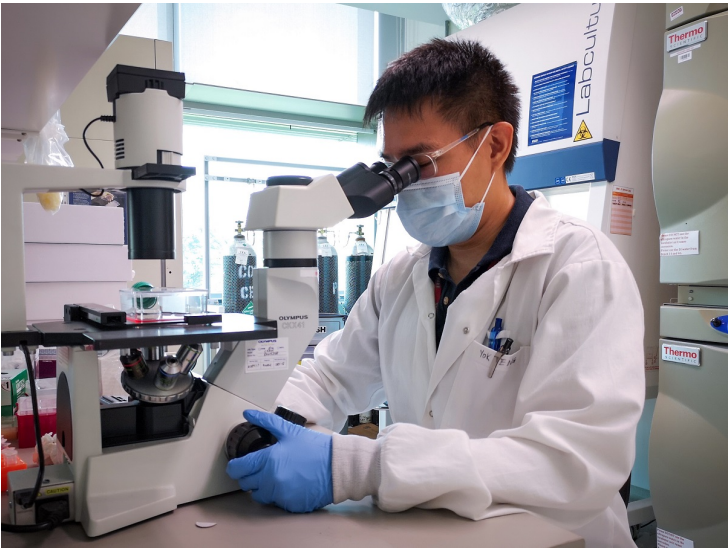


## Singapore develops potential antibody treatment for yellow fever

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**TY014 is developed by Rapid Response Strategy and can be extended to treat other infectious disease indications**



Researchers from [Antimicrobial Resistance](#) (AMR), an interdisciplinary group at [Singapore-MIT Alliance for Research and Technology](#) (SMART), MIT's research enterprise in Singapore, have developed TY014, a potential antibody treatment for yellow fever. SMART AMR collaborated with researchers from Massachusetts Institute of Technology (MIT), and local institutions such as the Singapore General Hospital, Duke-NUS and Tysana Pte Ltd to develop the antibody treatment within only seven months using a Rapid Response Strategy, a feat that usually takes several years.

In a paper titled "Phase 1 Trial of a Therapeutic Anti-Yellow Fever Virus Human Antibody" published in the *New England Journal of Medicine*, the researchers describe the methods and results of Phase 1 of the first-in-human TY014 study. The study has demonstrated the potential for yellow fever treatment using TY014, a fully engineered, human manufactured IgG1 monoclonal antibody that targets the yellow fever virus, with success in early-stage clinical trials in Singapore.

### **Reducing the time to make new drugs and therapeutics**

Monoclonal antibodies hold promise for treating a variety of infectious diseases including cancers, but these usually take several years to develop and test. The condensed timeline for TY014 was facilitated by a development process that carefully monitored product quality and correlated them with safety toxicology and pharmacokinetic studies using redundant orthogonal analytics; performing many of the steps necessary for drug development in parallel. The quick turnaround was also enabled by adapting an advanced proprietary computational platform technology, first developed at SMART and MIT, to identify and engineer the TY014 antibody.

It can be extended to other infectious diseases like, COVID-19 antibody treatment (named TY027) was developed by this team in just four months using this approach. Preliminary results from the Phase 1 trials show that no adverse events have been observed after the infusion of TY027 in healthy volunteers. Phase 3 clinical trials are expected to start in August in Singapore.

### **The lack of therapeutics for yellow fever**

Though vaccinating 80% or more of the population at risk can prevent the epidemic, the global manufacturing capacity is unable to meet a surge in demand, especially during an outbreak. Furthermore, the vaccine is contraindicated in infants and those above 60 years old, as well as in immunocompromised persons.

Researchers used a computational approach to develop the TY014 antibody to specifically target an epitope on the yellow fever virus envelope (E) protein in post-infection therapy. This will help alleviate the stress on global healthcare systems in managing a yellow fever outbreak, and also fill the current gaps in healthcare that cannot be safely addressed by vaccination alone.

### **Testing for safety and efficacy**

The clinical trial was conducted at the SingHealth Investigational Medical Unit in Singapore in healthy human volunteers. Researchers found that following TY014 treatment, the virus was undetectable in blood samples from people who received the antibodies. The treatment also reduced inflammation following vaccination, compared to people who received the vaccine but not the antibody treatment.

With the phase 1b trial completed in July 2019, the researchers will perform phase 2 clinical trials in patients infected with the disease.

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Yellow fever, an acute viral haemorrhagic disease transmitted by infected mosquitoes, infects about 200,000 people and causes an estimated 30,000 deaths each year. While currently endemic in 47 countries in Africa and Central and South America, the potential for large urban outbreaks is still present in other regions where the mosquitoes capable of transmitting yellow fever exist, especially in Southeast Asia due to the favourable ecology for the *Aedes aegypti* mosquito species. Same species of mosquito that spreads dengue is also capable of transmitting yellow fever, extending the risk of a yellow fever outbreak even to non-endemic regions including Asia and parts of USA.