16S, 18S rRNA and ITS sequencing: The 16S ribosomal RNA (rRNA) gene is a conserved gene that is present in all bacteria and archaea (Edwards et al., 1989). 18S rDNA and ITS (Internal Transcribed Spacer) sequencing are two commonly used approaches in molecular biology to study the diversity of eukaryotic microorganisms (Schoch et al., 2012). The rDNA sequences are analyzed using bioinformatics tools to identify the different microbial taxa present in the sample. This can involve comparing the sequences to reference databases, such as GenBank or SILVA, or using software packages, such as QIIME or mothur (Caporaso et al., 2010; Klappenbach et al., 2001)

Metatranscriptomics: Metatranscriptomics involves sequencing and analyzing the RNA transcripts in a microbial community (Urich et al., 2008; Shakya et al., 2019). This technique can provide insights into the metabolic activities, gene expression patterns and functional role of individual organisms within the community in specific environments (Poretsky et al., 2009).

Metaproteomics: Metaproteomics involves identifying and quantifying the proteins expressed by the microbial community. This technique can provide information about the functional activities and metabolic pathways of individual microorganism as well as identify the functional roles of microorganisms in specific environments (Wilmes and Bond, 2004).

3. Applications of metagenomic approaches to systems microbiology

Metagenomic approaches have revolutionized the field of systems microbiology, allowing researchers to study the structure, function, and interactions of microbial communities in different environments (Kitano, 2002). Systems microbiology has applications in a wide range of fields, including biotechnology, environmental science, and human health, some of which are discussed below:-

Microbial community profiling: Metagenomic sequencing can provide a comprehensive profile of microbial communities in different environments, including soil, water, and human gut (Collins and Greenberg, 2016). This information can be used to understand the diversity and abundance of microbial species, as well as their potential roles in biogeochemical cycles and other ecosystem processes (Gilbert et al., 2010; Riesenfeld et al., 2004)

Functional annotation and pathway analysis: Metagenomic sequencing data can be used to identify genes and functional pathways in microbial communities, providing insights into their metabolic potential and ecological roles (Edwards et al., 2008). This information can be used to predict the functional capabilities of microbial communities and to understand how they respond to environmental changes (Tyson et al., 2004).

Comparative analysis of microbial communities: Metagenomic sequencing data can be used to compare microbial communities in different environments, or to track changes in microbial community structure and function over time (Edwards et al., 2008; Fierer et al., 2012). This approach can provide insights into the factors that drive microbial community dynamics and ecosystem functioning under different stressors (Dinsdale et al., 2008).

Microbial interactions: Metagenomic approaches can be used to identify and characterize interactions between microbial species in different environments, such as mutualistic or competitive relationships. This information can be used to understand how microbial communities are structured and to predict how they might respond to environmental changes (Tringe et al., 2005). A metagenomic analysis of microbial communities in the ocean identified novel microbial taxa and genes involved in key biogeochemical processes, such as nitrogen and carbon cycling.

This study also revealed the presence of functional redundancy within microbial communities, indicating that multiple microbial taxa can perform similar functions in the ocean ecosystem (DeLong et al., 2006). A metagenomic analysis of soil microbial communities identified genes and metabolic pathways involved in carbon and nitrogen cycling, as well as the presence of antibiotic resistance genes and mobile genetic elements, highlighting sustainable land use practices (Fierer et al.2012).

Human Microbiome: Another application of systems microbiology is in the study of the human microbiome, which is the collection of microorganisms that inhabit the human body (Human Microbiome Project Consortium, 2012; Qin et al., 2010). The human microbiome has been implicated in a wide range of diseases, including obesity, diabetes, and inflammatory bowel disease (Sharon et al., 2013). By studying the interactions between the human microbiome and the host, systems microbiologists can gain insights into the underlying mechanisms of these diseases and develop new therapies to treat them (Verberknoes et al., 2009).

Human gut microbiome using metagenomic approaches identified a core set of microbial genes and pathways that are conserved across individuals, as well as inter-individual variability in the abundance of specific microbial taxa and functions. This study also revealed associations between microbial functions and host health, such as the enrichment of certain microbial pathways in individuals with a high body mass index (Qin et al., 2010).

Drug Discovery: In drug discovery, systems biology can be used to identify new drug targets, understand the mechanisms of drug action, and predict drug toxicity (Hood et al., 2004). Systems biology can be used to identify new drug targets by analyzing the interactions between genes, proteins, and metabolites in biological systems. For example, network analysis can be used to identify key nodes or hubs in biological networks that are essential for cell function and survival. These hubs can be potential drug targets for the development of new therapies (Liu et al., 2015). Gene expression profiling can be used to identify the pathways and processes that are affected by a drug. This information can be used to optimize drug efficacy and minimize side effects. Computational models can be used to simulate the effects of drugs on cellular metabolism and predict their impact on cell viability (Ramanathan et al., 2009). This information can be used to identify drugs that are less likely to cause adverse effects. Systems biology can be used to develop personalized medicine approaches by analyzing individual patient data and identifying drug targets and therapies that are specific to their disease or genetic profile (Oprea and Tropsha, 2011).

Bioremediation and industrial applications: Metagenomic approaches can be used to identify microbial genes and pathways involved in bioremediation or industrial processes, such as the degradation of pollutants or the production of biofuels. This information can be used to optimize bioremediation or industrial processes and to develop new technologies for sustainable resource use (Handelsman, 2004).

Sustainable Bioprocess development: One application of systems microbiology is in the development of bioreactors, which are used for the large-scale production of useful compounds such as biofuels and pharmaceuticals. By engineering microbial communities to optimize the production of these compounds, systems microbiologists can create more efficient and sustainable bioprocesses. A metagenomic analysis of microbial communities in a bioreactor used for the production of biofuels identified novel microbial taxa and metabolic pathways involved in biofuel production, as well as the presence of genes involved in stress response and cell-to-cell signaling.

4. **Conclusion:**

Systems microbiology offers a powerful approach for studying microbial communities and understanding their role in shaping the world around us. By combining the principles and techniques of metagenomics, microbiology, genetics, biochemistry, physics, and engineering, systems microbiologists can gain a more complete understanding of microbial communities and their interactions with their environment. This knowledge can be used to develop new biotechnologies, understand the impact of microorganisms on the environment, and develop new treatments for human diseases.

Acknowledgement

Authors are grateful to Department of Microbiology, Institute of Biosciences & Biotechnology for research facilities.

Reference

1. Alivisatos, A. P., Blaser, M. J., Brodie, E. L., Chun, M., Dangl, J. L., Donohue, T. J., ... & Paerl, H. W. (2015). Microbiome research needs a new approach. Proceedings of the National Academy of Sciences, 112(23), 7285-7288.
2. Caporaso, J. G., Kuczynski, J., Stombaugh, J., Bittinger, K., Bushman, F. D., Costello, E. K., ... & Knight, R. (2010). QIIME allows analysis of high-throughput community sequencing data. Nature methods, 7(5), 335-336.
3. Collins, J. J., & Greenberg, E. P. (2016). Foundations of microbiology: a systems approach. McGraw-Hill Education.
4. DeLong, E. F., Preston, C. M., Mincer, T., Rich, V., Hallam, S. J., Frigaard, N. U., ... & Karl, D. M. (2006). Community genomics among stratified microbial assemblages in the ocean's interior. Science, 311(5760), 496-503.
5. Edwards, R. A., Hall, D., Angly, F., Breitbart, M., Brulc, J. M., ... & Rohwer, F. (2008). Functional metagenomic profiling of nine biomes. Nature, 452(7187), 629-632.
6. Edwards, U., Rogall, T., Blöcker, H., Emde, M., & Böttger, E. C. (1989). Isolation and direct complete nucleotide determination of entire genes: characterization of a gene coding for 16S ribosomal RNA. Nucleic acids research, 17(19), 7843-7853.
7. Fierer, N., Lauber, C. L., Ramirez, K. S., Zaneveld, J., Bradford, M. A., & Knight, R. (2012). Comparative metagenomic, phylogenetic and physiological analyses of soil microbial communities across nitrogen gradients. The ISME journal, 6(5), 1007-1017.
8. Gilbert, J. A., Meyer, F., Antonopoulos, D., Balaji, P., Brown, C. T., Brown, C. T., ... & Wilke, A. (2010). Meeting report: the terabase metagenomics workshop and the vision of an Earth microbiome project. Standards in Genomic Sciences, 3(3), 243.
9. Handelsman, J. (2004). Metagenomics: application of genomics to uncultured microorganisms. Microbiology and Molecular Biology Reviews, 68(4), 669-685.
10. Hood, L., Heath, J. R., Phelps, M. E., & Lin, B. (2004). Systems biology and new technologies enable predictive and preventative medicine. Science, 306(5696), 640-643. doi: 10.1126/science.1104635
11. Human Microbiome Project Consortium. (2012). Structure, function and diversity of the healthy human microbiome. Nature, 486(7402), 207-214.
12. Kitano, H. (2002). Systems biology: a brief overview. Science, 295(5560), 1662-1664. doi: 10.1126/science.1069492
13. Klappenbach, J. A., Saxman, P. R., Cole, J. R., & Schmidt, T. M. (2001). rrndb: the Ribosomal RNA Operon Copy Number Database. Nucleic acids research, 29(1), 181-184.
14. Kultima, J. R., Coelho, L. P., Forslund, K., Huerta-Cepas, J., Li, S. S., Driessen, M., ... & Sunagawa, S. (2019). MOCAT2: a metagenomic assembly, annotation and profiling framework. Bioinformatics, 35(11), 2000-2002.
15. Liu, Y., & Chan, C. (2015). Using Systems Biology Approaches to Identify Pathways and Targets for Antifungal Drug Discovery. Journal of Fungi, 1(3), 409-427. doi: 10.3390/jof1030409
16. Oprea, T. I., & Tropsha, A. (2011). Systems biology and personalized medicine: current status and perspectives. Expert review of precision medicine and drug development, 1(3), 313-329. doi: 10.1586/erd.11.20
17. Poretsky, R. S., Hewson, I., Sun, S., Allen, A. E., Zehr, J. P., & Moran, M. A. (2009). Comparative day/night metatranscriptomic analysis of microbial communities in the North Pacific subtropical gyre. Environmental microbiology, 11(5), 1358-1375.

18. Qin, J., Li, R., Raes, J., Arumugam, M., Burgdorf, K. S., Manichanh, C., ... & Wang, J. (2010). A human gut microbial gene catalogue established by metagenomic sequencing. Nature, 464(7285), 59-65.
19. Ramanathan, A., & Schreiber, S. L. (2009). Directing evolution: the next revolution in drug discovery?. Nature chemical biology, 5(6), 394-397. doi: 10.1038/nchembio.175
20. Riesenfeld, C. S., Schloss, P. D., & Handelsman, J. (2004). Metagenomics: genomic analysis of microbial communities. Annual review of genomics and human genetics, 5, 247-277.
21. Shakya M, Lo CC, Chain PSG. (2019) Advances and Challenges in Metatranscriptomic Analysis. Front Genet., 10:904. doi: 10.3389/fgene.2019.00904.
22. Sharon, I., Morowitz, M. J., & Thomas, B. C. (2013). Time series community genomics analysis reveals rapid shifts in bacterial species, strains, and phage during infant gut colonization. Genome research, 23(1), 111-120.
23. Schoch, C. L., Seifert, K. A., Huhndorf, S., Robert, V., Spouge, J. L., Levesque, C. A., ... & Crous, P. W. (2012). Nuclear ribosomal internal transcribed spacer (ITS) region as a universal DNA barcode marker for Fungi. Proceedings of the National Academy of Sciences, 109(16), 6241-6246.
24. Tringe, S. G., von Mering, C., Kobayashi, A., Salamov, A. A., Chen, K., Chang, H. W., ... & Rubin, E. M. (2005). Comparative metagenomics of microbial communities. Science, 308(5721), 554-557.
25. Tyson, G. W., Chapman, J., Hugenholtz, P., Allen, E. E., Ram, R. J., Richardson, P. M., ... & Banfield, J. F. (2004). Community structure and metabolism through reconstruction of microbial genomes from the environment. Nature, 428(6978), 37-43.
26. Urich, T., Lanzén, A., Qi, J., Huson, D. H., Schleper, C., & Schuster, S. C. (2008). Simultaneous assessment of soil microbial community structure and function through analysis of the meta-transcriptome. PLoS One, 3(6), e2527.
27. Verberkmoes, N. C., Russell, A. L., Shah, M., Godzik, A., Rosenquist, M., Halfvarson, J., ... & Hettich, R. L. (2009). Shotgun metaproteomics of the human distal gut microbiota. The ISME journal, 3(2), 179-189.
28. Wilmes, P., & Bond, P. L. (2004). Metaproteomics: studying functional gene expression in microbial ecosystems. Trends in microbiology, 12(12), 506-509.
29. Zhou, J., & He, Z. (2018). Methods for the extraction of microbial DNA from environmental samples. In Handbook of Hydrocarbon and Lipid Microbiology (pp. 1-9). Springer, Cham.