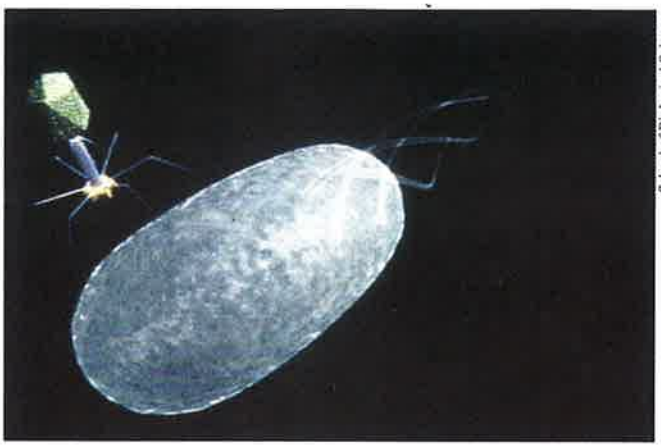
Revealing Some Nasty Little Secrets



School of Biological Sciences

This computer-simulated image shows a virus' size in relation to a host cell it is about to invade. Of the 1,500 or so types of viruses, about 250 can cause diseases in humans.

It's based on a simple scientific premise: to discover how to eliminate a process, one simply figures out how it originates and develops. Identify those steps and then outline ways to stop the process.

The complexity of viruses has puzzled scientists for years.

Viruses — obligate intercellular parasites — are some pretty tough opponents. They invade and conquer healthy cells, causing much pain and suffering. Herpes, rabies, influenza and the common cold are diseases caused by viruses.

But for George Thomas Jr., Curators' Professor in UMKC's School of Biological Sciences, unlocking the secrets of viral growth is a passion worth the effort.

Thomas and his team are making progress in solving viral secrets, as evidenced through the lab's status in its field. The team holds National Institutes of Health grants totaling nearly $400,000.

To date, the team has published 175 papers on the structure of viral proteins and nucleic acids and how they assemble themselves.

Viruses are the Davids of their world, as they are much smaller than their host-cell targets. Despite their size, viruses are vastly more complex than a cell; their mission is to find, invade, conquer.

Also unique, Thomas says, is a virus' ability to defy analysis because of its ability to mutate.

To understand one aspect of the architectural complexity of a virus particle, consider that viral DNA is encased in a complex protein shell, or capsid, designed to package the DNA efficiently and inject it into the host cell. In a typical bacterial virus, the capsid may have a specialized apparatus made of many protein molecules — a tail, really. The tail mediates the host hook up, which allows the DNA injection process to begin.

Once attached, the virus burrows through the cell's membrane and injects its own DNA into the host. Inside, the viral DNA starts duplicating and progeny viral particles are constructed. To live, the virus steals the host cell's biomechanical machinery, destroying normal cell growth. At maturity, the new viruses exit the host cell and seek out new healthy host cells to invade and destroy.

A key aspect of the "virus assembly" process involves the so-called "scaffolding" proteins, which direct the assembly of the virus' capsid shell. Thomas' team has recently focused on ways to interfere with the pre-programmed functions of the scaffolding proteins. If successful, this action could provide a way to prevent virus assembly. Stop the assembly and the virus cannot complete its deadly mission.

Thomas is quick to point out, however, that a far greater understanding of the basic rules governing protein recognition and interaction is necessary. Again, the complexity of viruses prevents clear-cut answers, at least for now.

Viral capsids, Thomas explains, are typically constructed from many hundreds, and sometimes thousands of protein molecules, which assemble in a highly symmetrical, often icosahedral shape. Many different types of protein-to-protein interactions are required for the intricate construction, and the pathways to shell assembly are just beginning to be understood.

Still, understand the pathways, Thomas says, and you can change the virus so it assembles itself into a nonharmful alternative.

— Michael Johnson