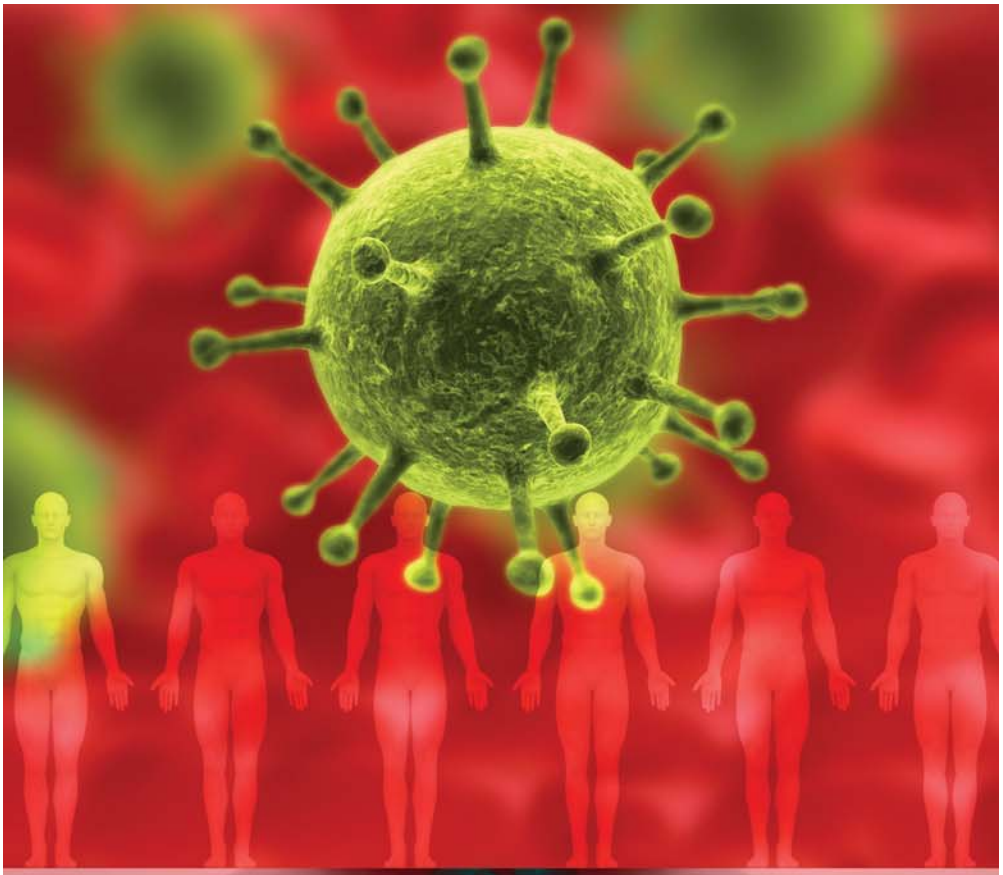
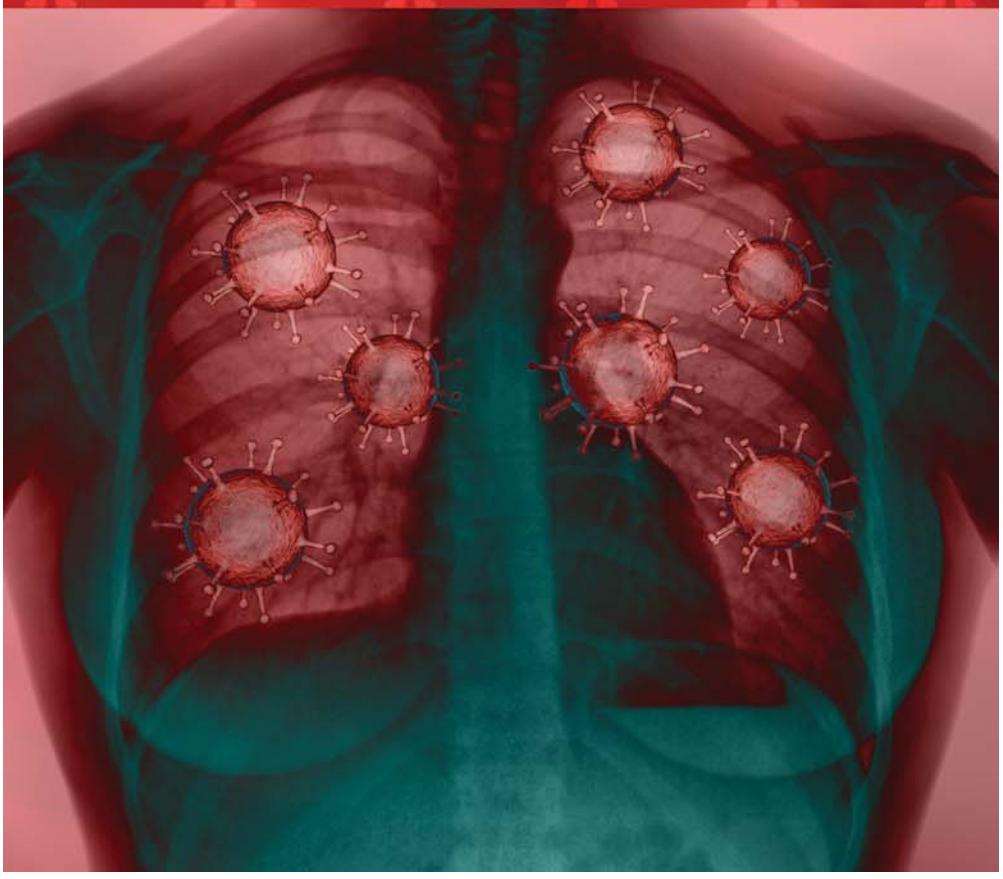




The Reality Behind a Movie Thriller

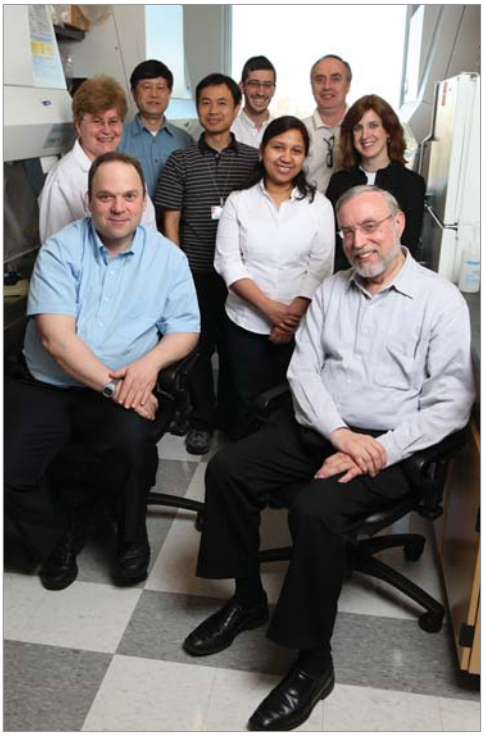
Steven Spielberg's film *Contagion* depicts the outbreak of a lethal virus pandemic threatening human life, but within the walls of PHRI, our experts deal every day with the real thing. **BY DAVID MCKAY WILSON**

A poster for the 2011 movie thriller, *Contagion,* hangs from the wall outside David Perlin's office at the Public Health Research Institute (PHRI). Perlin, a PhD researcher, is the executive director of PHRI. The poster stands as a sober reminder to staff and visitors that the new $38 million Regional Biocontainment Laboratory (RBL) managed by PHRI has the infrastructure — and the scientific firepower — to investigate a pandemic virus similar to the one portrayed in the film.

In *Contagion,* there's an outbreak of a lethal virus that spreads from bats to pigs, and then to humans. The film's heroes are the steadfast microbiologists who race against time to create a vaccine to stop its spread.

"Emerging infectious diseases are everywhere," says Perlin, who came to PHRI in 1985, when its labs were located at New York City's Department of Health Bureau of Laboratories. "They occur all the time, and no matter how clever we think we are, there's another one that comes along that throws us for a loop. It's good that we have the infrastructure to safely study these highly transmissible agents."

PHOTO ILLUSTRATION: SHEILA JOHNSTON SHERER



Far left: David Perlin, PhD; and members of the Pinter lab at NJMS, clockwise, from left, Charles Reichman, PhD, Kathy Revesz, Zhong Lai, Lianping Peng, Sholem Blobstein, Adhuna Phogat, PhD, Chavdar Krachmarov, PhD, Aidy Salomon, and Abraham Pinter, PhD

PHRI was established 70 years ago in New York City as a biomedical institute dedicated to infectious disease research. It relocated to the International Center for Public Health (ICPH) in 2002 and was established as a center of UMDNJ–NJMS in 2006. PHRI's faculty members study a broad range of infectious disease issues.

In fact, the effort underway at PHRI involves some of the world's most pressing—and intractable—public-health problems. Some investigators delve into the mysteries of the HIV virus, the world's leading infectious killer, which claims 3 million lives a year. Others study the bacterium that causes tuberculosis, the lung infection that kills up to 2 million annually. And some of the scientists are focused on hospital and community-acquired infections, as well as potential agents of bioterrorism. PHRI's researchers have developed novel molecular tools, such as molecular beacons, and they work with clinicians, helping to manage patients and track infectious disease as it spreads.

"We are interested in infectious agents with the potential to cause high morbidity and mortality," says Perlin. "And we want to develop counter-measures with new vaccines, new therapeutics, new diagnostics, and new understandings of the biology of the organisms."

Of growing concern to Perlin and Karl Drlica, PhD, a molecular biologist at PHRI, are the always-evolving pathogenic strains of bacteria that are resistant to antibiotics. Their new book, *Antibiotic Resistance: Understanding and Responding to an Emerging Crisis,* published in late 2011, details the misuse of antibiotics today and discusses the ramifications of using antibiotic doses that aren't strong enough to kill all the bacteria and their mutants that develop in a bad infection.

Drlica's research at PHRI focuses on the basic principles involved in the antibiotic flouroquinolone's ability to kill the organisms that cause a variety of lethal bacterial diseases. "If we can figure out the principles, then the drug companies can do the rest," says Drlica. "I think antibiotic resistance is second to global warming as the world's most serious issue. Imagine life without antibiotics. You couldn't get surgery because all the bugs would be there. And when you got pneumonia, you would die. People used to die a lot from infectious diseases."

Many of the studies involving highly transmissible agents occur within the specialized biosafety Level 3 laboratories of the new RBL, which is part of a network of 13 such laboratories in place across the U.S. These national centers were developed by the National Institutes of Health (NIH) in the aftermath of the anthrax attacks in the fall of 2001, which rattled a nation already reeling from the events of September 11.

When PHRI relocated in 2002, its biosafety Level 3 facilities included animal labs there in Newark's University Heights Science Park. So when the federal government sought partners in the national program, PHRI was well-positioned to participate.

The RBL, developed through the federal program, expanded its space for research scientists and the newly opened lab is already operating at about 50 percent capacity, says Perlin. "We needed a home for fundamental research," he explains. "It's good to have a place where we can study these dangerous pathogens safely."

"Imagine life without antibiotics. You couldn't get surgery because all the bugs would be there. And when you got pneumonia, you would die. People used to die a lot from infectious diseases." —**Karl Drlica, PhD**

TOP LEFT: JOHN EMERSON; TOP RIGHT: ANDREW HANENBERG

A walk through the high-security laboratory provides a glimpse of how the cutting-edge research moves forward. Safety systems are designed to protect both the research staff within the facility as well as the general public outside the laboratory.

The labs operate with a system of negative pressure, which means air is constantly moving into the labs from the outside. But it is only released after going through a high-efficiency particulate air (HEPA) filter that traps greater than 99.97 percent of contaminants 0.3 microns or larger in size. Back-up generators kick on in case of a power failure to maintain the lab's negative pressure.

When Steven Park, the lab's biosafety Level 3 manager, enters the lab, his first stop is an ante-room, which is under negative pressure. There, he dons what he calls his personal protective equipment, a Tyvek protective suit, gloves, booties, headgear that protects his face with a plastic shield, and a stream of air blowing out from an air-pack on his back.

Then his security clearance allows him into the actual lab where experiments take place in biosafety cabinets, which also keep the infectious agents from circulating in the air, using negative pressure.

"In addition to the negative pressure in the room, there's external air coming into the cabinet," says Park, who has worked with Perlin at PHRI since 1997. "It gets discharged through a filter, which prevents any infectious material from escaping."

These measures provide safe working conditions for about 40 investigators and research staff as well as a dozen technical, animal-care, and biosafety personnel.

Among the researchers is G. Marcela Rodriguez, PhD, who studies *Mycobacterium tuberculosis,* the pathogen that infects about one-third of the world's population and is responsible for at least two million deaths each year. Her research is aimed at understanding how the bacterium interacts with its human host to obtain the mineral iron, which it needs to survive. Iron is not freely available, but this bacterium has developed strategies to capture the iron from its host. Rodriquez studies the molecules that the pathogen uses to obtain the iron and transport it. "Those molecules are potential targets for drug therapy," she says.

Abraham Pinter, PhD, joined PHRI's staff in 1985, just as the HIV virus emerged in humans. More than two decades later, his research team is still exploring the mysteries of the virus and working to overcome barriers towards developing a vaccine. Pinter's research is focused on isolating antibodies from some infected patients that are highly protective against the virus and understanding the structure of the targets recognized by these antibodies.

His latest research has shown promise as his lab designs new immunogens and vaccination strategies that could induce broadly protective antibody responses in the human body. "This virus has been more challenging than any other virus studied to date."

As Pinter works on HIV and Rodriguez investigates the TB bacteria, Perlin and colleagues at PHRI and NJMS stand ready to battle the world's next bewildering bug. As Perlin says, "A lot of them are quite happy in their initial hosts. But when they jump to another host, they can cause very serious disease. We have the infrastructure to work safely with a wide range of pathogens and parasites." ●

Did You Know…

The Public Health Research Institute (PHRI) at NJMS has been on the cutting edge of infectious disease research since its founding? For seven decades, this institute has addressed challenges posed by infectious diseases. Scientists at PHRI have an impressive record of accomplishments during the past seventy years. Here are just a few of the historically dramatic highlights from past decades:

1940s PHRI produced and distributed the smallpox vaccine in New York City.

1950s The Institute's scientists developed methods to boost antibody response to infection.

1960s Work was done at PHRI which led to a vaccine for dengue fever.

1970s PHRI researchers identified cancer-causing oncogenes.

1980s Institute scientists discovered the gene for toxic shock syndrome.

1990s PHRI researchers identified the multi-drug-resistant TB strain "W."

JOHN EMERSON