International Journal of Research in Virology

Applications of Molecular Phylogeny in Disease Diagnosis

Aminu RF*, Emurotu MO, Mofolorunsho KC, Atokolo A and Okpanachi RO

Department of Microbiology, Prince Abubakar Audu University, Anyigba, Kogi State, Nigeria. *Correspondence:

Aminu RF, Department of Microbiology, Prince Abubakar Audu University, Anyigba, Kogi State, Nigeria.

Received: 09 Jan 2024; Accepted: 19 Feb 2024; Published: 27 Feb 2024

Citation: Aminu RF, Emurotu MO, Mofolorunsho KC, et al. Applications of Molecular Phylogeny in Disease Diagnosis. Int J Res Virol. 2024; 1(1): 1-8.

Keywords

Molecular biology, Genetics, Cancer research, Disease, Diagnosis.

Introduction

In the realm of modern medicine, the accurate and timely diagnosis of diseases stands as a cornerstone for effective patient care and public health management. Over the past few decades, advancements in molecular biology and genetics have revolutionized the field of disease diagnosis. One such powerful tool that has emerged as a game-changer is molecular phylogeny. Molecular phylogeny, the study of evolutionary relationships among organisms based on molecular data, has found extensive applications in the diagnosis and identification of various diseases. This multifaceted approach combines genetic information, computational analysis, and phylogenetic methods to unravel the complex web of pathogens, providing invaluable insights into their evolution, transmission, and virulence [1].

The traditional methods for disease diagnosis, which primarily relied on culturing and phenotypic characterization, were often labor-intensive, time-consuming, and sometimes unreliable, especially when dealing with fast-evolving pathogens or those that are difficult to culture. In contrast, molecular phylogeny leverages the genetic material of the pathogen, such as DNA or RNA, to unveil its identity and evolutionary history. This approach has had a transformative impact on disease diagnosis, offering rapid and precise results across various fields of medicine, from infectious diseases to cancer research [2].

Molecular phylogeny is a powerful tool in disease diagnosis and understanding the evolutionary relationships among organisms at the molecular level. It involves the study of genetic material, such as DNA and RNA, to construct evolutionary trees or phylogenies. These phylogenies can help identify the origins of pathogens, track their spread, and develop effective diagnostic tools and treatments.

Principles of Molecular phylogeny

Homology: Homology, as a fundamental principle in molecular phylogeny, plays a crucial role in disease diagnosis by enabling researchers and healthcare professionals to trace the evolutionary relationships between genes, proteins, and organisms. This concept stems from the idea that closely related species share common ancestors and, as a result, inherit genetic material with structural and functional similarities. These shared characteristics, or homologous traits, are essential for understanding the genetic basis of diseases and predicting their behavior across various species [3].

One key aspect of homology in molecular phylogeny is the identification of homologous genes and proteins. Researchers use comparative genomics and bioinformatics tools to detect sequences that have evolved from a common ancestral gene. By aligning sequences and analyzing their similarities and differences, scientists can pinpoint genes or proteins associated with specific diseases. This approach has been instrumental in identifying disease-causing mutations, understanding genetic predispositions, and developing targeted therapies. For instance, the study of homologous genes has greatly contributed to the field of oncology. Many cancer-related genes, such as the BRCA1 and BRCA2 genes associated with breast and ovarian cancer, have homologs in various species. By examining these homologous genes across different organisms, researchers gain insights into the evolution of cancer susceptibility and can develop more effective diagnostic tests and treatments [4]. Furthermore, the principle of homology extends beyond genes and proteins to include anatomical structures and pathways. Comparative anatomy and embryology allow scientists to identify homologous structures in different species, shedding light on the evolutionary history of organisms and their susceptibility to diseases. This information aids in the diagnosis of genetic disorders and informs the development of therapies tailored to specific species [5].

In disease diagnosis, homology-based approaches also enable the prediction of disease outcomes and the assessment of potential treatments. By studying how similar genes or proteins function in closely related species, researchers can infer how a disease might progress and respond to interventions. This knowledge is invaluable for personalized medicine, as it allows healthcare providers to tailor treatments based on an individual's genetic makeup and the homologous traits they share with other species [6].

Sequence Alignment

Sequence alignment in molecular phylogeny is a fundamental process that involves comparing genetic sequences, such as DNA or protein sequences, to identify similarities and differences among species or organisms. This alignment is crucial for reconstructing evolutionary relationships and building phylogenetic trees. It helps researchers infer common ancestry, estimate divergence times, and understand evolutionary history. Various algorithms, like ClustalW or MAFFT, are used to align sequences by optimizing the placement of gaps and substitutions to maximize similarity, facilitating accurate phylogenetic analysis [7].

Phylogenetic Trees: A phylogenetic tree is a graphical representation used in molecular phylogeny to depict the evolutionary relationships among species or genes. It illustrates the branching patterns that result from genetic divergence over time. The tree's structure is based on molecular data, such as DNA or protein sequences, and is constructed using various methods like maximum likelihood or neighbor-joining [8].

Genetic Distance

Genetic distance plays a crucial role in molecular phylogeny, especially in the context of disease diagnosis. Genetic distance measures the evolutionary divergence between two sequences, providing insights into their common ancestry and evolutionary history. In disease diagnosis, understanding genetic distance helps scientists and healthcare professionals identify the origins and mutations of pathogens, enabling more accurate diagnoses and effective treatment strategies [9].

To grasp the concept of genetic distance, one must first appreciate the idea of molecular evolution. Over time, genetic material accumulates changes, or mutations, due to various factors like random genetic drift, natural selection, and environmental pressures. These mutations accumulate in a clock-like manner, leading to the formation of genetic diversity among populations. Genetic distance quantifies the number of differences, or mutations, between two sequences. The greater the genetic distance, the longer the time since their common ancestor, suggesting a more distant evolutionary relationship [10].

In disease diagnosis, genetic distance is employed to classify and trace the origins of pathogens. For instance, in the case of viral infections like HIV or SARS-CoV-2, scientists analyze the genetic distance between viral strains isolated from different patients. By comparing the genetic sequences of these strains, they can infer

their evolutionary relationships and identify the source of the outbreak. This information is crucial for implementing targeted interventions and tracking the spread of the disease [11].

Phylogenetic Inference Methods

Phylogenetic inference methods are a fundamental principle in molecular phylogeny, playing a crucial role in disease diagnosis. One widely used phylogenetic inference method is Maximum Likelihood (ML). ML estimates the evolutionary history that maximizes the probability of observing the given genetic data under a specific model of evolution. This method is highly versatile and can accommodate complex evolutionary processes, making it suitable for analyzing the genetic diversity of pathogens. Another commonly employed method is Bayesian Inference (BI), which uses probability distributions to estimate the phylogenetic tree and model parameters. BI allows for the incorporation of prior knowledge and uncertainty in the analysis, providing a robust framework for phylogenetic reconstruction [3].

Furthermore, Distance-based methods like Neighbor-Joining (NJ) and character-based methods like Parsimony are also employed in disease diagnosis. These methods use genetic distance or character state changes to infer evolutionary relationships. While they may be less statistically rigorous than ML and BI, they are computationally efficient and can be useful for preliminary assessments [12]. These phylogenetic inference methods rely on extensive datasets of genetic sequences, obtained from various sources such as patient samples, clinical isolates, and genomic databases. By comparing these sequences and applying phylogenetic methods, researchers can trace the transmission pathways of pathogens, identify potential sources of infection, and determine the degree of relatedness between different strains [13].

In the context of disease diagnosis, phylogenetic inference methods provide valuable insights into the evolution of pathogens and their interactions with host populations. For instance, during disease outbreaks, these methods can help identify the index case, track the spread of the disease, and assess the effectiveness of control measures [10].

Techniques in Molecular Phylogeny

This basic technique in molecular phylogenic analysis includes: **DNA Sequencing**: DNA sequencing is a fundamental tool in molecular phylogeny, the study of evolutionary relationships among organisms. It involves determining the order of nucleotide bases (A, T, C, G) in a DNA molecule. By comparing these sequences across different species, scientists can infer evolutionary history, construct phylogenetic trees, and understand genetic relatedness. This method revolutionized the field, enabling more accurate and detailed insights into the evolutionary tree of life.

PCR (Polymerase Chain Reaction)

Polymerase Chain Reaction (PCR) is a fundamental molecular biology technique used in molecular phylogeny to amplify and analyze specific DNA sequences. It plays a crucial role in reconstructing evolutionary relationships among organisms by providing researchers with the ability to obtain sufficient DNA for analysis, even from limited or degraded samples. It involves three main steps: denaturation, annealing, and extension [14].

Phylogenetic Markers

Phylogenetic markers are a fundamental technique in molecular phylogeny, a field dedicated to unraveling the evolutionary relationships among species by examining their genetic material. These markers, also known as molecular markers or genetic markers, are specific regions within the DNA or RNA of organisms that are used to infer evolutionary relationships based on shared ancestry. Rather than relying on visible traits or morphological characteristics, molecular phylogenetics leverages the power of molecular biology to elucidate the evolutionary history of organisms [15].

The utility of phylogenetic markers lies in their evolutionary conservation. These markers are selected based on their relatively slow mutation rates and are typically present across a wide range of species. By comparing these markers across different organisms, scientists can construct phylogenetic trees that depict the branching patterns of evolutionary relationships. The primary advantage of molecular markers is their objectivity; they provide quantitative data that can be analyzed statistically, reducing subjectivity in phylogenetic reconstructions [16]. Commonly used phylogenetic markers include genes like ribosomal RNA (rRNA), mitochondrial DNA (mtDNA), and protein-coding genes such as cytochrome c oxidase subunit 1 (COI) in animals or ribulose-1,5-bisphosphate carboxylase/oxygenase (rbcL) in plants. These markers are selected for their stability and widespread presence, which ensures that they provide informative data for a wide range of organisms. Researchers also often use multiple markers to increase the robustness of their phylogenetic reconstructions [17].

Multiple Sequence Alignment

Multiple Sequence Alignment (MSA) is a technique in the field of molecular phylogeny, a branch of biology that seeks to understand the evolutionary relatedness between different species or organisms based on their genetic sequences, typically DNA or protein sequences. MSA plays a pivotal role in this process by allowing scientists to compare and analyze the similarities and differences in sequences from multiple organisms, enabling the reconstruction of evolutionary trees or phylogenetic trees. These trees provide insights into the evolutionary history and relationships among species [18].

MSA begins with the collection of sequences from various species of interest. These sequences can represent a specific gene, a group of genes, or even entire genomes. The primary objective of MSA is to align these sequences in a way that maximizes the similarity between homologous positions, where homologous positions are those that share a common ancestor. By aligning sequences, researchers can identify conserved regions, which are indicative of functional constraints, and variable regions, which may provide insights into evolutionary changes [19]. One of the most commonly used algorithms for MSA is the progressive alignment

method, such as the ClustalW or Clustal Omega algorithm. These algorithms employ a step-by-step approach, beginning with the pairwise alignment of sequences, followed by progressively building the alignment by adding sequences one at a time based on their similarity scores. Other algorithms like MUSCLE and MAFFT use different strategies to achieve MSA [13]. While MSA is a powerful tool in molecular phylogeny, it is not without its challenges. The "multiple" in MSA signifies that it deals with more than two sequences, which increases the complexity of the problem. Additionally, MSA is an NP-hard problem, meaning it becomes computationally intensive as the number of sequences or sequence length increases. As a result, heuristic algorithms are often employed to approximate the optimal alignment quickly. Despite its challenges, MSA is essential for constructing accurate phylogenetic trees. The alignment produced by MSA serves as the basis for various phylogenetic analysis methods, including maximum likelihood and Bayesian inference. By comparing aligned sequences, researchers can infer evolutionary relationships, estimate divergence times, and gain insights into the molecular evolution of species [18].

Phylogenetic Software

Phylogenetic software employs various computational algorithms to analyze molecular data and infer evolutionary relationships. One of the fundamental methods used is sequence alignment, where software aligns sequences by identifying similarities and differences, helping to establish evolutionary connections. Commonly used phylogenetic software packages include MEGA (Molecular Evolutionary Genetics Analysis), PHYLIP (PHYLogeny Inference Package), and RAxML (Randomized Axelerated Maximum Likelihood). These tools apply different mathematical models and algorithms to estimate phylogenetic trees based on sequence data, and their effectiveness often depends on the size and complexity of the dataset [20]. Furthermore, these software packages offer methods to assess the reliability of the inferred trees. Bootstrapping, a resampling technique, is frequently used to estimate the confidence level associated with specific branches on the phylogenetic tree. This provides valuable insights into the robustness of the evolutionary relationships inferred from the data [21].

Molecular Clocks

This approach relies on the assumption that mutations accumulate in a linear fashion over time in the DNA or protein sequences of different species. By comparing these genetic sequences, scientists can estimate the time of divergence between species or the common ancestor they share [22]. One of the key advantages of molecular clocks is their ability to provide a temporal framework for phylogenetic trees. Traditional methods of phylogenetic analysis, such as morphological characteristics, can be imprecise when inferring evolutionary relationships and divergence times. Molecular clocks, on the other hand, offer a quantitative approach to estimate when two species or lineages split from a common ancestor. This is particularly valuable when dealing with species that lack a rich fossil record or when fossils are insufficient to construct a comprehensive evolutionary timeline [13]. Molecular clocks can be applied to various types of genetic markers, including DNA sequences and amino acid sequences in proteins. Commonly used molecular clock genes include ribosomal RNA (rRNA), mitochondrial DNA (mtDNA), and nuclear genes like those coding for histones. Researchers calibrate these clocks using known divergence times from the fossil record or other historical data, allowing them to calculate the rate of genetic change for a given gene or region [18].

Application in Disease Diagnosis

Molecular phylogeny, the study of evolutionary relationships among organisms based on molecular data, has revolutionized various fields of biology, including disease diagnosis. This essay explores the applications of molecular phylogeny in disease diagnosis, highlighting its significance in understanding disease origins, tracking disease outbreaks, and developing targeted treatment strategies.

Phylogenetic Analysis for Pathogen Identification

One of the primary applications of molecular phylogeny in disease diagnosis is the identification of pathogens. Molecular techniques such as DNA sequencing allow researchers to analyze the genetic material of unknown microorganisms and compare it to known sequences in databases. By constructing phylogenetic trees, scientists can pinpoint the evolutionary relationships between pathogens, aiding in their accurate identification. For instance, the Human Immunodeficiency Virus (HIV) has multiple strains with varying drug resistance profiles, and phylogenetic analysis plays a crucial role in tailoring antiretroviral therapy [22].

Tracking Disease Outbreaks

Molecular phylogeny is instrumental in tracking the spread of infectious diseases. During outbreaks, genomic sequences of pathogens can be rapidly analyzed to determine the source and transmission routes. For example, during the COVID-19 pandemic, scientists used phylogenetic analysis of SARS-CoV-2 genomes to trace the virus's origins, understand its transmission dynamics, and develop effective containment strategies [23]. Molecular phylogeny has become an indispensable tool in the field of disease diagnosis and tracking of outbreaks. It provides valuable information about the origins, transmission patterns, and evolution of pathogens, helping public health officials and researchers respond effectively to disease threats. By harnessing the power of genetic data and phylogenetic analysis, we can better understand and control infectious diseases, ultimately safeguarding public health [24].

Evolutionary History of Pathogens

The evolutionary history of pathogens is a fascinating field of study that leverages molecular phylogeny to enhance disease diagnosis and management. This approach relies on the principles of evolutionary biology to trace the ancestry and genetic relationships among various disease-causing agents, such as bacteria, viruses, and parasites. By understanding the evolutionary history of pathogens, scientists and healthcare professionals can make more informed decisions regarding disease prevention,

treatment and surveillance [25]. Molecular phylogeny, a powerful tool in this context, involves the analysis of genetic material such as DNA and RNA sequences, to reconstruct the evolutionary relationships among pathogens. This is achieved by comparing genetic sequences of different strains or species of pathogens and constructing phylogenetic trees that depict their evolutionary divergence. Notably, the technique is based on the assumption that closely related pathogens share a more recent common ancestor, whereas those that are distantly related diverged from a common ancestor further back in time [26]. The evolutionary history of pathogens is instrumental in understanding drug resistance. By studying how pathogens evolve and adapt to selective pressures such as antibiotic use, researchers can anticipate the emergence of drug-resistant strains. This knowledge informs the development of new therapies and treatment guidelines to combat drug-resistant infections [25].

Zoonotic Disease Identification

Zoonotic diseases, which are infectious diseases that can be transmitted between animals and humans, pose significant public health threats. Identifying and tracking the sources and transmission routes of these diseases is crucial for effective disease control and prevention. Molecular phylogeny, a field of biology that examines the evolutionary relationships among organisms using genetic data, has emerged as a powerful tool in the diagnosis of zoonotic diseases [23]. One key application of molecular phylogeny in zoonotic disease diagnosis is the identification of reservoir hosts. Reservoir hosts are animal species that harbor and transmit a pathogen to humans or other susceptible hosts. Understanding which animals serve as reservoirs for zoonotic diseases is essential for targeted surveillance and control efforts. Molecular phylogenetic analyses can help identify the closest relatives of a pathogen found in humans, shedding light on potential reservoir species [13]. For example, the identification of bats as reservoir hosts for various coronaviruses including the one responsible for the COVID-19 pandemic was made possible through molecular phylogenetic studies. By comparing the genetic sequences of coronaviruses found in bats and humans, researchers established a link between the two, highlighting the role of bats in the transmission of these viruses [27]. Moreover, molecular phylogeny plays a crucial role in tracking the evolution of zoonotic pathogens. As these pathogens adapt and evolve, they can become more virulent or acquire resistance to existing treatments. By monitoring genetic changes over time, scientists can identify emerging strains of zoonotic pathogens and assess their potential for increased transmission or resistance. This information informs the development of diagnostic tests and vaccines to combat evolving threats [23].

Antimicrobial Resistance

Antimicrobial resistance (AMR) poses a significant global health threat as infectious diseases become increasingly difficult to treat due to the resistance of pathogens to antibiotics and other antimicrobial agents. Molecular phylogeny plays a crucial role in disease diagnosis by helping to understand and combat AMR. This approach leverages the genetic diversity of microorganisms to track the spread of resistant strains and inform treatment strategies [24]. Molecular phylogeny employs techniques such as DNA sequencing and comparative genomics to analyze the genetic makeup of pathogens. By examining the genetic sequences of bacteria, viruses, and fungi responsible for infectious diseases, researchers can identify the genetic mutations or variations associated with antimicrobial resistance. These mutations can confer resistance to specific antibiotics or antimicrobial agents, making the pathogens harder to eradicate. Studying the evolutionary relationships among resistant and non-resistant strains helps scientists pinpoint the origins and transmission routes of AMR [28].

One practical application of molecular phylogeny in AMR diagnosis is the identification of resistance genes within microbial populations. Researchers can use genomic sequencing to identify the presence of genes that code for resistance mechanisms, such as beta-lactamases in bacteria or efflux pumps in fungi. Knowing which resistance genes are present in a particular strain allows healthcare professionals to choose the most effective treatment and avoid prescribing antibiotics that the pathogen is already resistant to. Moreover, molecular phylogeny can provide insights into the spread of AMR at both local and global scales. By comparing the genetic profiles of resistant pathogens collected from different geographic regions, scientists can trace the movement of resistant strains. This information is invaluable for public health efforts to monitor and control the spread of AMR. It helps authorities implement targeted interventions such as infection control measures or the restriction of certain antibiotics in regions where resistance is prevalent [22].

Forensic Epidemiology

Molecular phylogeny is also applied in forensic epidemiology, where it helps in solving disease-related mysteries. By comparing the genetic fingerprints of pathogens found at different crime scenes or in outbreaks, investigators can establish connections and pinpoint sources of infection. This has been instrumental in solving cases involving foodborne illnesses and bioterrorism [22].

Successful Applications of Molecular Phylogeny in Disease Diagnosis

Molecular phylogeny has played a crucial role in disease diagnosis by helping researchers understand the evolutionary relationships among microorganisms and enabling more accurate identification of pathogens. Here are a few case studies and examples that highlight successful applications of molecular phylogeny in disease diagnosis:

HIV/AIDS: Molecular phylogeny has been instrumental in tracking the evolution of the human immunodeficiency virus (HIV) and understanding its transmission dynamics. By analyzing the genetic diversity of HIV strains, researchers can identify the source of infection and monitor the spread of drug-resistant variants. For example, a study published in the journal "Nature" in 2014 used molecular phylogeny to trace the origin and spread of HIV in North America, providing valuable insights for prevention and treatment strategies [29].

Influenza Virus: The influenza virus undergoes frequent genetic changes, making it challenging to develop effective vaccines and antiviral drugs. Molecular phylogeny has been used to analyze the genetic diversity of influenza strains and predict which strains are likely to be prevalent in future seasons. This information guides the selection of influenza vaccine components. The Global Initiative on Sharing All Influenza Data (GISAID) is a platform that uses molecular phylogeny to track the evolution of influenza viruses worldwide [30].

Tuberculosis (TB): *Mycobacterium tuberculosis*, the causative agent of TB, exhibits genetic diversity that can impact drug resistance and transmission patterns. Molecular phylogeny has been applied to study the evolutionary history of *M. tuberculosis* strains. For instance, a study published in "Science Translational Medicine" in 2015 used whole-genome sequencing and phylogenetic analysis to identify transmission patterns in a TB outbreak, helping public health officials to control the spread of the disease.

Ebola Virus: During the 2014-2016 Ebola outbreak in West Africa, molecular phylogeny played a vital role in understanding the origin and spread of the virus. By sequencing viral genomes from patient samples and wildlife reservoirs, researchers were able to reconstruct the Ebola virus's evolutionary history. This information aided in tracking the transmission chains and developing containment strategies [29].

COVID-19: The ongoing COVID-19 pandemic is a prominent example of the use of molecular phylogeny in disease diagnosis. Researchers worldwide have sequenced SARS-CoV-2 genomes to track the emergence of new variants and assess their potential impact on vaccine efficacy and transmission. This information has guided public health measures and vaccine development efforts.

Limitations and Challenges of Molecular Phylogeny in Disease Diagnosis

Molecular phylogeny has significantly advanced our understanding of the evolutionary relationships among organisms by analyzing genetic material, primarily DNA sequences. While it has been a powerful tool in various scientific fields, including evolutionary biology and ecology, it also has important applications in disease diagnosis. However, like any scientific technique, molecular phylogeny has its limitations when applied to disease diagnosis.

Data Availability and Quality

Genetic Variability: Molecular phylogeny relies on genetic data, such as DNA sequences, to infer relationships. However, not all pathogens have sufficient genetic variability to differentiate them effectively. Some closely related strains may have nearly identical sequences, making it challenging to distinguish them accurately [31].

Sampling Bias (Limited Sampling): The accuracy of molecular phylogenetic analysis is highly dependent on the availability and quality of genetic samples. Limited sampling, especially in under-

studied regions, can result in incomplete or biased phylogenies, potentially missing important strains or variants [14].

Recombination

Horizontal Gene Transfer: Some pathogens, such as bacteria, can undergo horizontal gene transfer, where genetic material is exchanged between unrelated lineages. This can blur the phylogenetic signal and complicate the accurate reconstruction of evolutionary histories [32].

Convergent Evolution

Convergence: Molecular phylogenetic methods assume that similar genetic sequences indicate close evolutionary relationships. However, pathogens can evolve convergently, leading to similar sequences in distantly related lineages. This can result in misclassification [33].

Temporal Resolution

Lack of Temporal Information Molecular phylogeny provides insight into evolutionary relationships but may not offer precise temporal information about when a specific strain emerged or when it entered a population. This can be crucial for tracking disease outbreaks [34].

Limited Predictive Power

Functional Insights: Molecular phylogeny typically focuses on genetic relationships, but it may not provide direct insights into the functional characteristics of pathogens, such as virulence or drug resistance, which are critical for disease diagnosis and treatment [35].

Computational Challenges

Big Data Handling: Analyzing large-scale genetic data for phylogenetic reconstruction can be computationally intensive and may require specialized software and expertise [36].

Interpreting phylogenetic trees: Some pathogens can form polyphyletic groups, where genetically similar strains are found in distinct branches of the tree. This can challenge our understanding of their evolutionary history. Also, Interpreting the meaning of branch lengths in a phylogenetic tree can be complex, as they represent genetic divergence but not necessarily time [28].

Clinical Relevance (Linking Phylogeny to Clinical Outcomes): While molecular phylogeny can provide insights into the evolutionary history of pathogens, translating this information into actionable clinical decisions can be challenging 37].

Advancements of Molecular Phylogeny in Disease Diagnosis

Molecular phylogeny, a branch of biology that investigates the evolutionary relationships among species or organisms using molecular data has witnessed remarkable advancements in recent years. While its primary focus has traditionally been on evolutionary biology and taxonomy, molecular phylogeny has found increasingly significant applications in the field of disease diagnosis. This article explores the key advancements and innovations in molecular phylogeny for disease diagnosis, highlighting how it has revolutionized our ability to identify and combat various diseases.

DNA Sequencing Technologies

The most significant advancement in molecular phylogeny for disease diagnosis is undoubtedly the rapid progress in DNA sequencing technologies. The advent of next-generation sequencing (NGS) has enabled researchers to generate vast amounts of DNA sequence data quickly and cost-effectively. This has been pivotal in identifying disease-causing pathogens, elucidating their genetic diversity, and tracking their evolution. For example, NGS has been crucial in studying the genetic diversity of HIV, which has implications for vaccine development and treatment strategies [38].

Metagenomics

Metagenomics is a powerful tool within molecular phylogeny that has transformed our understanding of microbial communities in various environments, including the human body. It involves sequencing the collective genetic material from a complex mixture of microorganisms, allowing for the detection of pathogens in clinical samples without the need for culture-based methods. Metagenomics has been instrumental in identifying novel viruses responsible for outbreaks such as the discovery of the Ebola virus in bats.

Phylogenetic Analysis

Advancements in phylogenetic analysis software and algorithms have facilitated the reconstruction of evolutionary trees with higher accuracy and speed. Phylogenetic trees are invaluable in tracking the transmission of infectious diseases, understanding the origin of outbreaks, and identifying potential reservoirs of pathogens. For example, during the COVID-19 pandemic, real-time phylogenetic analysis played a crucial role in monitoring the virus's spread and detecting new variants [39].

The revolutionary CRISPR-Cas technology has been adapted for disease diagnosis, allowing for the rapid and precise detection of pathogens. CRISPR-based diagnostics are highly sensitive and specific, making them valuable tools for identifying infectious agents. This innovation has the potential to revolutionize pointof-care testing for diseases, including bacterial and viral infections [40].

Conclusion

The applications of molecular phylogeny in disease diagnosis has been able to revolutionized the ability to understand, track, and combat infectious diseases. Its role in pathogen identification, transmission dynamics, evolutionary insights, drug resistance monitoring, personalized medicine, and forensic epidemiology underscores its versatility and importance in healthcare. As technology continues to advance, molecular phylogeny will remain at the forefront of disease diagnosis, contributing to better public health outcomes and a deeper understanding of the microbial world.

References

- Smith GJD, Vijaykrishna D. Bats and the emergence of bats. In Bats and Viruses John Wiley & Sons. 2011; 325-344.
- Prahallad A, Bernards R. Opportunities and challenges provided by crosstalk between signalling pathways in cancer. Oncogene. 2015; 35: 1073-1079.
- 3. Felsenstein J. Confidence limits on phylogenies: An approach using the bootstrap. Evolution. 1985; 39: 783-791.
- Koonin EV, Galperin MY. Sequence–Evolution–Function: Computational Approaches in Comparative Genomics. Springer. 2003;
- Visscher PM, Brown MA, McCarthy MI, et al. Five years of GWAS discovery. The American Journal of Human Genetics. 2012; 90: 7-24.
- Carroll MW, Matthews DA, Hiscox JA, et al. Temporal and spatial analysis of the 2014–2015 Ebola virus outbreak in West Africa. Nature. 2015; 524: 97-101.
- Wang C, Horby PW, Hayden FG, et al. A novel coronavirus outbreak of global health concern. Lancet (London, England). 2020; 395: 470-473.
- 8. Hasegawa, M, Kishino H, Yano T et al. Dating of the humanape splitting by a molecular clock of mitochondrial DNA. Journal of Molecular Evolution. 1985; 22: 160-174.
- 9. Nei M, Kumar S. Molecular evolution and phylogenetics. Oxford University Press. 2000; 352.
- Holmes EC, Drummond AJ. The evolutionary genetics of viral emergence. Current topics in microbiology and immunology. 2007; 30: 51-66.
- 11. Lee RS, Ma X. Molecular techniques in the diagnosis of systemic fungal infections. Expert review of molecular diagnostics. 2018; 18: 277-290.
- Pybus OG, Rambaut A. Evolutionary analysis of the dynamics of viral infectious disease. Nature Reviews Genetics. 2009; 10: 540-550.
- Katoh K, Standley DM. MAFFT multiple sequence alignment software version 7: improvements in performance and usability. Molecular Biology and Evolution. 2013; 30: 772-780.
- Pybus OG, Rambaut A. Evolutionary analysis of the dynamics of viral infectious disease. Nature Reviews Genetics. 2009; 10: 540-550.
- 15. Soltis DE, Soltis PS. Applying the bootstrap in phylogeny reconstruction. Project Euclid. 2003; 18: 256-267.
- Hillis DM, Bull JJ. An empirical test of bootstrapping as a method for assessing confidence in phylogenetic analysis. Systematic Biology. 1993; 42: 182-192.
- 17. Holmes EC. Evolutionary history and phylogeography of human viruses. Annual Review of Microbiology. 2008; 62: 307-328.
- Thompson JD, Higgins DG, Gibson TJ. CLUSTAL W: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice. Nucleic Acids Research. 1994; 22: 4673-4680.

- Edgar RC. MUSCLE: multiple sequence alignment with high accuracy and high throughput. Nucleic Acids Research. 2004; 32: 1792-1797.
- Stamatakis A. RAxML version 8: A tool for phylogenetic analysis and post-analysis of large phylogenies. Bioinformatics. 2014; 30: 1312–1313.
- 21. Ronquist F, Teslenko M, van der Mark P, et al. MrBayes 3.2: Efficient Bayesian phylogenetic inference and model choice across a large model space. Systematic Biology. 2012; 61: 539–542.
- 22. Palacios G, Druce J, Du L, et al. A new arenavirus in a cluster of fatal transplant-associated diseases. New England Journal of Medicine. 2008; 358: 991-998.
- Worobey M, Pekar J, Larsen BB, et al. The emergence of SARS-CoV-2 in Europe and North America. Science. 2020; 370: 564-570.
- Manson AL, Cohen KA, Abeel T, et al. Genomic analysis of globally diverse Mycobacterium tuberculosis strains provides insights into the emergence and spread of multidrug resistance. Nature Genetics. 2017; 49: 395-402.
- 25. Smith DJ, Lapedes AS. Predicting the emergence of human h5n1 influenza in pandemic. Influenza and Other Respiratory Viruses. 2006; 1: 105-116.
- 26. Dudas G, Andrew JT, Baele G, et al. Virus genomes reveal factors that spread and sustained the Ebola epidemic. Nature. 2017; 544: 309-315
- 27. Duffy S, Shackelton LA, Holmes EC. Rates of evolutionary change in viruses: patterns and determinants. Nature Reviews Genetics. 2008; 9: 267-276.
- Drummond AJ, Rambaut A. BEAST: Bayesian evolutionary analysis by sampling trees. BMC evolutionary biology. 2007; 7: 214.
- 29. Dudas G, Carvalho LM, Bedford T, et al. Virus genomes reveal factors that spread and sustained the Ebola epidemic. Nature. 2017; 544: 309-315.
- 30. Gire SK, Goba A, Andersen KG, et al. Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. Science. 2014; 345: 1369-1372.
- 31. Streicker DG, Turmelle AS, Vonhof MJ, et al. Host Phylogeny Constrains Cross-Species Emergence and Establishment of Rabies Virus in Bats. Science. 2010; 329: 676-679.
- 32. Didelot X, Maiden MC. Impact of recombination on bacterial evolution. Trends in Microbiology. 2010; 18: 315-322.
- Cui Y, Achtman M, Balloux F, et al. Historical variations in mutation rate in an epidemic pathogen, Yersinia pestis. Proceedings of the National Academy of Sciences. 2013; 110: 577-582.
- 34. Volz EM, Siveroni I. Bayesian phylodynamic inference with complex models. PLoS Computational Biology. 2018; 14.
- 35. Harrison A. The use of genomics in microbial epidemiology and antimicrobial surveillance. The Lancet Infectious Diseases. 2012; 12: 641-650.

- 36. Suchard MA, Lemey P, Baele G, et al. Bayesian phylogenetic and phylodynamic data integration using BEAST 1.10. Virus Evolution. 2018; 4: 016.
- Morelli MJ, Phylogenetic analysis of rubella virus in western countries of the WHO European Region. Virology Journal. 2010; 7: 279.
- 38. Gonzales MJ, Delwart E, Rhee SY, et al. The Impact of Next-Generation Sequencing in the Understanding of HIV

Diversity. Viruses. 2012; 4: 2858-2873.

- 39. Faria NR, Claro IM, Candido D, et al. Genomic characterisation of an emergent SARS-CoV-2 lineage in Manaus: preliminary findings. Virological. 2021 372: 1-9.
- 40. Chen JS, Ma E, Harrington LB, et al. CRISPR-Cas12a target binding unleashes indiscriminate single-stranded DNase activity. Science. 2018; 360: 436-439.

© 2024 Aminu RF, et al. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License