

## From the Director

Otto J. Schwarz, Ph.D.



The year has traveled its course, the academic year that is, and I am still able to sit upright in my office chair and enjoy the never

ending parade of challenges that are a daily part of the business of the Division of Biology.

For the most part, the Division has been able to hold its own in the face of the beginning of the year University shutdown and a year long search for ways to trim an already slender budget, all culminating in the announcement of an across the board nine percent budget cut by our State's governor.

The University responded beautifully in trying to minimize the effect of the budget mandate by trimming its spending and allowing normal attrition to work toward meeting the nine percent goal. Within the Division, no sitting positions were lost and all educational needs were supported through the help of the College of Arts and Sciences. Unfortunately we continue to lose valuable personnel at [See DIRECTOR, on page 4](#)

### Table of Contents

|                                |   |
|--------------------------------|---|
| From the Director .....        | 1 |
| Spotlight on Microbiology..... | 1 |
| From the Head .....            | 2 |
| New Faculty.....               | 4 |
| Focus on Staff .....           | 6 |
| Alumni News .....              | 7 |

## Battling SARS at UT

Professor Dr. David Brian's studies on coronaviruses have been funded by the National Institutes of Health (NIH) for 25 years. This partnership has helped to put Dr. Brian near the front lines of the battle to understand the causative agent of severe acute respiratory syndrome or SARS.

He said, "The general approach by NIH is wise. It is to fund basic research for all known animal viruses, and then when something like this appears, they can move rapidly to analyze both the genetics and behavior of the new virus and maybe have a jump start on diagnosing, making vaccines, and treating infections by the new virus."

Dr. Brian was contacted by the Centers for Disease Control (CDC) shortly after SARS made its appearance. He has a standing conference with the CDC every Wednesday, giving his opinion and sending reagents of the bovine and other animal coronaviruses his laboratory has worked on for comparison. SARS virus has been found to belong to a family of virus called coronavirus.

Dr. Tony Fauci of the NIH is spearheading the government's attempt to develop a vaccine or antiviral drug for SARS. The NIH has

been in contact with Dr. Brian because of his continuing work on coronaviruses. As was previously reported in last year's *In Vivo* article (Volume 2, Number 2), Dr. Brian's laboratory focuses on the replication strategy and elements that direct the RNA synthesis of the coronavirus family. In the past NIH dollars have been targeted to develop drugs to block replication of the influenza and AIDS viruses. Dr. Brian's work will



Left to right: Gwyn Williams, Hung-Yi Wu, Kimberly Nixon, Sharmila Raman and Dr. Brian

contribute to an effort to find such drugs for a coronavirus.

Dr. Brian has received extra support from NIH to spend more time on SARS research. He will study RNA structures in the SARS virus genome, material extracted from SARS virus infected cells at CDC. Fortunately, the material in this form can be studied safely.

Coronaviruses are found in many species of animals, birds and in domesticated animals. In chickens

[See BRIAN, on page 3](#)



## From the Head

by Jeffery Becker, Ph.D.

It is with great enthusiasm that I take on the responsibility of being Head of the Microbiology Department. I have been at UT since November, 1972. Thirty years! It is time for me to serve my Department. The job is demanding, but I look forward to its challenges and to building the Department from the strong base provided by the Heads during my tenure here: **Arthur Brown**, **Dwayne Savage**, and **“Buddy” Moore**.

My career at UT has been filled with many rewarding moments involved in research and teaching. Perhaps the task in which I take the most pleasure is in mentoring graduate and undergraduate students toward careers in science and medicine.

Thus, I would like to yield the rest of this column to Munira Basrai, one of my former students. Munira recently started her independent career as a staff scientist at the National Cancer Institute in Bethesda, MD. Below is her “story.”

**Munira Adnan Basrai, Ph.D.** is a Tenure Track Investigator with the Genetics Branch of the National Cancer Institute. She received her B.S. and M.S. at the Abasaheb Garware College, University of Pune, India and her Ph.D. at the University of Tennessee, Knoxville (Mentor, **Dr. Jeffrey Becker**). Her research objective was: characterization of fluid phase endocytosis and peptide transport system in the opportunistic pathogen, *Candida albicans*.

She conducted her Postdoctoral Research, at The Johns Hopkins School of Medicine, Baltimore, Maryland (Mentor, **Dr. Philip Hieter**). Her research objective there was: identification of molecular determinants of genome stability in budding yeast and their evolutionarily conserved human homologs.

She said, “I was born and grew up

in Pune, India, which is 160 miles from Mumbai. I came to the United States to pursue my graduate education and career goal of establishing a research laboratory. I still recall the day when I first saw a living cell under the microscope, an observation that piqued my research interest in how cells divide and propagate.

I quickly learned that the process of faithful transmission of chromosomes



**Deziree Elliott, Dr. Becker, and Carole Vosdingh**

was the key factor that determined genome stability. Since budding (bakers) yeast offers the “AWESOME POWER OF GENETICS” it became the obvious model system of choice.

After my degree in Dr. Becker’s lab at UT, I found a postdoctoral research laboratory that offered me an excellent opportunity to continue this long-standing research interest.

I have continued my research as a tenure track investigator in the Genetics Branch at the National Cancer Institute of the NIH. Research in our laboratory focuses on defining the molecular determinants of faithful chromosome segregation and cell cycle checkpoint responses in budding yeast.

These studies are important as most of the genetic information that provides the blueprint for an organism is contained in the chromosomes of its cells. The maintenance, replication and segregation of these chromosomes

are controlled by the mitotic cell division cycle. Checkpoints ensure the sequential execution of the events in the cell division cycle.

Not surprisingly, errors in chromosome segregation have dramatic consequences and have been implicated in cancer, aging, and congenital birth defects. Hence, we are also developing and implementing yeast/human cross species approaches to identify evolutionarily conserved genes in these pathways.

The relevance of our studies is reinforced by the fact that, to date, about one-third of all human disease-associated genes have functional homologs in yeast, including mammalian homologs of yeast genes required for chromosome segregation and checkpoint function. Detailed analysis of chromosome segregation and checkpoint responses in yeast will help us understand how these processes operate successfully

(health) or fail to operate (disease) in humans.

For our studies, we use a combination of genetic, cell biology, biochemistry and genomics approaches. For the latter, we have constructed a whole genome array of budding yeast for studies on gene regulation, gene function, chromosome structure and the identification of Non-Annotated ORFs (NORFs). We are particularly interested in the NORFs that represent small genes not yet annotated by genome sequencing efforts. We have previously reported the biological significance of one of these NORFs, encouraging us to pursue the characterization of others.

I have immensely enjoyed the past few years here at NIH and especially being a part of the National Cancer Institute. The leadership at every level including the Genetics Branch with which I am affiliated has been extremely

*See HEAD, on page 7*

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### BRIAN, from page 1

and turkeys they cause severe and costly diseases. Should such a virus jump to the human species it could prove to be a very important human pathogen. A similar jump from an animal is the possible origin of SARS. This virus is spread through the air and is difficult to avoid, hence the wearing of surgical masks by many people in China and other countries.

One concern of developing a vaccine is to get the right one. Dr. Brian refers to a vaccine developed years ago to combat feline infectious peritonitis virus. He said that the vaccine made the situation worse because it resulted in an immune enhancement of the disease. The immune response to the surface protein of the virus enhanced subsequent virus infection and disease.

The SARS genome features elements resembling, but not identical to, those in currently studied coronaviruses of mammals and birds. This suggests that the virus existed in either a mammalian or avian host for a period of time prior to its jump to humans.


As with all RNA viruses, mutations occur at a high rate as the virus replicates in its host, so the SARS virus as it replicates in humans will undergo changes, too. Dr. Brian said that SARS looks much like the coronavirus disease in chickens in which there is pneumonia with systemic infection and involvement of the kidney and other organs. The mortality rate in humans is high, 15% overall, 50% in people over 60, which compares with mortality rates of up to 70% in chickens infected with avian coronavirus.

There are many questions left to answer about SARS. One main question is the origin of the virus. The study of the SARS genome sequence, soon to be featured in *Science*, would suggest that the virus has been residing in nature somewhere for a long period of time.

Dr. Brian said, "In general we, that is the larger international biomedical community, need to try to isolate and study more coronaviruses from animals, especially the wild animals, to learn more about the coronavirus gene pool. There may be several new coronavirus species to discover. What has been studied to date are coronaviruses that infect and cause diseases in domestic animals and humans."

Another question Dr. Brian faces involves the transmission of SARS. The virus in chickens can cause a life-long persistent infection and can be shed in the feces for a very long time. In the feces it can remain infectious for weeks. It is possible this same method of transmission, in addition to the aerosol method of spread, could be involved in human transmission of SARS virus.

There is also the question of longevity of the pathogenic properties of the SARS virus. Dr. Brian said, "My guess is that SARS will become attenuated, that is, become less virulent over time as it adapts to the human host. However, it could then recombine with a currently known respiratory coronavirus and maybe lead to another virulent pathotype. It's just not possible to predict the future properties of a continuously mutating virus."

Dr. Brian said, "Viruses with new species or tissue tropisms and viruses with new pathogenic properties like SARS virus arise with quite high frequency in nature among plants and animals, especially with RNA viruses such as coronaviruses. It is their very nature to mutate and to often jump species. One can't afford to be complacent about our study of any group of viruses." 

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## Designing more effective vaccines

Assistant Professor **Dr. Mark Sangster** is studying the mechanisms of antibody production by B cells in response to virus infection. He is also interested in the B cell memory that enables a more rapid and effective antibody response to be generated on re-exposure to a virus. This work could lead to improved approaches to vaccination.



Dr. Sangster began his research career in his hometown of Perth at the University of Western Australia. His graduate studies focused on genetically determined resistance to flaviviruses such as West Nile virus and yellow fever virus. He developed mouse models to investigate a genetic basis for the increased susceptibility of some individuals to flavivirus infection.

To obtain mice for these studies, Dr. Sangster's Ph.D. advisor decided to take advantage of a mouse plague that was occurring at the time to the north of Perth.

With approximately one mouse per square yard, Dr. Sangster had no trouble trapping more than 300 mice in two night's work. He then spent several years breeding flavivirus-resistant mice and even developed a liking for the little mammals. Dr. Sangster said, "It was fun at the time, but a little inappropriate for a Ph.D. program. However, a resistance gene that we discovered in the wild mice has now been introduced into other mouse strains and is still being studied in Perth."

In 1992 Dr. Sangster accepted a

post-doctoral position at St. Jude Children's Research Hospital in Memphis, Tennessee. It was there that he changed his focus from genetics to immunology, and developed an interest in the antibody response to infection.

From 1997 to 2003 he worked as an Associate Investigator in the laboratory of Nobel Laureate **Dr. Peter Doherty**, and studied viruses such as

influenza virus that infect the respiratory tract. An added bonus of Dr. Sangster's time in Memphis was meeting his wife, **Linda**.

He accepted a position in the Department of Microbiology at UT last August,

and moved with his wife to Knoxville in February.

As soon as his laboratory is established, he plans to hire a technician and attract students. He will be responsible for teaching an immunology course next year.

Dr. Sangster will continue his studies of virus infections of the respiratory tract, initially focusing on aspects of the antibody response to influenza virus. A particular interest is the process by which anti-viral IgA antibodies are generated in the respiratory tract.


These antibodies have an important role in clearing virus infections from mucosal surfaces such as the respiratory tract, and providing a barrier to re-infection. Dr. Sangster also plans to examine the role of IgA and other antibodies in the long-term "memory" responses that occur on re-exposure to a virus.

He will use mouse models in his studies of the immune response to infection and vaccination, and will make extensive use of the campus Animal Facility. He hopes to interact with ORNL and take advantage of the mutant

strains of mice that have been generated there. He will also continue his collaborations with researchers at St. Jude Children's Research Hospital.

Here in Microbiology, Dr. Sangster looks forward to collaborating with **Dr. Barry Rouse**, **Dr. Tim Sparer** (see facing), and **Dr. David Brian** (see page 1).

Dr. Sangster's work may have important implications for the optimization of vaccination regimens. The effectiveness of many vaccines in current use may be substantially improved by strategies that ensure a strong IgA response, just like the one generated by natural virus infection.

Dr. Sangster plans to apply to the NIH and the American Lung Association for grants to support his research. 

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### **DIRECTOR**, from page 1

all levels because of noncompetitive salaries and at times for our inability to provide a continuing program of job advancement.

I could spend many words in telling you of the good things that the Division was able to do for itself, the departments and our students, however I am sure that future issues of *IN VIVO* will do just that.

For myself, I have had a satisfying year as the Interim Director. In thinking about how I have rationalized this point of view I can only come to one conclusion. I have had the good fortune to be surrounded by many very competent, dedicated and enthusiastic people. Add in a stimulating environment populated by creative minds working to explore the very fabric of life, who wouldn't appreciate such an opportunity.

Dear reader, you don't have to travel farther than across these pages to visit a dash of what Biology

**See DIRECTOR**, on page 7

## Smart viruses

Until recently, it was commonly held that viruses attempt to avoid detection by the body's immune system. However, Assistant Professor **Dr. Tim Sparer** is engaged in research that points to a more insidious plot. He explains, "Discoveries in the last five years have shown that many viruses have stolen our genes for their own benefit."

His research indicates that some viruses may have modified our own genes, enabling them to "disguise" themselves and attract the attention of the immune system of the host. This



helps viruses spread to other people because instead of being targeted for attack by the host's immune system, the virus is actually aided by the immune system to spread throughout the body.

Dr. Sparer studies cytomegalovirus (CMV), a member of the herpesvirus family. He has found that CMV is one of the viruses that uses subterfuge and manipulation to spread. CMV spreads easily between people because it is carried by saliva and other secretions (breast milk and urine). Since infection is usually asymptomatic, most people do not know that they have been infected with CMV. However, those that have been infected will carry the virus for life.

CMV infection is not without some consequences. In people with compromised immune systems, such as those with AIDS and transplant patients, the virus can reactivate and

contribute to inflammation of the lungs and intestines, often leading to death. CMV's most dramatic effect occurs when pregnant mothers are infected for the first time during pregnancy. The virus can then spread to the developing fetus and lead to mental retardation, learning disabilities, or hearing loss. Approximately 1% of all newborns in the US are infected with CMV *in utero*.

In addition, CMV has recently been implicated as a contributing factor for the development of heart disease in heart transplant patients.

Whether this occurs in non-transplants remains to be investigated. Even though in most cases CMV does not cause disease, when it does, the effects can be devastating.

Current treatments for CMV include antiviral drugs such as gancyclovir. Unfortunately, gancyclovir is so toxic that it can only be tolerated for short-term use. Additionally, drug-resistant viruses can develop, rendering the antiviral drug ineffective. Dr. Sparer hopes that studying how CMV manipulates our immune system and spreads will lead to a safer, more effective vaccine.

Because CMVs are highly species-specific (i.e., human CMV only infects humans), Dr. Sparer uses mouse CMV infection to model how human CMV proteins manipulate the immune system. Both human and mouse CMVs have proteins that activate the immune system. These proteins attract and activate the immune system just like the host's own chemokines.

In other words, CMV chemokines mimic the activity of our bodies' own chemokines. As Dr. Sparer asks rhetorically, "If you were a virus, why would you want to turn on your host's immune system? Normally, most

viruses are trying to hide from the immune system." He hopes that his work will help solve this seemingly contradictory puzzle.

Dr. Sparer has found one clue to the puzzle by studying a protein called MCK. MCK, which is produced by mouse CMV, appears to mimic the mouse chemokines that normally activate the immune system. The MCK protein appears to aid the spread of murine CMV by attracting immune cells; these cells then help the virus spread to the salivary gland, which in turn helps CMV spread to another mouse when mice bite or lick each other. Clever.

Work in Dr. Sparer's laboratory is currently focused on a similar protein in human CMV called the vCXCL-1 protein. In order to discover whether this protein plays a role in the spread and dissemination of human CMV, the way that MCK helps to spread murine CMV, Dr. Sparer is making murine CMVs that express the vCXCL-1 protein in place of MCK. He hopes this will allow him to see whether vCXCL-1 can replace the function of MCK and allow the virus to spread to the salivary gland.

One hurdle Dr. Sparer has faced is the fact that the vCXCL-1 protein does not function in mice. When vCXCL-1 is tested on mouse cells nothing happens. "To circumvent this problem," Dr. Sparer explains, "I made a transgenic mouse expressing the human vCXCL-1 receptor." So far, this step has been successful. He continues, "If I'm able to show that a virus lacking vCXCL-1 cannot spread, then eliminating that gene from human CMV would make a good vaccine candidate."

Dr. Sparer came to UT in January and will be joined by his wife, **Cathy Shuck**, in August. He has an army of undergraduates that are helping him to get established. The undergraduates **Jennifer Janowitz**, **Helena**

*See SPARER, on page 6*

## To say she is loyal is an understatement

**Carole Vosdingh**, Administrative Aide to the Department Head, has served Microbiology faithfully for nearly 30 years. She started at UT in 1974, two years before Walters Life Sciences Building was completed. Carole remembers watching the building go up and even getting to tour it before it opened.



She has worked for four department heads; **Dr. Arthur Brown**, **Dr. Dwayne Savage**, **Dr. Robert Moore**, and **Dr. Jeffery Becker**. Carole worked the longest for Dr. Brown, 15 of the 19 years he served as head.

Dr. Becker said, "A major reason for my being enthusiastic about

heading Microbiology is the opportunity to work on a daily and regular basis with Carole, one of the most professional and experienced administrators at The University of Tennessee."

Dr. Becker goes on to say, "Carole knows more than anyone about the Microbiology Department. Her wealth of knowledge and experience, combined with her skills as a manager and her generally wonderful personage, bring a unique and highly valuable combination of skills to the office. Microbiology is indeed fortunate to have Carole as its chief administrative assistant."


Her favorite part of her job is getting to know the students. She said, "It's really been nice helping the students get started, and then watching as they go on in their careers. That's why I stayed in an academic department; I really like the contact with students."

Carole notes that the most noticeable change in her job over

the years has involved the office equipment. She said, "We went from mimeographs, carbon paper and a centralized copy machine to computers. It's been amazing."

Carole is originally from Vinton, Iowa, which is 40 miles from Cedar Rapids. She grew up on a farm helping to raise cattle and hogs. She married her high school sweetheart, **Larry**, and soon his job moved them to Seymour, Tennessee, just south of Knoxville.

She was happy to leave the snow and bitter cold of Iowa winters; however, her first day here introduced her to East Tennessee "snow panic." It snowed five inches when they arrived with the moving van and Carole went a local store to stock up on staples for her new house. She found the cupboards empty and the stores all locked up.


Carole has three daughters. One lives in nearby Maryville and the other two live near Spartanburg, South Carolina. She is happy to be close to her nine grandchildren. In her spare time she enjoys gardening and yard work. 

## Golf Update

By Jan Hudson

The "Friends of Biology" golf tournament went well and I am so glad it did not fall on a rainy week! The weather was beautiful and I think a good time was had by all.

**Glen Makin's** team won, and yours truly took second place. **Sandy Coward** won the longest drive for the women and **Brad Bennett** won for the men's longest drive.

**Jody Watson** and **Stephanie Hicks** graciously helped out with registration and selling mulligans. Centennial does a great job with the tournament every year. 

## SPARER, from page 5

**Geissler**, and **Chris Bell**, were with him during the spring semester and three others will be joining him this summer. Along with graduate student, **Mindy Miller-Kittrell**, he is hoping to hit the ground running. He has submitted grant proposals to the NIH and the American Heart Association with the hopes that they will see the importance of CMV in human diseases.

Originally from Cincinnati, Ohio, Dr. Sparer completed his undergraduate degree in Molecular and Cellular Biology at Northwestern University in 1989. He received his Ph.D. at Emory University School of Medicine in

Atlanta in 1995 studying adenoviral suppression of immune responses.

His first postdoctoral fellowship was at the National Heart and Lung Institute at Imperial College in London, UK where he studied respiratory syncytial virus' alteration of the immune responses. He went on to study CMV virology at Stanford University School of Medicine during his second postdoc. He is now looking forward to exploring all that Tennessee has to offer.



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## HEAD, from page 2

supportive of our program. This has allowed me to explore areas of interest and use approaches that would be otherwise difficult in other places.

The flexibility has fostered much fruitful collaboration with investigators both within and outside the NIH to pursue whole genome approaches in defining new genes and their function.

The NIH campus offers, by far, the



**Dr. Basrai**

maximum resources, seminars and workshops conducted by reputable leaders in the field. It may be appropriate to say that at the

NIH "sky is the limit" in terms of opportunities to broaden ones horizon, network and grow as a scientist.

The trainees including summer interns, post-baccalaurate and post-doctoral fellows become a major driving force in the laboratory. Each individual brings different strengths to the group and we all benefit from this diversity. In turn, the laboratory group plays a pivotal role in mentoring a trainee to address the biological problem under investigation and pursue approaches with possible interpretations of the data.

The latter is one of the most stimulating parts of my job as I learn to view the research problem from

someone else's viewpoint. These interactions are very rewarding. A testimony to this is the initiation during the past year of a new project based on the observation and intellectual pursuit of a summer intern. I also enjoy teaching, a passion that is, in part, satisfied by mentoring the research program in our laboratory.

In addition, since NIH is not a typical academic setting, I volunteer some of my time to give talks at workshops/courses at other institutes or colleges.

Every day is somewhat different in terms of prioritizing responsibilities. The daily activities include interactions with my trainees, writing (manuscripts, review articles, progress and site visit reports), attending seminars, networking and participation in various faculty interest groups.

My first priority is the research efforts in the laboratory, which includes conducting some of my own experiments and mentoring the fellows/trainees in the laboratory. The best part of this involves the discussions of hypothesis/models and the possible experiments to be done as well as interpretation and analysis of the data generated from such efforts.


I have learned over the years that one has to keep an open mind when interpreting data and be prepared to accept the "story" that the "cell" is trying to tell rather than forcing the data to fit the hypothesis.

Research is extremely rewarding especially when your group thrives to meet the challenges of defined objectives. However, family, friends and cultural heritage are also part of my priorities. Over the years, I have balanced my professional career with family activities and traveling agendas. During my travel to different parts of the world I have witnessed and learned about the historical, cultural, wild-life and natural beauty that each land has to offer." 

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## Alumni News

**Betty R. Davis** received her bachelor's degree in 1949 and her master's in 1955 from Bacteriology. She became a research microbiologist at the Centers for Disease Control in Atlanta. She is now retired and living in Knoxville.


**Doug Tremblay** graduated with a Ph.D. in 1997 working with **Dr. David Hacker**. Afterwards, Doug worked with **Dr. Steven Lommel** at North Carolina State University in Raleigh studying movement of plant viruses and for the last year and a half has been working at BASF Plant Science in Research Triangle Park, North Carolina studying abiotic stress in crops. Doug and his wife have a four year old daughter and all are doing well. 

## DIRECTOR, from page 4

at UTK has to offer. Microbiology has a new permanent Head, but an old hand at meeting the challenges of research and teaching, **Dr. Jeffery Becker**. Enjoy his "From the Head" column.

The other faculty profiled, **Drs. David Brian, Mark Sangster, and Tim Sparer** offer a brief glimpse into the research world of the modern microbiologist. Lastly don't miss the much deserved staff profile of **Carole Vodingh**, Administrative Aide to the Department Head. All of what Dr. Becker says about her is the absolute truth.

A final appeal (for now). Let's hear from you, our friends and alumni. Let us know what you are up to and give us the benefit of your wisdom and perspective.

Peace. 

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## In Vivo

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# IN VIVO

Newsletter of the University of Tennessee Division of Biology

VOLUME 3, NUMBER 2

JUNE - JULY 2003



**Otto J. Schwarz and Christopher Pack**

## **Hollaender Recipient Announced**

By Otto J. Schwarz

It is my pleasure to announce that **Christopher D. Pack**, from the Department of Comparative and Experimental Medicine, is the recipient of the Alexander Hollaender Fellowship for 2003-2004.

Pack is a graduate research assistant in **Dr. Barry Rouse's** laboratory. He is a native of Knoxville. He received his B.S. in Microbiology in 1996 and his M.S. in Microbiology in 2000 from The University of Tennessee, Knoxville. His research focuses on prophylactic approaches to vaccinate neonatal mice against infection with herpes simplex virus-1.