How to Read a Scientific Paper

Dissecting the Format

- Abstract
- Introduction
- Methods
- Results
- Discussion
- Conclusion (not always present)

Functions of the Parts - Abstract

- Provides a comprehensive overview of the paper
- Allows readers to know at a glance if the paper answers a question of interest to them
- Allows readers to note the key findings of the paper

- Focus is on clarity and brevity

Functions of the Parts - Introduction

- Provides background information for readers who may be from a different area and are not as familiar with the specifics of the topic
- Allows the authors to put their questions and findings in a research context

- Serves to focus reader interest to the hypothesis or hypotheses in the paper
- Provides the background critical to understanding the question(s) addressed in the paper

Functions of the Parts - Methods

- Provides enough detail for those familiar in this area to evaluate the strengths and weaknesses of the approach
- Allows other scientists to evaluate the replicability of the experiments

- Many readers less familiar with research in this area will just skim this section, so need to call out important points
- Details that do not affect the results and are typically standardized among scientists in this area do not need to be included

Functions of the Parts - Results

- Provides the data necessary to answer the questions posed in the introduction
  - Interpretation is provided in the discussion

- Focus is on providing data with as little bias as possible
- Almost always includes visual representations of the data as well as statistical results

Functions of the Parts - Discussion

- Answers the questions posed in the introduction by interpretation of results
- Explains the results in the context the authors set up in the introduction
- Explains why the findings are significant to the field
- If a conclusion is absent, may explain the practical or political implications of the findings

Functions of the Parts - Conclusion

- Explains the significance of the findings in a broader context
  - E.g. relevance to policy or management decisions or further theoretical development of the field

Walking through - Introduction

Mycobacterium tuberculosis occurs world-wide and is still killing 2–3 million people each year (7). New tools for tuberculosis control are urgently needed, including a more effective vaccine (8). A series of genotyping tools for M. tuberculosis have been developed (9). Most of these make use of mobile genetic elements or repetitive DNA. Even though these tools have been invaluable for detecting ongoing tuberculosis transmission, the markers upon which they are based change relatively rapidly, making it difficult to define deep phylogenetic relationships (4). In contrast, large sequence polymorphisms (LSPs) represent unique event polymorphisms that can be used to construct robust phylogenies for M. tuberculosis (10). An additional advantage is that, once LSPs have been identified (e.g., by comparativewhole-genome hybridization), simple PCR can be used to screen large numbers of strains in a high-throughput fashion.

In this study, we used comparative genomic and molecular epidemiological tools to define the global population structure of M. tuberculosis and to investigate its influence on the transmission dynamics of M. tuberculosis in San Francisco during an 11-year period.

Walking through - Methods

In an ongoing population- based molecular epidemiological study in San Francisco, CA (19), 2,807 tuberculosis patients were enrolled between January 1991 and December 2001. Of these patients, 2,382 (84.9%) had M. tuberculosis isolated in culture. Demographic and epidemiological data, including place of birth and self-defined ethnicity, were recorded for each patient, and IS6110 RFLP genotyping was performed on 2,141 (89.9%) of the bacterial isolates following standardized methods (19). Isolates with fewer than six IS6110 copies were further genotyped by polymorphic GC-rich sequence (PGRS) RFLP (9). Isolates with matching (clustered) RFLP patterns were considered part of a chain of relatively recent tuberculosis transmission. The protocols and the procedures for the protection of human subjects were approved by Stanford University and the University of California, San Francisco.

Walking through – Results

The analysis of our global sample of 875 strains revealed six main lineages and 15 sublineages of M. tuberculosis (Fig. 1a, Tables 1 and 3, and Table 6, which is published as supporting information on the PNAS web site). Some of these lineages correspond to strain groupings that have previously been reported. For example, the Indo-Oceanic lineage includes a group of strains that have been referred to as ‘‘ancestral’’ due to the fact that they conserve the TbD1 genomic region, which is deleted in ‘‘modern’’ strains of M. tuberculosis (14). The East-Asian lineage includes, but is not limited to, the Beijing family of strains (13). The West-African lineages 1 and 2 correspond to strains that have traditionally been named Mycobacterium africanum (12), and the Euro-American lineage regroups strains that have generally been described as principal genetic groups 2 and 3 (15–17).

Walking through - Discussion

The analysis of our global sample of 875 strains revealed six main lineages and 15 sublineages of M. tuberculosis (Fig. 1a, Tables 1 and 3, and Table 6, which is published as supporting information on the PNAS web site). Some of these lineages correspond to strain groupings that have previously been reported. For example, the Indo-Oceanic lineage includes a group of strains that have been referred to as ''ancestral'' due to the fact that they conserve the TbD1 genomic region, which is deleted in ''modern'' strains of M. tuberculosis (14). The East-Asian lineage includes, but is not limited to, the Beijing family of strains (13). The West-African lineages 1 and 2 correspond to strains that have traditionally been named Mycobacterium africanum (12), and the Euro-American lineage regroups strains that have generally been described as principal genetic groups 2 and 3 (15–17).

Walking through - Conclusions

Overall, our findings demonstrate a global genetic population structure for M. tuberculosis and support the notion that this pathogen has adapted to specific human populations. These results have implications for tuberculosis control efforts, especially for the development of new vaccines. The importance of strain genetic variation for vaccine escape has been documented in several bacterial species (24–26). In bacillus Calmette-Gúerin (BCG), the currently available tuberculosis vaccine, significant geographical variation in protective efficacy has been observed (8). Environmental factors and differences in vaccine strain have been invoked (8, 27–29), but our findings suggest that regional differences in host–pathogen interactions could be partially responsible. Although recent progress has been made in the development of new tuberculosis vaccines (30), the global population structure of M. tuberculosis and host-specific pathogen adaptation may need to be considered when engineering and evaluating new vaccine candidates.

Walking through - Abstract

Mycobacterium tuberculosis remains a major cause of morbidity and mortality worldwide. Studies have reported human pathogens to have geographically structured population genetics, some of which have been linked to ancient human migrations. However, no study has addressed the potential evolutionary consequences of such longstanding human–pathogen associations. Here, we demonstrate that the global population structure of M. tuberculosis is defined by six phylogeographical lineages, each associated with specific, sympatric human populations. In an urban cosmopolitan environment, mycobacterial lineages were much more likely to spread in sympatric than in allopatric patient populations. Tuberculosis cases that did occur in allopatric hosts disproportionately involved high-risk individuals with impaired host resistance. These observations suggest that mycobacterial lineages are adapted to particular human populations. If confirmed, our findings have important implications for tuberculosis control and vaccine development.