

stars insights: 1 February 2019

Overcoming Challenges Facing the Development of Medicines for Tropical Diseases

*Despite the high number of people who are infected with the Dengue and Zika viruses around the world, there are currently no drugs to treat those tropical diseases, and only one vaccine for Dengue. With a high risk of failure, coupled with a potentially low profit margin, some pharmaceutical companies have scaled back or even stopped their drug development programmes for tropical diseases. stars alumna Dr. **Katja FINK**, Principal Investigator at Singapore Immunology Network A*STAR – who also hosts one of the site visits of the upcoming [stars Singapore symposium 2019](#) – explains in this article how these challenges can be overcome.*

How much damage does Dengue or Zika cause?

Both Dengue and Zika are viruses that are transmitted by *Aedes* mosquitoes. Every year, an estimated 390 million people are infected with the Dengue virus. Up to 80% of those infections are asymptomatic, meaning that infections result in little or no symptoms. There are, however, about 100 million people who experience clinically apparent dengue infections each year.

Although rarely fatal if treated in a hospital, Dengue causes symptoms such as high fever, muscle and joint pain, rashes, as well as headaches. A serious effect of dengue is vascular leakage (the liquid component of our blood leaks out of the blood vessels) and coagulopathy (inability of the blood to clot properly). If a patient with severe vascular leakage does not receive intravenous fluid replacement, shock and organ failure can ensue. Due to the coagulopathy, patients often do not stop bleeding from small injuries or experience severe bleeding, hence the term “dengue hemorrhagic fever”. Patients with severe dengue should seek medical advice, and could be provided intravenous fluids to maintain circulating fluid volume and paracetamol to bring down fever and ease the pain. This is effective but requires that a patient is hospitalized and closely monitored.

The Zika virus is closely related to Dengue and causes similar symptoms such as fever and pain. The symptoms are comparatively mild compared to those of Dengue. The main concern with Zika, however, is its damaging effect on fetuses. This is similar to the damaging effect of other viruses like measles or rubella. While a Zika infection poses a relatively low risk for healthy individuals, it has been known to cause birth defects in developing fetuses. For newborns without obvious defects, the potential impact of Zika infection during pregnancy on their later development is only starting to be studied.

Only one vaccine and no drugs for treating Dengue and Zika

There are currently no drugs to treat Dengue and Zika, and only one vaccine for Dengue, despite the high number of infections globally. One reason for this is that Dengue exists in four distinct serotypes, which means that a mixture of four different vaccines needs to be developed to offer someone full protection from the disease.

However, it has been found that a mixture does not seem to work well because there is competition between the four vaccines, and the immune system recognizes them with different efficacies, providing insufficient protection. This insufficient protection could in rare cases even worsen subsequent infections. This phenomenon can at least partially be

1/4

associated with pre-existing antibodies, a part of our immune response, that do not block the virus sufficiently and instead are “tricked” by the virus to infect more cells throughout the body.

While Zika only has one serotype, it occurs more sporadically compared to Dengue and an important target population for a vaccine are pregnant women. These factors make it very difficult to plan clinical trials and extra care is needed to ensure the safety of the foetuses.

Challenges faced when developing drugs for infectious diseases

The development of drugs for infectious diseases comes with many challenges. For example, the pathogenesis and the body's response to diseases like Dengue are not fully understood, which makes it difficult to develop drugs that effectively target the disease. The risk of failure is high. Additionally, drugs developed for infectious diseases could have a limited target population due to the possible physiological requirements in order for the drugs to work. For example, the dengue vaccine Dengvaxia® is only recommended for persons with previous dengue infection.

Another crucial factor is cost. The development of new drugs requires large investments and because of this, pharmaceutical companies tend to focus on highly prevalent illnesses such as cancer. In 2017, the top cancer drug generated USD 8.2 billion, compared to USD 5.6 billion generated from the top selling product for infectious diseases (a pneumococcal vaccine). In addition, many infectious diseases are prevalent in developing countries where little or no profit can be made to offset the cost of development.

With a high risk of failure, coupled with the potentially low profit margin, some pharmaceutical companies have scaled back or stopped their drug development programmes for infectious diseases.

Reducing the drug development cost for infectious diseases

The most obvious way to counter high costs, and to encourage the development of drugs for infectious diseases would be to reduce the total cost of drug development. In order to have a real impact on total cost, all phases of development should and can be optimised, as taking a drug or molecule through each phase of drug development involves a large cost.

Optimisation could start with the research labs in universities and other public institutions where many drug discoveries are made before being acquired by industry. A good way to do so is to train researchers and equip them with knowledge of what is needed for a drug to be successful. This includes knowledge of how treatments work and how biological mechanisms can be measured and quantified. Application-focused training guides researchers to look at scientific results from a different angle.

With such training, researchers would understand that the next phase of drug development involves a study of a molecule's suitability as a drug (for example the ability to reach a target organ in the body) and its potential toxicity. This means that they would be able to identify and address potential pitfalls earlier, and thus save time and resources.

Other potential solutions that will help fund drugs for infectious diseases

There are also other potential solutions in the form of biologics, or products that are naturally produced in living organisms or contain components of living organisms. Antibodies, naturally produced as part of a body's immune defense, belong to this class.

The potential for antibodies in treating infectious diseases is immense. Antibodies are highly efficient in binding and blocking viruses, and are less prone to causing side-effects. This, combined with the fact that biologics can perform successfully for companies make biologics a viable candidate for infectious disease drug development.

However, the uncertainty in market size remains a risk factor for development of infectious diseases medicines. A potential solution to address such concerns comes in the form of public-private partnerships. There are a number of organisations that pharmaceutical companies can partner to de-risk their investments in the area of drug development for infectious diseases. Good examples are the Global Health Innovative Technology Fund ([GHIT](#)) or the Coalition for Epidemic Preparedness Innovations ([CEPI](#)). CEPI's mission is to "stimulate, finance and co-ordinate vaccine development against diseases with epidemic potential in cases where market incentives fail".

The need for continued research and partnership between the public and private sectors

It is also important to note that the study of antibodies that are not suitable for manufacturing can still make ground-breaking contributions to drug development. The knowledge gained from these studies helps us better understand the mechanisms of the body's response to diseases. This will be instrumental in the development of antibodies that are suitable as medicines.

Public-private partnerships become a viable solution where the public institute does not have the funds (and knowledge) to develop a drug candidate into a drug, and where the risk for the private partner is too high to fully fund the program.

For these endeavours to be successful, trust between the public and private sectors is of the utmost importance. This sounds very obvious but what people underestimate is the time and effort it takes to build this trust. Clear communication channels and a good understanding of each other's capabilities can greatly facilitate the transition of research discoveries into drug candidates. One way to build this trust is through small collaborations that do not necessarily result in huge market impact. Once the frame for concerted and collaborative efforts is established, future projects have a much higher chance to be successful. This partnership, and to some extent, dependency, should benefit niche areas like medicines for tropical diseases in particular.

*Dr. [Katja FINK](#) received her doctor in natural sciences (Dr. sc. nat) from the Swiss Federal Institute of Technology (ETH) where she studied anti-viral immune responses. She moved to Singapore in 2006 to work for the Novartis Institute for Tropical Diseases, where she held a position as post-doctoral fellow and where she started to work with dengue virus. Since 2009 Dr. Fink is a Principal Investigator at the Agency of Science, Technology and Research (A*STAR), Singapore. Her research is on the development of immuno-therapies including vaccines and therapeutic antibodies. Dr. Fink is also an Adjunct Associate Professor at the Nanyang Technological University NTU and the Lee Kong Chian School of Medicine-NTU, Singapore.*

The views expressed here are solely those of the author and they do not necessarily represent or reflect the views of the official policy or position of her employer, the stars Foundation or any other group or individual.

[stars insights](#) are exclusive contributions by business leaders and experts who scan the horizon to discuss geopolitical, economic, technological and further trends and developments which will impact society and business in the next few years.

www.the-stars.ch