VIROLOGY

New Finding Heats Up The Hot Zone

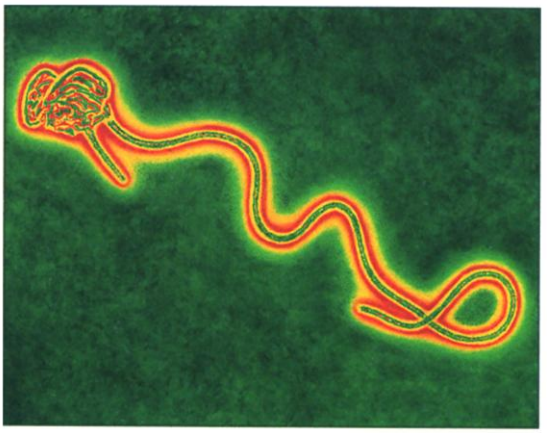
Ebola and its equally gruesome cousin, Marburg, fascinate the public. They've even played starring roles in best-selling books and Hollywood movies. But these terrifying viruses, which typically cause death by hemorrhage within weeks of infection, have attracted relatively few research groups (and scant funding) since they were discovered some 25 years ago. As a result, the modus operandi of these viruses is largely unknown. Now a team led by Mark Goldsmith at the Gladstone Institute of Virology and Immunology in San Francisco, California, has uncovered an intriguing lead: a molecule that helps both viruses infect cells.

As Goldsmith, Stephen Chan, and co-workers describe in the 13 July issue of *Cell*, these viruses have an intimate relationship with folate receptor–α (FR-α), which is found on the surface of many cell types. "It's an important finding," says Paul Bates of the University of Pennsylvania in Philadelphia. "We're now going to get into the nitty-gritty of taking [the discovery] apart and trying to figure out the nature of the interaction," says Bates, whose own lab also studies how Marburg and Ebola establish infections. If FR-α does turn out to be an important accomplice for viral entry, this insight might point the way to novel treatment and vaccine strategies.

Many viruses cause infections by first docking onto receptors on cell surfaces. But the Goldsmith team carefully avoids calling FR-α a "receptor" for Ebola and Marburg. Rather, they describe it as a "cofactor for cellular entry"—which is another way of saying that they don't yet know the precise role that FR-α plays in opening the cellular door to these invaders. "At this point we're happy to have any clues about how [these viruses] enter cells," says Gary Nabel, who heads the Vaccine Research Center at the National Institutes of Health and is part of the small club of investigators who study Ebola.

The Gladstone researchers found FR-α by exploiting an earlier finding—that Ebola and Marburg do not infect T cells. These cells thus provide an ideal system for testing, one by one, possible factors that control viral entry. Specifically, the researchers made a library of DNA from cells that the viruses *can* infect, reasoning that these genes produce the missing factor (or factors). They next engineered new T cells to contain one or more of those genes, then "challenged" the modified cells with a chimeric virus that combined a surface protein from Marburg with HIV. (Researchers routinely use such "pseudotype" viruses of both Marburg and Ebola because few labs have the biosafety capabilities to work with the real pathogens.) They soon found that the pseudotype Marburg virus could infect T cells that contained FR-α. The same held true for a pseudotype Ebola virus.

"We did many, many, many experiments to try and convince ourselves that the results were real," says Goldsmith. For example, they found that blocking FR-α inhibits viral entry. And, working with Alan Schmaljohn at the U.S. Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland—which has one of two labs in the country equipped to handle the hottest viruses—the researchers demonstrated that wild-type Marburg virus could infect T cells only if they were modified to contain FR-α.



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Breaking and entering. Researchers have found a molecule that helps Ebola (above) and Marburg viruses enter cells.

Several caveats remain. Nabel cautions that rather than serving as a receptor for Ebola and Marburg, FR-α might send signals that tell the cell to let the viruses enter. Pennsylvania's Bates adds that he'd like to see more studies done with other cell types. "The three most important targets [for these viruses] aren't addressed in this paper: macrophages, hepatocytes, and endothelial cells," says Bates. (All have FR-α, to varying degrees.) And both Goldsmith's group and Bates have unpublished data that Ebola and Marburg can infect cells that do not have FR-α—evidence that the viruses may use different pathways to enter different types of cells.

Goldsmith, too, is cautious about the FR-α findings. "We don't know how things will play out," he says. But for the small cadre of Ebola and Marburg researchers, the new work offers a tantalizing clue about two diseases that, famous though they are, largely remain a mystery. **–JON COHEN**

ScienceScope

New Faces A trio of prominent research institutions is getting new leaders. The European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, this week appointed two women to lead key outposts. Janet Thornton, a structural biologist at University College London, will become research director at the European Bioinformatics Institute near Cambridge, U.K. Nadia Rosenthal, a biomedical researcher at Harvard University, will take over EMBL's mouse biology program in Monterotondo, Italy. Both programs are emerging reinvigorated from financial crises (*Science*, 18 May, p. 1275, and 15 June, p. 1985).

In the United States, veteran virologist Edmund Tramont has taken the helm of the government's largest AIDS program. Tramont, former head of the U.S. military's AIDS research program and the University of Maryland Biotechnology Center, will lead the National Institute of Allergy and Infectious Diseases' $1 billion Division of AIDS.

Celera, NIH Make a Deal After 7 months of painstaking review, the National Institutes of Health (NIH) has agreed to let some of its scientists use private DNA databases maintained by Celera Genomics of Rockville, Maryland. NIH's largest unit, the National Cancer Institute (NCI), signed a memorandum of understanding with Celera in late June that permits NCI scientists to pay for Celera's data from their own budgets. The decision was controversial because NIH has already used public funds to create its own DNA data archive, GenBank (*Science*, 12 January, p. 223).

NCI's decision does not signal a loss of confidence in the public system, says NIH intramural chief Michael Gottesman. "Some people at NCI were interested" in seeing Celera's data, he said, so NCI managers made a deal that would give them access and serve as a model for other NIH institutes. He doubts many researchers will sign up but hasn't taken a "head count" of potential users.

Celera president J. Craig Venter says NIH was pushed into the decision by its own researchers, especially those who want to check out the company's assembled and annotated mouse genome. (The public mouse genome may not be available for years.) The agreement "will put behind us" old battles, Venter says. He predicts Celera will bill NCI "less than $20,000 per lab" for use of all its databases, including the mouse genome.

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