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Paratuberculosis Molecular Epidemiology and Genotyping Techniques

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Abstract

The underlying cause of Johne's disease (JD), which primarily affects ruminants and is characterised by chronic diarrhoea and emaciation, is Mycobacterium avium subsp. paratuberculosis (MAP). Johne's illness is extremely widespread around the world and causes significant economic losses due to diminished production. The study of population genetics, pathogenesis, and molecular epidemiology, including disease surveillance and outbreak research, could all benefit from the genotyping of the involved pathogen. Primarily, scientists have presummated the existence of two distinct MAP strains linked to the animal host species (cattle and sheep). In contrast, genetic testing using genetic marker including insertion elements, repetitive sequences, and single nucleotide polymorphisms is now the major method used for MAP characterisation. This project intends to give a general overview of the MAP molecular epidemiology's future prospects are discussed in light of the developments in molecular biological tools used for MAP typing over the last two decades, how these techniques have been applied to answer intriguing epidemiological questions, and the potential uses of these techniques in the future.

Keywords: Emaciation; Paratuberculosis; Mycobacterium; ruminant

Introduction

The M. avium complex includes Mycobacterium (M.) avium subsp. paratuberculosis (MAP) (MAC). It is the primary cause of paratuberculosis, often known as Johne's disease (JD), a chronic gastroenteritis that mostly affects domestic ruminants and results in significant financial losses, particularly for the global dairy industry. It was also discovered that the disease occasionally affected wild ruminants. MAP was also found in a variety of hosts, including non-human primates, non-ruminant fauna, dogs, feral cats, rabbits, parrots, and bears, albeit these hosts did not exhibit any clinical symptoms. A potential function for MAP in the aetiology of Crohn's disease (CD), a chronic, disabling gastroenteritis that affects humans, has been disputed for more than a century [1]. The "Linda" isolates, one of the first MAP samples to come from a Crohn's patient one of the major challenges to proving or disproving this idea for such a long time was the difficulties of consistent and reproducible MAP isolation from human CD patients. A subfield of epidemiology called molecular epidemiology of infectious illnesses uses molecular biology methods to investigate the causes and distribution of disease incidence in a given population. In this review, we'll concentrate on the state-of-the-art knowledge of MAP diversity, the developments made in MAP genotyping molecular biology methods over the past two decades, and the epidemiological uses of these methods [2].

Materials and Method

Historically, epidemiologic and phenotypic traits were used to describe different MAP kinds. Researchers recommended the cattle (C) and sheep (S) type strains as the two main MAP types infecting cattle and sheep, respectively, based on the host from which MAP strains were first recovered. However, improvements in molecular biology have given classification a more solid foundation. Two MAP genetic groups that displayed just host preferences but not exclusivity were found using pulsed-field gel electrophoresis (PFGE), and as a result [3], a new nomenclature for MAP types (type I and II) has been proposed. When compared to type II isolates, which were quickly developing strains typically isolated from cattle but with a larger range, type I isolates were slow growers requiring more than 16 weeks to acquire noticeable growth. It was also determined that a third group, referred to as "intermediate" or "type III," was distinct from type S and type C isolates. However, a recent study using whole genome sequencing found that both types are sheep or type S subgroups. A novel MAP type known as "bison" or "type B" was described for isolates coming from bisons (Bison bison) in Montana, USA, based on an SNP at bp 223 of the insertion element IS1311. In contrast to type S isolates, all IS1311 copies in "type B" isolates showed a thymidine transition [4]. Some copies of the type C isolates had T and others had C nucleotides (NT). The type B is a subgroup of type C, and whole genome sequencing analysis later revealed that some type C strains displayed the IS1311 profile of type S, raising questions about the validity of IS1311 analysis as the go-to approach to distinguish between types C, S, and B. Variations were found after further molecular study of Indian MAP type B isolates.

Result

The designation "Indian bison type" was applied to the isolates that were derived from those that were isolated in the USA. Later, a TG deletion was discovered in the Indian bison type isolates at bp locations 64 and 65 of the IS1322 locus 2. MAP types are currently categorised based on a recent whole genome sequencing-based analysis [5]. Numerous genotyping techniques have been created and used to characterise MAP. The various techniques detailed in this review are listed. A quick and affordable method for PCR-based finger printing is RAPD analysis (Figure 1). In this research, a single short primer (10-22 bases) with any sequence is used to directly amplify the genomic DNA under low stringency PCR conditions. RAPD was frequently employed for subtyping many species, including Mycoplasma, M. TB, and M. avium, in the final decade of the 20th century [6]. For the first time

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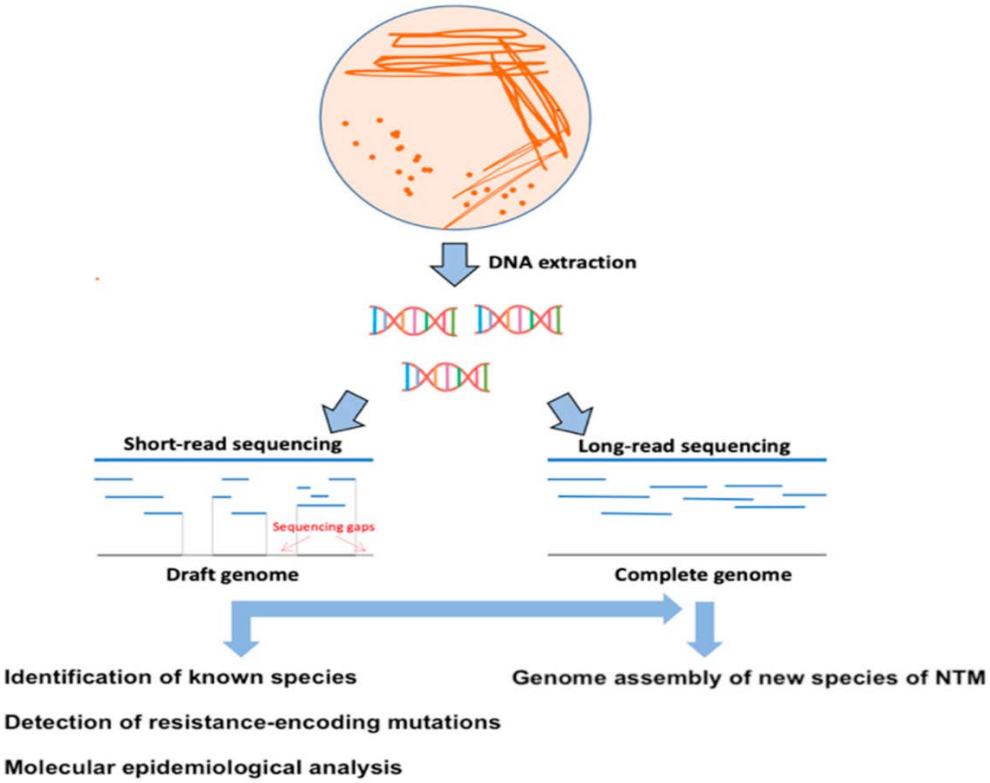

Figure 1: Paratuberculosis Molecular Epidemiology and Genotyping Techniques.

in Germany, RAPD was employed to describe MAP isolates (n = 16) from cattle. The isolates showed heterogeneity, but there wasn't enough information to say that RAPD could be used for MAP genotyping. More recently, one primer was discovered to be suitable for the identification and subtyping of MAP and M. avium utilising a commercial kit's 20 distinct primers.

Discussion

RAPD evaluation. For both the MAP and M. avium isolates under investigation, six distinct genotypes were found. A sheep isolate showed a unique genetic profile, unlike the MAP isolates from cattle, goats, and humans, which were all genetically similar [7]. A quick PCR-based fingerprinting method is AFLP. It entails the use of restriction enzymes to fragment DNA, followed by the ligation of adaptors that complement the restriction areas. Following PCR amplification, the modified restriction fragments are subsequently detected on polyacrylamide gels using autoradiography or fluorescence-based techniques. Since multiple restriction enzymes and adaptors/primers can be mixed, AFLP is a versatile tool that can be used for a number of tasks, including genetic characterisation and genetic mapping.

Additionally, AFLP is capable of detecting polymorphisms across the entire genome. In one study conducted in the USA, 104 genetically heterogeneous MAP isolates collected from various hosts and geographical areas were characterised using AFLP [8]. Unlike past investigations, the MAP isolates isolated from people had AFLP fingerprints. Neither clustered with the ovine isolates nor the bovine isolates. Bovine MAP isolates, regardless of their place of origin, had a low level of genetic variety, whereas isolates from people and sheep showed a higher level of genetic heterogeneity. On the other hand, a different American study team discovered that MAP isolates identified by AFLP utilising 96 primer set had a significant level of genetic diversity. The same research team has more recently reported that AFLP can distinguish between MAP isolates based on epigenetic changes. MAP isolates isolated from tissue samples have distinctive AFLP fingerprints compared to isolates cultivated from faecal samples, even though no sequencing changes were found. It's interesting to note that they were able to pinpoint restriction sites that weren't digested in the tissue-associated isolates, accounting for the ostensible heterogeneity. The authors hypothesised that this might be caused by the presence of a DNA sequence they found upstream of potential methyltransferase recognition sites. First introduced the fingerprint-based genotyping method known as PFGE in 1984 for the division of yeast chromosomes. Even so, it continues to be the benchmark for characterising many harmful microorganisms [9]. In order to improve DNA fragment separation, PFGE is a unique type of gel electrophoresis in which constrained DNA fragments are periodically subjected to periodic reorientation of the electric field relative to the gel direction. For the first time, MAP isolates from various ruminant species were genotyped in Australia using PFGE. The three primary MAP types could be distinguished using PFGE. It has divided the pigmented and non-pigmented MAP isolates into two genetic groupings as a preliminary stage. The restriction endonuclease-based typing method known as RFLP includes fragmenting the genome of an organism using one or more restriction endonuclease enzymes, followed by electrophoresis. The MAP-specific insertion sequence is targeted using a tagged DNA probe, which is subsequently hybridized with these pieces on a membrane [10]. The randomness of the IS900 insertion sites, which vary from one MAP strain to another, is used in IS900-RFLP. As a result, each MAP strain would display a unique banding pattern after hybridization. BstEII, PvuII, and PstI are the three enzymes that have been employed in the majority of investigations. But combining the outcomes of two or more IS900-RFLP experiments with various restriction enzymes raises the MAP genotyping's overall

discriminatory power/index (DI). DI is a number with a range of 0 to 1 [11]. It calculates the likelihood that two strains of a specific microbial population that are not epidemiologically related might be distinguished by a particular typing technique. Additionally, the three main MAP types type I or S, type II or C, and type III or intermediate could be distinguished using IS900-RFLP.

Conclusion

DNA sequences that are repeated head to tail are referred to as tandem repeat (micro- or minisatellites). Prokaryotic genomes frequently contain them, and even strains that are closely related can have different repeat copy numbers. Tandem repeats are divided into three primary types according to the repeat size [12]. Microsatellites, short sequence repeats (SSR), and short tandem repeats are all terms used to describe repetitions that range from 1 to 9 NT. While repeats of more than 100 nt are referred to as macrosatellites, larger repeats are typically referred to as minisatellites or variable number tandem repeats (VNTR). The addition or deletion of repeat copies was thought to be influenced by two different mechanisms, strand slippage brought on by DNA polymerase errors on one side and recombination events on the other. Tandem repeats are a PCR-based method for typing that has several benefits over other approaches. They have simplified and accelerated the characterisation process. They also made direct typing from clinical samples or non-viable cultures possible. Reproducibility, standardization, and the ability to compare data among laboratories are further benefits [13].

Acknowledgement

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Conflict of Interest

None

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