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Leveraging Natural Immunity to Find New Vaccines

There are few effective vaccines against infectious diseases such as malaria and tuberculosis that are caused by parasites or bacteria capable of growing within human cells.

However, some individuals do develop immunity that protects them from these diseases. One company has developed a way to rapidly explore this immunity in the hopes of more quickly discovering new vaccines and improving existing ones.

Genocea Biosciences is working with the Naval Medical Research Center to apply its new screening technique to malaria, one of the top five global killers. The project is funded by the U.S. Army Medical Research and Materiel Command's Telemedicine and Advanced Technology Research Center. Says Dr. John Carney, who manages TATRC's infectious disease research portfolio, "This is a different approach. The Genocea effort examines immune cells from people who have developed their own sterilizing immunity—those who could survive when exposed to malaria—to identify how their immune system responded differently so we can generalize this knowledge to vaccine development."

Because the parasites that cause malaria grow sequestered within host cells, immunity requires triggering a response from the body's T cells, which only react to certain proteins in the parasite. According to Genocea Biosciences principal investigator Dr. Jessica Flechtner, many vaccine programs have been ineffective because no one had found a way to efficiently screen all possible antigens (proteins) from a disease-causing pathogen to find the ones that stimulate T cells.

Flechtner explains, "Genocea was founded on the premise that we could learn from natural immunity. We theorize that we can intelligently design vaccines by targeting the same part of the pathogen as the people who naturally mount protective immune responses."

Genocea has developed a core technology that allows them to rapidly determine which antigens from the entire proteome of an organism are able to elicit T cell responses in humans.

The U.S. Military Malaria Vaccine Program, a research enterprise harnessing the talents of vaccine developers from NMRC and from the Walter Reed Army Institute of Research, is vitally interested in developing a malaria vaccine to protect military personnel deployed to malarious areas throughout the world, many of which are potential locations for U.S. military engagement.

Navy Capt. Tom Richie, research coordinator for USMMVP, believes that Genocea's technology may help: "As the malaria parasite consists of more than 5,000 proteins, identifying which of

these proteins could be most immunogenic and protective in a vaccine is of vital concern. For this reason, we have partnered with Genocea, and have provided banks of T cells from human volunteers immunized with an experimental vaccine and protected against malaria challenge, to support the company's screening technology. We have also provided *Plasmodium falciparum* sporozoites, the infectious form of the parasite."

The Genocea team recently used the sporozoites from USMMVP to develop a library of antigens from the parasites, and in the first half of 2011 will be screening them against the T cell samples the NMRC has collected from immunized volunteers. Half of the samples are from those who produced a protective T cell immune response, and half are from those who did not. The group will use the identified antigens to develop a malaria vaccine that takes best advantage of the body's natural immune defenses.

According to Flechtner, a vaccine would have great advantages over current anti-malarial drugs because there would be fewer side effects and no worries about taking medication on schedule or developing drug resistance.

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