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Time vs swine: Working agains the clock to stop the next pandemic

It was 2003, just four years after the first known outbreak of Nipah virus occurred in Malaysia and around the time a second outbreak occurred in Bangladesh. Dr. Hector Aguilar-Carreño had just decided to focus his research on the Nipah virus, instead of expanding on his postdoctoral lab's research on HIV. "The more I looked into the Nipah virus the more interested I became," says Aguilar-Carreño. In retrospect, he made the right choice: "We became famous for being the pioneers for studying how the Nipah virus makes its way into cells." Now an associate professor in the Department of Microbiology & Immunology at Cornell, Aguilar-Carreño continues working towards unveiling how this virus causes disease.

The break-in

The Aguilar-Carreño lab

The Nipah virus enters the body via the respiratory route and infects the brain and lung cells, specifically those lining the outer surface of these organs and the interior of their blood vessels. The Aguilar-Carreño group found that Nipah does this in several sequential steps that involve the interaction of two proteins. One viral protein first attaches to the cell and the other viral protein fuses the viral membrane with the membrane of the cell. This was an interesting finding because "for decades scientists thought that the two proteins did not interact in a concerted way, and that it was just the close proximity of the membrane of the virus with the membrane of the cell that made the two fuse almost magically," Aguilar-Carreño explains.

His lab studies how both proteins interact with each other to cause fusion of the virus to the cells it infects. So far, it is unclear what part (or parts) of the attachment protein causes fusion, or where the points of contact between the two proteins are.

"The beauty of all this is that once we answer these questions it doesn't only help our knowledge of the Nipah virus; it also contributes to our knowledge of other viruses that are in the same family which enter cells using a similar mechanism," Aguilar-Carreño explains. Other such viruse include measles and mumps, which are still a problem in many parts of the world.

One of the end goals of these studies is to develop anti-virals that target the virus membranes "I am very proud of this approach because when developing anti-virals most people target the proteins of the virus. Instead, we target the membrane," says Aguilar-Carreño. Viruses are unable t repair a damaged membrane. Therefore, damaging viral membranes will prevent the virus from fusing with healthy cells and spreading. This approach is significant because membrane viruses (those that have an envelope around them) cause most of the viral diseases with high mortality rates. "The world health organization has a list of pathogens that are most likely to cause the future epidemics, and every single pathogen on the list is a membrane virus," Aguilar-Carreño says. "That tells me that the work we are doing is very important."

Just a matter of time

Nipah is the featured virus of the 2011 film *Contagion*, where-to quote the movie- "somewhere in the world the wrong pig met up with the wrong bat," causing a global pandemic and widespread panic. Although a fictional drama, Nipah does have the potential to cause a pandemic and is currently listed as a bioterrorism agent.

The first Nipah virus outbreak happened in Malaysia in 1999, sickening pigs that became infected through contact with bats, and then sickening pig farmers and people in close contact with pigs . In Bangladesh, where mini-outbreaks have occurred every year since the first outbreak in 2001, drinking date palm sap contaminated with bat urine and/or saliva was quickly singled out as the culprit.

Nipah virus has the power to jump from human to human, but infection cases have remained confined to Southeast Asia. This is because all the outbreaks have happened in remote villages with a very low density of human population. "It may take just one person traveling from that remote area to a big city for us to have a big outbreak," says Aguilar-Carreño.

Dr. Aguilar-Carreño. Behind him, an artistic representation of Nipah and Ebola viruses

Others just like it

Nipah belongs to the henipavirus genus along with other related viruses such as Hendra, which Aguilar Carreño also studies. He explains that 20 other henipaviruses have been discovered in bats in the last few years, but it is unknown whether they can infect humans. "It is important to study Nipah and Hendra because there might be other related viruses who might be coming our way, or that might be already killing people without us knowing." A 2014 study reported that three to four percent of human serum samples from 500 individuals living in various villages across southern Cameroon tested positiv for antibodies against Nipah and Hendra, which means that they had been infected with these or othe closely related viruses. "I believe that there is a percentage of people who are dying every year from henipaviruses that we don't know about," says Aguilar-Carreño. His work could provide answers not only about Nipah and Hendra but also about related viruses which likely have similar mechanisms of causing disease. If an entirely new virus emerges, Aguilar-Carreño is prepared to tackle it. "Working with Nipah virus was a great learning experience because I feel prepared to work with a new emerging virus. Now I know what to do and how to get started."

-Luisa Torres, Postdoctoral Researcher in Microbiology & Immunology

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