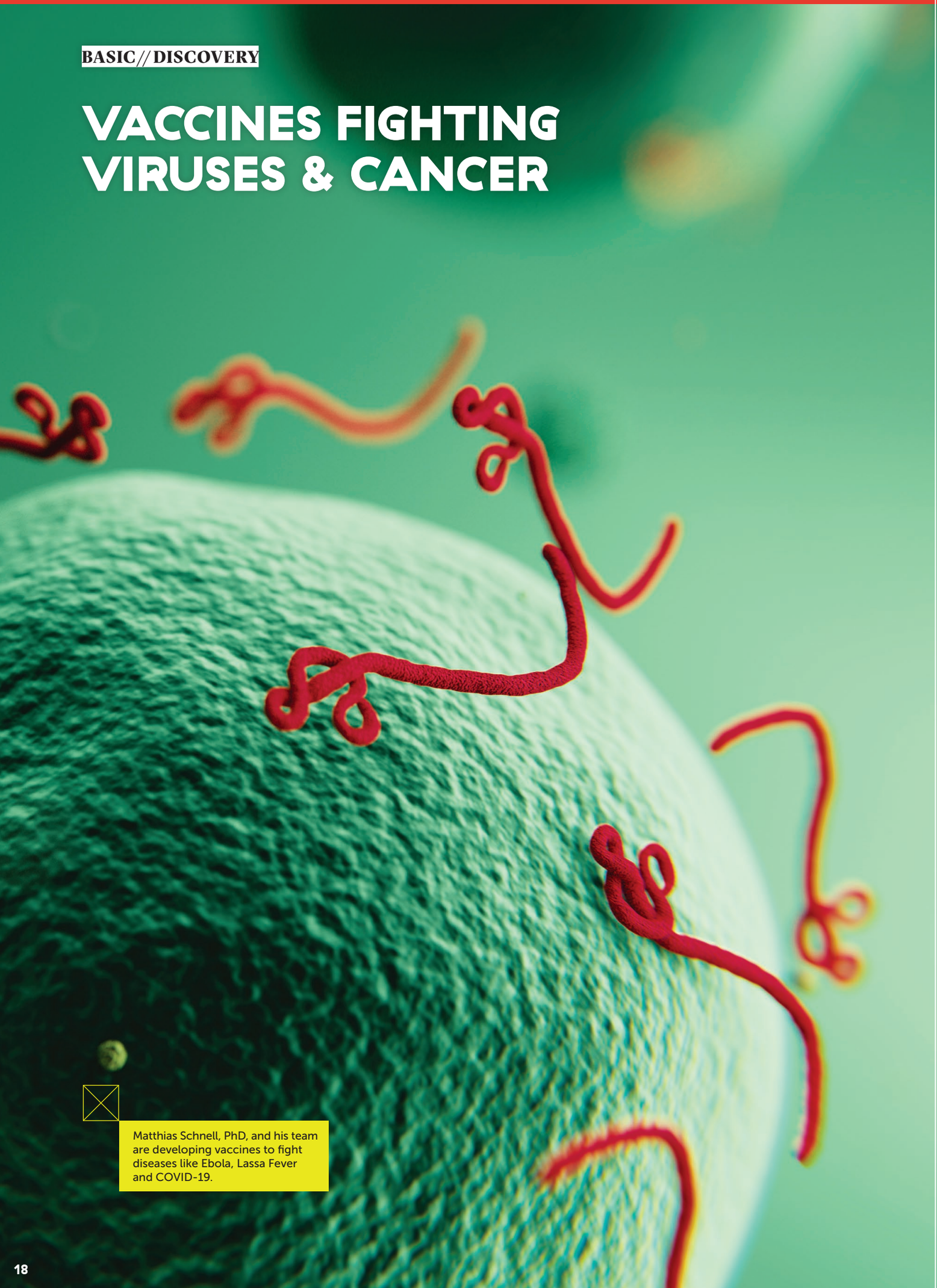
VACCINES FIGHTING VIRUSES & CANCER



Matthias Schnell, PhD, and his team are developing vaccines to fight diseases like Ebola, Lassa Fever and COVID-19.

A GROUP OF JEFFERSON VIRAL VACCINE RESEARCHERS LED by **Jefferson Vaccine Center (JVC)** director and professor of microbiology and immunology **Matthias Schnell, PhD** have been using rabies vaccine as a potent tool for understanding and fighting hemorrhagic viruses—such as Ebola, Marburg, Sudan and Lassa Feve—as well as coronavirus. By the end of 2019, the team had developed a tetravalent vaccine that uses an established dead-virus rabies vaccine modified with specific antigens for the viruses. In animal models, the immune system develops a reaction to the vaccine that is specific and can defend against rabies and some viruses. Soon after COVID-19 first emerged, Schnell and his team created a killed-rabies vaccine that incorporates the spike portion of the SARS-COV-2 virus, which causes the disease. The resulting COVID-19 vaccine candidate—CORAVAX™—was put into animal trials as a prelude to expected phase 1 clinical trials.

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"Rabies is a prevalent problem in much of the world, and it is extremely hard to prevent spread of hemorrhagic viruses—evidenced by the most recent Ebola outbreak. It would be valuable to be able to provide immunity against these diseases simultaneously," Dr. Schnell says. "And the importance of leveraging our approach to create a coronavirus vaccine candidate is clear."

The NIH-funded project involves a bench-to-bedside range of work: From identifying and applying the antigens and observing the quality of the antibody response to developing a scalable production process to planning clinical trials. With the vaccine having proved effective and safe in small and large animal models, Dr. Schnell's team is working with a production facility to ensure Good Manufacturing Processes of the vaccine formulation. That process, which should be completed in the coming year, will be prelude to a subsequent phase I clinical trial testing toxicity. If early clinical trials are successful, the vaccine could be ready to test in actual disease outbreaks within five years.

JVC is the cornerstone of the University's programmatic research in immunology and infection disease. Building on basic and translational studies in immunology, microbial pathogenesis and tumor immunology, JVC researchers pursue multifaceted investigations on vaccines that combat viruses and those that provoke immune response to diseases such as cancer.

JVC researchers are also seeing robust results from their rabies-based vaccine for Nipah virus, which is transmitted from animals to humans and causes severe respiratory illness that can progress into encephalitis, seizure and coma. Outbreaks have occurred in Malaysia, Singapore, Bangladesh and India; and because no vaccine is available, the World Health Organization has listed Nipah as needing urgent action. A recent study in mice—testing a rabies vector that incorporates a Nipah virus gene—showed that one dose of the vaccine was safe and elicited strong antibodies response against both Nipah and rabies. A second, chemically killed version of the vaccine—which could be ideal for immunocompromised individuals—also safely induced strong immunity.

Rabies' unique method for attacking the brain—it bypasses the blood system and the blood-brain barrier by entering the central nervous system (CNS) through muscles at the site of an infecting bite—makes it a perfect tool to learn about ways of harnessing the power of the immune system to fight tumors in the brain. Results from recent studies by JVC investigators found that delivering rabies vaccine through a mouse's jaw muscles promoted an immune response in the brain—one sufficient to prompt CNS immune memory and protect against rabies in a way current vaccines do not. The study also demonstrated that for immune mechanisms to properly protect the brain long-term, immune "memory" cells must become resident in the CNS. That suggests immunity established in the blood is insufficient to fight brain cancer—a potentially pivotal finding for development of vaccines against the disease.

That study was one in a series of projects in which Jefferson researchers are translating their basic science discoveries into immune-based cancer treatments that have proven effective in early trials. See *Advancing Cellular and Immune-based Cancer Therapies* on page 6 for a look at that work. ■