at the tip of a fully assembled pilus. Throughout this process, chaperone molecules stabilize pilus subunits, shuttling them one by one to the usher. Subsequently, a conformational change in the β-barrel domain of the usher (FimD) along the outer membrane helps to move and secrete the subunits of the growing pili. When closed, the barrel-like pores are kidney-shaped when viewed from outside the cell. When activated by a chaperone-adhesin, they become nearly circular. It and other β-barrel proteins on the outer membrane of gram-negative bacteria were believed to be rigid, according to Li. “We always assumed the outer barrel proteins were rock solid and rigid to protect cells from the harsh outside environment,” he says, adding that he and his collaborators do not know what that unanticipated shape change might accomplish for E. coli.

Another surprise was that the chaperone-adhesin binds to the C-terminus site of the usher. The new observation, made with electron paramagnetic resonance spectroscopy, suggests that the chaperone subunit is first recruited at the N-terminus site, and then transferred to the C-terminus site during pilus assembly. “Before this, we thought that only the N-terminus was important for assembly. Now we know the C-terminus is just as important,” Li says.

“There are a number of machines that transport proteins across membranes, but never before have we seen one in action,” says molecular biologist Thomas Silhavy of Princeton University in Princeton, New Jersey. “It’s a remarkable finding. You can look at the structure and imagine how the machine works.”

Type 1 pili on uropathogenic strains of E. coli are critical for causing urinary tract infections (UTI). Their adhesin subunits such as FimH bind, invade, and form biofilm communities in bladder cells. In the United States, 15 million UTI occur yearly, mostly in women. Because antibiotics are not very effective in treating such infections, about 10% of UTI progress to chronic cystitis, a condition that requires long-term suppressive therapy. “There’s a real need for better ways to treat UTI, and women and urologists want better therapies,” says microbiologist Scott Hultgren of Washington University School of Medicine, who collaborated with Li on this structural analysis.

This new crystallography-based understanding of pilus assembly could “help to zero in on new critical nodes for rational drug development,” Hultgren continues. He and his collaborators in St. Louis are designing and testing potential “pilicides,” compounds that can interrupt pili assembly, adherence to bladder cells, and biofilm formation. They also are testing mannose derivatives as a way to block the FimH adhesin.

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Model for Malaria Tracks Impact of Simulated Interventions

Malaria Tools, a model for tracking this parasitic disease, is robust enough to predict outcomes of interventions now being contemplated, according to its developers, Azra Ghani and colleagues at Imperial College in London, England. It simulates various means for controlling malaria against the dynamics of transmitting the disease, while taking into account important factors such as climate and public health interventions. Users can evaluate, for example, the extent of mosquito net use, access to standard treatments, and how much pesticide is being sprayed in a particular geographic sector. The model simulates how those strategies fare against the population dynamics of the malarial parasite, Plasmodium falciparum, and the female Anopheles mosquitoes that deliver it to humans.

Malaria Tools can also help in eval-

Efforts To Improve Influenza Vaccines and Track Them and the Virus

Recent developments affecting influenza vaccines or the virus include:

- An antibody, designated F16, is the first known to neutralize both group 1 and 2 influenza A viruses, and it can protect against such infections in mice and ferrets, according to Antonio Lanzavecchia of Humabs in Bellinzona, Switzerland, and his collaborators there and at several other institutions. Details appear in the 28 July 2011 Science.
- By tracking specific gene activity in white blood cells, it is possible to predict who will eventually make high levels of protective antibodies within a few days after receiving the influenza vaccine, according to Bali Pulendran of the Emory University School of Medicine in Atlanta, Ga., and his collaborators there. Details appear in the July 10, 2011 Nature Immunology.
- Gold nanoparticles coated with antibodies that bind the influenza virus can detect it in minutes via laser light scattering patterns, according to Ralph Tripp of the University of Georgia College of Veterinary Medicine in Athens and his collaborators. Details appear in the August 2011 Analyst.
Virus Developments and a Broad-Spectrum Antiviral Agent

Recent developments affecting assorted viruses include:

- A newly recognized adenovirus infects both humans and monkeys, causing fever and respiratory tract symptoms, marking the first time an adenovirus is known to jump between species while remaining infectious, according to Charles Chiu of the University of California, San Francisco, and his collaborators. Details appear in the July 1, 2011 PLoS Pathogens.
- An experimental vaccine consisting of viruslike particles coated with the envelope protein of the hepatitis C virus protects mice and monkeys against that virus, according to David Klatzmann of Inserm in Paris, France, and his collaborators at several institutions, including the biotechnology company Epixis. Details appear in the August 3, 2011 Science Translational Medicine.

Evaluating the effectiveness of a malaria vaccine, such as one now in Phase 3 trials, according to John Marshall of Imperial College. When the model runs with the (wildly optimistic) assumption of 90% vaccination coverage across Africa, it shows the area of malaria sufferers steadily decreasing over 20 years. Thus, it predicts that the vaccine virtually vanquishes the disease.

To produce such scenarios, the Malaria Tools program relies on data summarizing the population dynamics of P. falciparum at six locations in Africa, across a range of seasonal patterns and infection intensities. Vectors are accounted for by species, according to Jamie Griffin, also of Imperial College, since the behavior of any one mosquito species affects the impact of control measures at each of those sites. For example, some Anopheles species bite indoors and rest on interior walls after feeding. The model accounts for people as individuals to reflect, for instance, differing immune responses to infections. Tracking such details bedeviled other modelers, he says.

The complex interactions between parasites and hosts partly account for why malaria is so difficult to control. Decades of simulating this disease with models failed to capture its shifting patterns. “There are individual factors, household factors, and geographic factors, but they’re not as predictable as you’d think,” says David Smith from the University of Florida.

Researchers belonging to malERA, a loose affiliation of modelers, recently wondered: “How can models and model systems ask key questions?” Their subsequent efforts yielded a blueprint for harmonizing several models, including Malaria Tools, according to malERA scientist Marcel Tanner, with the University of Basel in Switzerland. Under that plan, various teams will employ competing modeling strategies in parallel, rather than follow any single approach, while testing those models with hard data. “There’s a new way to use models,” says Tanner. “Modelers aren’t just lunatics staring at a computer screen.”

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Final Shuttle Flight Carried Several Microbial Experiments

When Atlantis launched in July for the final mission of the U.S. Space Shuttle program, it carried microbial experiments probing bacterial biofilms, the genetic makeup of yeast, microgravity effects in a plant-bacterial model system, and a candidate live-attenuated vaccine for combating Streptococcus pneumoniae infections. Other experiments in biology aboard STS-135 looked at the effects of tissue regeneration and wound-healing, the effectiveness of experimental drug therapies against bone loss resulting from microgravity, and how spaceflight affects sleep patterns.

BioServe Space Technologies of the University of Colorado, Boulder, a group that specializes in developing and packaging microgravity life-science experiments, handled the logistics of preparing and loading the microbiological experiments aboard STS-13, according to Cynthia Collins of Rensselaer Polytechnic Institute in Troy, N.Y. Among those packages, the shuttle carried experiments that she designed to test how microgravity affects the growth of biofilms. The experiments, which included samples of Pseudomonas aeruginosa and Staphylococcus aureus, follow up earlier findings indicating that biofilms are altered during spaceflight and that different microorganisms respond differently in microgravity, she says. This July after the shuttle launch, she ran duplicate samples on Earth, starting...