

Creating vaccines appropriate for Asian infectious disease strains

NUANCED VARIATIONS IN BACTERIA GENOMES indicate a need for vaccines that better treat Asian strains, and could help countries in the region track and treat outbreaks.

Tuberculosis is a top 10 cause of death globally. Thailand ranks among the top 20 countries most burdened by the infectious bacterial disease, with nearly 100,000 cases each year. However, most studies in which vaccines are tested use the Euro-American strain of the tuberculosis bacteria, and so their results may not be fully applicable to strains found in Thailand.

Whole genome sequencing studies by Professor Prasit Palittapongarnpim, Executive Vice President of Thailand's National Science and Technology Development Agency, are helping clarify the strains of tuberculosis bacteria affecting Thai populations.

Palittapongarnpim hopes this will help researchers improve vaccine versatility. He also sees whole genome sequencing as a means for middle-income countries, including Thailand, to affordably monitor for infectious disease outbreaks and better manage drug resistance.

Diverse tuberculosis strains

Palittapongarnpim's team has studied tuberculosis patients in Chiangrai, northern Thailand,

since 2003. "We've analyzed genetic sequences from 1,200 patients and the bacteria they were infected with. We've just begun sequencing an additional 600," he says.

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Tuberculosis is thought to have emerged 70,000 years ago, expanding globally as humans migrated out of Africa. It's thought to have then co-evolved with humans, as the occurrence of each of the seven major strains differ among language families. For instance, the Philippines strain is the predominant type in groups of people who speak Austronesian languages, a language group common in Pacific islands such as the Philippines and Indonesia. In neighbouring Thailand, however, the predominant

strains are the Indo-Oceanic strain and Beijing strain.

The study in Chiangrai demonstrates that the reality is even more complex, with unique sub-strains dispersed everywhere. Chiangrai is an ethnically diverse region of Thailand, where many descend from minority tribes. While the research team did not initially observe an association, a different picture emerged when dividing patients into three ethnic subgroups: Akha, Lahu and Thai. In particular, the Akha and Lahu subgroups tended to be infected by a sub-strain with a unique mutation, which was not the case in the Thai subgroup.

"Some of the sub-strains we found in Chiangrai had never been described before in the literature," Palittapongarnpim notes. He says that highlighting this diversity and their prevalence is the first step toward improving vaccines.

"Most tuberculosis studies were based on the Euro-American strain, which is considered the standard for research. But it's actually only the major strain in Europe and the US. Prominent strains in Asia behave quite differently,"



More universally versatile vaccines could better treat different *Mycobacterium tuberculosis* strains.

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he points out. "Now that we're seeing such diversity around the world, we need to accumulate more data on each strain so that drug developers can prioritize making vaccines more universally versatile."

Avoiding drug resistance

The decrease in whole genome sequencing costs means it's now also a useful to screen for strains of drug-resistant bacteria.

Thailand's current tuberculosis drug resistance rate is 2–3%, for example. Whole-genome sequencing data is making identifying when to test for drug resistance more efficient. "We're seeing that drug resistance is concentrated in just a handful of sub-strains,"

explains Palittapongarnpim.

Standard procedure also tests tuberculosis bacteria for drug resistance with multiple tests; with whole genome sequencing all the tests could be done in one.

This could help quickly identify which drugs to use first: one of five first-line drugs that are usually initially administered; or second-line drugs that are usually administered if first-line drugs don't work due to drug resistance.

"For first-line drugs, we have enough WGS data to be able to spot genetic characteristics for drug resistance quite accurately. We're currently trying to run a pilot for whole genome sequencing tests in the health

system. This isn't the case for second-line drugs yet. We still need to collect more data," says Palittapongarnpim.

Spotting outbreaks

Whole genome sequencing could also prove cost-effective for spotting infectious disease outbreaks. "In Thailand, where the population is large, having an overwhelming number of patients is nothing out of the ordinary, so an increase in the number of infectious disease patients can easily slip off the radar," says Palittapongarnpim.

"To add to that, most countries can't afford to send trained staff to trace infections, in the way some did to decipher the origin of COVID-19 in their

countries. For us, it's not realistic to visit a patient's house and begin investigating anyone they had close contact with."

The hope, he says, is that routine sequencing of whole bacterial genomes can raise red flags early.

"If we see that the bacteria's genetic sequence is the same between a large number of people, it implies that patients are transferring the bacteria to one another. That's a warning signal that an outbreak might be occurring." If clinicians start being able to identify outbreaks, authorities can start prioritizing target locations for intervention, says Palittapongarnpim. "The implications for public health control would be enormous."

For public health control measures for infectious diseases to work, orchestrated international efforts are key, he adds. "Infectious diseases don't obey borders, so it's our job to cross borders and compare data. This would be tons more impactful than having each country investing in sporadic initiatives." ■



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