The Enemy of My Enemy is My Friend: Viral Version

All organisms live in an ecosystem, even a virus. The viral ecosystem is its host, and as such, a human virus lives with our adaptive immune system. Of course, the premise of vaccines is to bias the adaptive immune system with an antibody memory to enable it to recognize and eliminate an invading microorganism quickly. So, we typically worry that we lack an antibody memory and assume having such is a good thing in our internal ecosystem. However, in **antibody-dependent enhancement (ADE)**, cognate antibodies in the pool instead advance viral disease progress.

While incredibly important, it was difficult to rigorously demonstrate that ***residual antibodies in memory generated from a previous infection enhance the disease state in a later infective round***. This ADE hypothesis was originally forwarded by Dr Scott Halstead and colleagues in the 1970's in order to explain observations made of severely ill patients and their immune-reactivity against various Dengue serotypes which threaded back to research in the 1960's with patients in Thailand. So while one of the earliest suspected examples of ADE, Dr. Sujan Shresta and colleagues robustly established such for Dengue only in 2010 using a mouse model they developed. At the molecular level, a poorly neutralizing antibody appears to assist viral entry into memory B cells by way of the antibody Fcγ-R receptor, allowing that cell to be infected and further propagate the disease. Of course, this presents multiple "land mines" in developing a Dengue vaccine with 4 different serotypes, variants to those serotypes, and an antibody memory that wanes over time, all which might lead to pools of poorly neutralizing antibodies to a particular Dengue strain.

Zika, a related flavivirus, has sandwiched itself into this complex picture, dancing with Dengue in the immune ecosystem. Zika infection during pregnancy has been associated with congenital microcephaly as well as other neural and ocular issues in newborns, and the virus has been shown to cross thru the placenta to the fetus. Recently, a study has revealed that human placental macrophages have a higher rate of infectivity of Zika in the presence of Dengue antibodies, thus suggesting augmented infectivity against the fetus if the mother previously had a Dengue infection. In an animal study, Zika antibodies in female mice trigger more serious cases of Dengue in their offspring that will carry the maternal antibodies. ***These studies appear to reveal the evolution of a tag-team between Zika and Dengue, with the first round of infection from one opening the immune system to a more vicious attack by the other***, a particularly perilous issue for the fetus and newborns with the capability of Zika to cross the placental lining. The enemy of their enemy is a friend for these viruses, and potentially deadly for humans.

eEnzyme makes high quality infectious disease proteins and antibodies to help researchers to advance research in our understanding and sort through these complicated issues, including Zika proteins and their corresponding antibodies.

General Interest Reading

https://www.sciencedaily.com/releases/2010/02/100211121756.htm

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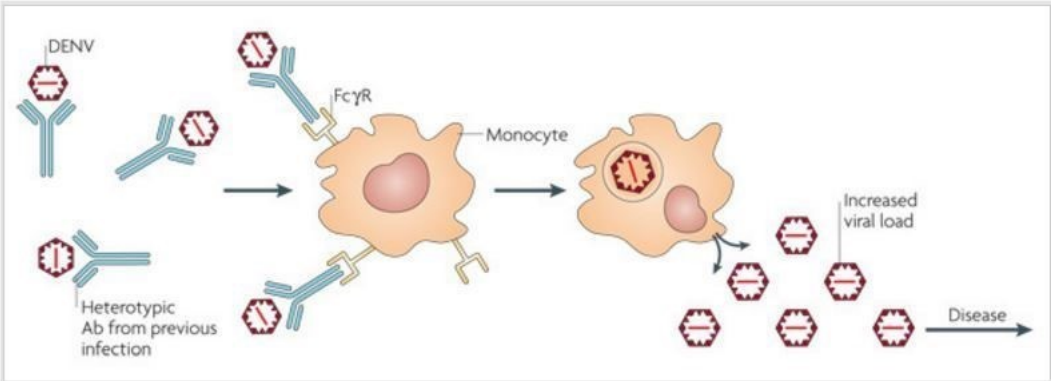
Model of antibody-dependent enhancement of dengue infection



Model of antibody-dependent enhancement of dengue infection
Antibody (Ab)-dependent enhancement of infection occurs when preexisting antibodies present in the body from a primary (first) dengue virus (DENV) infection bind to an infecting DENV particle during a subsequent infection with a different dengue serotype. The antibodies from the primary infection cannot neutralize the virus. Instead, the Ab–virus complex attaches to receptors called Fcγ receptors (FcγR) on circulating monocytes. The antibodies help the virus infect monocytes more efficiently. The outcome is an increase in the overall replication of the virus and a higher risk of severe dengue.