SFBR
Southwest Foundation for Biomedical Research
PROGRESS
Spring 2009

Fighting Disease Around the Globe

By John VandeBerg, Ph.D., Chief Scientific Officer, SFBR

Research in progress at the Southwest Foundation offers real hope for developing vaccines to prevent infectious diseases that afflict millions of people worldwide. And the opportunities and potential to capitalize on new vaccine strategies against illnesses ranging from Ebola hemorrhagic fever to tuberculosis within the next few years have never been better. In this column, I survey some of the groundbreaking work that promises to change the face of disease around the world.

Hepatitis C Virus

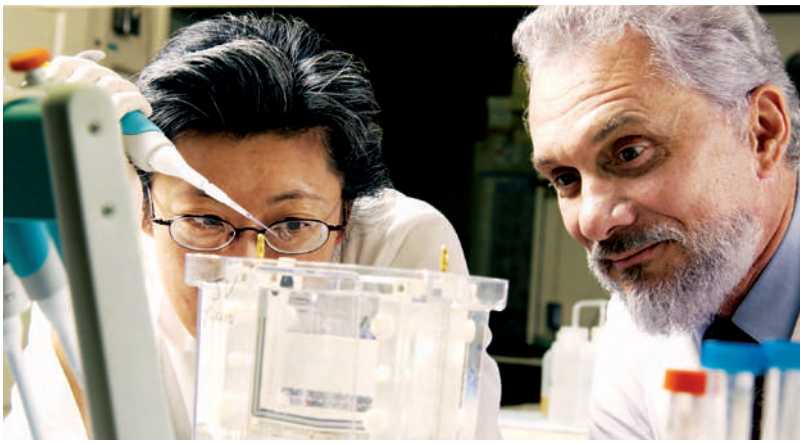
This virus infects 170 million people worldwide and two percent of the US population. There is no vaccine for prevention. It is the primary cause of liver cancer, the most rapidly increasing cause of cancer death, and is the leading cause of liver transplantation.

One strategy investigated by SFBR's Dr. Kris Murthy and scientists at the National Institutes of Health (NIH) involves virus-like particles (VLPs) containing genes for the outer coat of the virus and the core of the virus particle. In previous studies, vaccinated chimpanzees developed very mild infection that was rapidly cleared, whereas unvaccinated chimpanzees developed robust infection and became chronic carriers. To further strengthen this promising vaccine approach, additional VLPs have been constructed containing other viral genes. They have been selected for further studies in baboons before determining their efficacy in chimpanzees.

HIV

SFBR's Dr. Luis D. Giavedoni is working on a vaccine based on a combination of genetic material and part of a virus to deliver it into cells. Rhesus monkeys were immunized with genetic material entrapped in very small particles, which were delivered directly to the nose of the animals. This vaccination primed the immune system so that animals reacted with stronger responses when they were boosted with a second vaccine. When the monkeys were exposed to an HIV-like virus, half of the vaccinated animals resisted infection. These very encouraging results will be repeated in a larger study.

In other HIV vaccine development efforts, SFBR's Dr. Marie-Claire Gauduin focuses on the immune responses of lymph nodes and organs that are involved in the initial reaction to HIV infection. Approaches include vaccination with a weaker live virus,



Dr. John VandeBerg in his laboratory at the Southwest Foundation for Biomedical Research.

or with an HIV virus that is coated with a particular protein. In working on a vaccine for pediatric HIV, Gauduin has shown that newborn monkeys infected with a less virulent form of simian immunodeficiency virus can control infection even in the absence of antiviral treatment. This suggests that treatment may be quite successful in "rescuing" or preserving the infant's immune response.

Tuberculosis

The World Health Organization estimates that more than a third of the world's population, or 2 billion people, has latent or inactive infections with tuberculosis bacteria. Each year, 9 million people will develop the disease, and some 2 million will die from it. In 2008, 1,501 TB cases and 88 deaths were reported in Texas, according to the Texas Department of State Health Services.

Vaccine development against TB has been a challenge. The most widely used vaccine, called BCG, offers some protection to children. But studies on its effectiveness in adults have produced mixed results worldwide. At SFBR, we are collaborating with Brazilian scientists who have developed a vaccine that uses bits of genetic material and protein from tuberculosis bacteria that are packaged so that a single injection initiates two rounds of immune response. It is now being tested at SFBR in rhesus monkeys.

Ebola Viruses

In a recent report, SFBR scientists showed that protection against Ebola, one of the world's deadliest viruses, can be achieved

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An Interview with Kenneth P. Trevett, SFBR's President

Kenneth P. Trevett became SFBR's President and CEO in September, 2008. An attorney, Trevett has 27 years of senior management experience at independent research institutes, including his most recent position as head of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, one of the largest independent biomedical research organizations in California. Previously, he served as a senior administrator and legal counsel for The Schepens Eye Research Institute in Boston, an affiliate of Harvard Medical School; general counsel for the Dana-Farber Cancer Institute, also in Boston; and assistant to the director and house counsel for The Jackson Laboratory in Bar Harbor, Maine.

Kenneth P. Trevett, J.D.

Progress: Please tell us something about your career and what brings you to the Southwest Foundation.

Trevett: I've spent the majority of my professional career working in legal and management positions at independent, not-for-profit biomedical research institutions. It's been a very satisfying and exciting career. I had an opportunity this summer to consider the position here at the Southwest Foundation, and it was really an opportunity I couldn't ignore. This is one of the premier life sciences research institutions in the country, and the world.

Progress: Of the variety of jobs you have taken on in your career, what is it that has made you say, "I want to work there."

Trevett: I would say that it is because of new challenges, additional responsibilities and a clear opportunity to bring whatever professional skills I have to the particular situation. There certainly are some organizations where it might not be a fit if I became the CEO. Here, I really do believe that it was a good fit, and I think that I can add some real value to the institution.

Progress: What's unique about the Southwest Foundation?

Trevett: Well, it is truly an independent research institution. We do not have an institutional affiliation with a medical school or university, so all the scientists report up to a chief scientific officer here. There aren't dual roles. Now, some scientists do have adjunct appointments at either University of Texas at San Antonio or at the Health Science Center, but institutionally we are independent. So that's number one. Number two, we have great resources here for the scientists to do their work with the Southwest National Primate Research Center, with the AT&T Genomics Computing Center, with the San Antonio Family Heart Study, with very good laboratory facilities – some like the maximum containment lab are so unique. So that's very special. A third point is that Southwest Foundation has a real tradition of philanthropy. There is considerable revenue that comes in from grants and contracts, but that never covers the full cost of doing research. We have a robust philanthropic program, which is very, very instrumental in allowing us to support a sophisticated research program and also to develop new facilities and instrumentation.

Progress: Much of what you've said focused on strengths. What are your challenges here?

Trevett: The work of the Southwest Foundation really needs to be known more broadly. In San Antonio it is generally known, although there is some confusion with our sister institution, the Southwest Research Institute. I would question whether the lay community in parts of Texas and nationally knows about the work of the Foundation and its importance. So that's one thing. The second is that I think we can enhance our technology transfer efforts to take discoveries to people in a more expeditious way. And the third is that we do need to modernize some of our facilities and expand our capacity to do research, and that will take a building program, which we will be putting into place over time.

Progress: So these are really the challenges for the first part of your tenure as CEO here. What's the plan for addressing those issues?

Trevett: We must focus on updating some of our laboratories and support facilities as well as keeping up with the latest in technology. We have come a long way in the last decade in renovating labs, but we still have some very old ones remaining. We must marshal resources from a multitude of places to do some of the necessary things in terms of facilities. Another challenge we face is to give our scientists the very latest in laboratory technology. In almost every instance, this technology and the updated, efficient laboratory facilities can mean years of time saved in our advances and discovery. The promise of our research has never been stronger, so we must continue to invest even in these challenging economic times.

Progress: Are there any new areas in science that you see SFBR pursuing, or will the Southwest Foundation adhere to its core areas as they are now?

Trevett: We will build on some tremendous strengths. I see the continuing thrust being genetics, virology and immunology. The non-human primates are not only a resource but are really, effectively, a third area of research. There are life-saving advances that will come out of the laboratories of this nation's boldest researchers and the non-human primate will be invaluable as these advances move from lab to people. All three areas are historic strengths of the Foundation and I see us being

opportunistic about new scientific situations in these areas in which we've been so successful.

Progress: There's been some discussion of perhaps applying to the Gates Foundation for a grant related to international health. Is that something you're ready to talk about now or is it too far out in the planning stages?

Trevett: Unquestionably, the Southwest Foundation has the most significant basic research program in areas of international health of any independent research institute in the country. We're doing work in malaria, in TB, in HIV, in Chagas disease, in dengue fever, in Ebola, and others. Intestinal worm infections are another significant area of our study. There are just a number of diseases that impact large populations. So we are continuing to make a huge impact in international health, and I would like to see us promote that to foundations that have a particular interest in world health issues. I think we could attract additional resources and increase capacity to do work in this field.

> **". . . the Southwest Foundation has the most significant basic research program in areas of international health of any independent research institute in the country. . ." — *Kenneth P. Trevett***

Progress: You mentioned earlier your experience in facilitating technology transfer at some of the institutions where you've worked. Are there are any specific areas or projects that are underway at the Foundation that you see as right for pursuing in the technology transfer arena?

Trevett: Yes, there certainly are. One of them is genetics software that we have that helps to identify disease genes. I think we can do more in terms of promoting that particular software technology which has been developed by Dr. John Blangero and his colleagues. Second, we've got some very exciting work in the area of pre-eclampsia, which is a difficult medical condition that affects about five percent of women in the United States. One of our investigators, Dr. Eric Moses, is really homing in on the genetic basis for pre-eclampsia. So we could develop within a pretty short timeframe a genetic screen for pre-eclampsia that would be extremely helpful. A third area is a better understanding and analysis of people who are at risk for diabetes and other metabolic syndromes, and we are doing some excellent work in genetic analysis of that. We've got some fine vaccine development programs, one of them in TB, another in Chagas disease potentially. So there are some very specific projects that I think lend themselves to a technology transfer approach.

Progress: It's been said that one of the most important information technology revolutions of the 21st Century is going to be the intersection between computers and the biological sciences, which as you know is a field that seems to be moving at an ever-faster pace all the time. How do you see that having an impact here?

Trevett: Computers and "smart technology" power almost every lab, but one of the most striking examples that comes to mind is the AT&T Genomics Computing Center. That is a resource literally unparalleled in the world. We have about 3,000 computer processors generating data seven days a week and that allows us to help identify disease genes and potential pathways for addressing disease problems. So I think we are absolutely at the forefront of applying information technology to biological problems.

Progress: You mentioned a few new areas that the Southwest Foundation may be headed in over the next few years. How does an institution like this handle new directions while adhering to its core mission?

Trevett: I think it's always a challenge to keep your focus on what your strengths are while also looking for new opportunities, and we have outstanding scientific leadership here in the chief scientific officer and the department chairs. I trust in their judgment to really take advantage of opportunities that present themselves that are appropriate for the Foundation environment.

Progress: With some of these challenges in mind, how do you view your role here as the Southwest Foundation president? What's your style? How do you deal with people here, not only the scientists here, but also the Board of Trustees?

Trevett: First of all, I think my primary role is to try to enhance the scientific infrastructure so that the researchers can do their work. We have a first-rate faculty and they deserve a first-rate environment in which to do their research. I see that as a continuing responsibility. The second is to promote a climate with my management colleagues and scientist colleagues so that this is an enjoyable place to work as well as a productive environment. Thirdly, I really need to be the public face of the organization so that I can attract additional supporters whether they be in government, or donors, or local businesses, or possibly companies where we might do technology transactions. This is again a continuing responsibility of mine to promote the Foundation's good work.

Progress: How about your relationship with the board? How do you see your interactions there?

Trevett: We've got a first-rate board and first-rate board leadership, starting with the chair, J.R. Hurd. I believe it is one of the strongest boards in the state, if not the nation. My responsibility is to keep them in the know about issues that are important to us or of concern to us. Second, it is to take advantage of their professional expertise because this is a highly complex organization, as all research institutions are. I very much appreciate advice on investment, business, public relations, and accounting. Just the variety of professional skills that we see on that board, I want to be sure that we're taking advantage of those skills to maximize the effectiveness of the organization. ■

Separating fat from fiction

SFBR's Anthony Comuzzie focuses on possible role of fast-food diet in obesity and diabetes

Is it more important to control fat or sugar in the diet? Are some forms of sugar worse than others?

Those questions are part of a new pilot study led by SFBR's Anthony Comuzzie, Ph.D., a nationally recognized leader in the field of obesity, diabetes and related illnesses, including heart disease.

Comuzzie's team is focusing on the Western "fast-food diet" high in fat and processed sugars. Grants from the Voelcker Foundation and the Southwest National Primate Research Center provide funding for this ongoing study seeking genetic roots for metabolic disorders reaching epidemic proportions in people. The team includes staff scientist Raul Bastarrachea, M.D., postdoctoral scientists Liz Tejero, Ph.D., Juan Carlos Lopez Alvarenga, M.D., Ph.D., Saroja Voruganti, Ph.D., Paul Higgins, Ph.D., and Mike Proffitt, Ph.D.

The new study is a spinoff of SFBR's longest-running research program, "Diet and Genotype in Primate Atherosclerosis," commonly called the "Baboon Program Project." The program, started in 1972 with funding from the National Institutes of Health (NIH), supports a number of separate but related research projects that rely on the baboon model, due to baboons' genetic and physiological similarity to humans.

Comuzzie, a scientist in the Foundation's Department of Genetics, serves as co-principal investigator on the baboon project with John VandeBerg, Ph.D., SFBR's chief scientific officer.

In the new study, Comuzzie's team seeks data on how much we can blame saturated fat, or simple carbohydrates – or some deadly synergy of the two – on cardiometabolic dysfunction, such as poor regulation of fat and sugar, with an eye on finding potential genetic targets for preventions and therapies.

"So we came up with a diet that is formulated to mimic the nutritional content of a fast-food value meal," Comuzzie said.

Dr. Anthony Comuzzie holds a food pellet containing a specially developed diet for obesity studies.

One group of 10 baboons received a high-fat diet, with water. A different group received identical food, but had a choice of water or a beverage loaded with high-fructose corn syrup, which they would drink instead of water. The baboons underwent basic metabolic measurements, then were re-measured after eight weeks on the diet.

The group that got the high-fat diet and water did not show much change in overall health. But the group with the sweet drink showed a number of negative changes, including a shift in body composition in which fat increased and muscle decreased.

"So if you are losing muscle mass, you're not going to be as efficient at burning glucose, so you're going to start having glucose build-up in the blood, which is diabetes," Comuzzie said. Glucose, which fuels the body, gets metabolized and utilized in muscle.

Other metabolic markers also took a bad turn in the sweet beverage-drinking group, including:

- Triglycerides, a fat, which in high levels is associated with cholesterol readings, increased up to six-fold.
- HbA1c, or glycosylated hemoglobin, which can cause the type of blood vessel damage resulting from diabetes, increased dramatically.
- Physical activity declined, causing a decrease in muscle.
- Adiponectin, which regulates insulin sensitivity, declined.
- Leptin, a negative factor at high levels, increased.

Comuzzie suspects that something is disrupting the function of body fat, which produces numerous significant proteins, including leptin and adiponectin.

As the study progresses, the team will alter the diet, such as using sucrose, rather than high fructose corn syrup, and changing fat composition.

Comuzzie said examining dietary sugars has strong public health implications.

"At least for the past 15 or 20 years, there's been a big push relevant to heart disease: saturated fats and the problem with fats," Comuzzie said. "But while we've reduced some of the heart disease during that time, which I think is attributable to the reduction of consumption of saturated fats, obesity and diabetes prevalence has continued to increase."

Comuzzie began to establish himself in obesity and diabetes research after joining SFBR as a postdoctoral scientist in 1993, after earning his Ph.D. in biological anthropology at the University of Kansas. He began working on the San Antonio Family Heart Study, a collaboration with the University of Texas Health Science Center at San Antonio, which since 1991 has studied the contribution of genes to heart disease risk in Mexican Americans, focusing on 1,400 members of more than 40 large families. The project, funded by the National Heart, Lung and Blood Institute (NHLBI), part of the NIH, continues to yield rich data on the genetics of cardiovascular disease and other related conditions, including diabetes and obesity.

A native of Corpus Christi, Comuzzie earned his bachelor's and master's degrees at Texas A&M, and arrived at the Foundation wanting to expand genetic analyses of these public health challenges. He found himself in an important role, because no one in the group was analyzing obesity data.

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— Anthony Comuzzie

In 1993, obesity research was just beginning to take off. The Obesity Society had only been formed a couple of years earlier, when members of the American Diabetes Association and American Heart Association wanted both organizations to pay more attention to the topic of obesity.

His expertise in this increasingly important field has put Comuzzie in a leadership position, including his current membership on the NHLBI's expert panel revising guidelines on treatment of obesity and overweight, the Council of the Obesity Society, and the editorial board of a new scientific publication, the *Journal of Nutrigenetics and Nutrigenomics*.

Comuzzie and his wife Diana, a biology professor and dean of the School of Science and Math at Schreiner University in Kerrville, have two teenage sons. He is active with the Boy Scouts and enjoys camping and other outdoor activities, playing guitar, gardening, wood work, and cooking.

Apart from these activities, how does Comuzzie avoid the disorders he's studying?

For one, he's stopped drinking regular soft drinks. "I'll drink the diet ones, but I just gave up drinking any of the sweetened drinks, because, just from the data we had years ago on the effect on triglycerides," he said. "But I'm a native South Texan and things like chicken fried steaks and cheese enchiladas are a hard thing to forego." ■

Editor's Note

This redesigned issue of Progress *has several goals. One is to provide information about the work and activities of SFBR which is both concise and clear. Another goal is to publish three times annually, to give our readers more frequent information about what is happening at SFBR. Third, you will notice our smaller size, which makes the newsletter easier to carry. Editorially, each issue will include a profile or Q&A of an SFBR scientist, and pieces focusing on new developments in SFBR science and philanthropy.*

We also plan to include alternating columns by Dr. John VandeBerg, our chief scientific officer, and by Kenneth P. Trevett, our president. They will discuss issues important to SFBR and where and how this organization may evolve in the years to come. To comment on our new format and make suggestions, please e-mail Joseph Carey, SFBR's Vice President for Public Affairs, at jcarey@sfbr.org. Thank you for your continuing interest in, and support of, the Southwest Foundation for Biomedical Research. ■

Southwest Foundation Forum Gala Set for May 2 at The Argyle

The Southwest Foundation Forum is holding its 39th annual gala, "Out of Africa," on Saturday, May 2, 2009, at The Argyle. Through its annual gala, the Forum raises vital seed money for grants that enable pilot study research. That research, in turn, develops important preliminary data to make SFBR scientists more prepared in the highly competitive world of funds from the National Institutes of Health and other organizations. Over the last eight years, the gala proceeds have exceeded $1 million, which has enabled SFBR researchers to qualify for more than $23 million of additional funding.

The Forum gala is made possible by the generous support of individual and corporate sponsors, who underwrite the event by reserving tables and giving to the gala grants program. Gala grants are an opportunity to give a 100 percent tax-deductible donation to the Southwest Foundation Forum, which includes the gift in its total donation to the SFBR. Table sponsorships range from $2,500 to $20,000; individual tickets, $250 each.

This year's event will begin at 6 p.m. with sundowners on the lawn, and a chance to win one of seven amazing raffle prizes.

The 2008 gala chairs and leadership gather on The Argyle's steps on last year's big night. Kim Shepperd, Gala assistant; Anne Heaner, Gala co-chair; Anne Johnston, Gala chair; and Allison Zeller, president.

You'll also have the first-ever chance to bid on an original oil painting done by one of SFBR's very talented chimps, Bunky! The African safari tickets are $100 a chance, and the other six package tickets are $50 a chance.

For more information, to make reservations, to purchase raffle tickets, or to make a gala grants donation, please log on to swff.org or call Karen Lee Zachry at 829-8585. ■

▶ ***Continued from page 1***

by a vaccine produced in insect cells. (See p. 7 for more.)

Lassa Virus

SFBR's Drs. Jean Patterson and Ricardo Carrion are developing two vaccines for Lassa virus with collaborators from the Institute of Human Virology at the University of Maryland at Baltimore. Lassa virus causes 5,000 deaths annually in West Africa from Lassa fever. One vaccine combines the immune response of Lassa virus with the safety of a virus that does not cause disease. In separate studies, both marmoset monkeys and guinea pigs given the vaccine and then challenged with the virus were protected. The scientists plan larger studies in monkeys which, if successful, would lead to human trials.

In other studies, the team has developed a vaccine in which protective Lassa virus genes were integrated into the existing Yellow Fever vaccine. Guinea pigs immunized with this vaccine were protected from a lethal dose of Lassa virus, which provides hope that the combination vaccine can be used to treat both Yellow Fever and Lassa fever in the same regions of Africa.

West Nile Virus

Working with colleagues at the University of Texas Medical Branch at Galveston, Carrion also reports initial success in immunizing rhesus macaque monkeys with an experimental vaccine for West Nile virus. This virus can cause serious neurologic disease and currently, no treatment or vaccine is available. In 2008, 674 cases were reported in the US, including 40 in Texas, according to the Centers for Disease Control. In initial tests in macaques, the vaccine – which employs a pseudo-infectious particle – prevented viral replication. While human tests are still several years away, this vaccine could help protect vulnerable populations, particularly those with weakened immune systems.

Herpes B Virus

SFBR scientists are also helping to improve the safety of research animal care staff. Herpes B virus (BV) is a zoonotic agent, meaning that it can "jump species" from monkeys to humans. Untreated, BV infection in humans has a fatality rate of about 80 percent. Even with timely antiviral therapy, the fatality rate is about 20 percent.

Dr. Anthony Griffiths is developing a vaccine to protect monkeys from BV infection. He is employing the simian foamy virus as a way to carry small sections of BV in a vaccine that should produce an immune response in vaccinated animals. He anticipates that this vaccine will greatly improve safety for animal care workers, and improve public health.

As you can see, our vaccine strategies are aimed at many diseases and, from an economic perspective, represent the best hope to overcome these disorders. Developing vaccines is important for those living in Africa, Asia and Latin America, and the US and Texas, where some of these diseases occur. It also speaks to the importance of adequate funding for this vital work for which we are grateful to the NIH, many foundations, and our local philanthropies and donors. Only through their support will we continue to make the progress so essential to creating a healthier world. ■

SFBR Science Update

Advances vs. Ebola Viruses; Cancer Model May Aid Treatment

In separate new research developments, SFBR scientists report that an experimental vaccine can achieve protection against Ebola, one of the world's deadliest viruses, and that a new animal model of cancer may represent a new method for understanding and treating virtually all tumors.

Scientists study Ebola viruses in SFBR's biosafety level 4 laboratory.

In the Ebola virus vaccine study, SFBR scientists Ricardo Carrion and Jean Patterson report protection through the use of a vaccine using Ebola virus-like particles (VLPs) produced in insect cells using traditional bio-engineering techniques and injected into laboratory mice. A VLP vaccine is based upon proteins produced in the laboratory that assemble into a particle that, to the human immune system, looks like the virus but cannot cause disease.

Two high-dose VLP immunizations produced a high level immune response in mice. And when the twice-immunized mice were given a lethal dose of Ebola virus, they were completely protected from the disease. In contrast, mice that were not immunized had a very low immune system response and became infected. In another experiment, a three low-dose VLP immunization effectively boosted immune system response in mice and protected them against the Ebola virus. This finding is important because it demonstrates that since the vaccine produces immunization in dilute quantities, many more vaccine doses can be generated compared with a weakly immunogenic vaccine.

Dr. Ricardo Carrion

The new study was published in the January 2009 issue of *Virology*, and was supported by the National Institutes of Health.

There is no effective treatment for Ebola. Since its first identification in Africa in 1987, Ebola outbreaks have caused some 1,800 human infections and 1,300 deaths. Outbreaks have become increasingly frequent in recent years, and are likely to be caused by contact with infected animals followed by spread among humans through close person-to-person contacts. Ebola viruses cause acute infection in humans, usually within four to 10 days. Symptoms include headache, chill and muscle pain, followed by weight loss, delirium shock, massive bleeding and organ failure leading to death in two to three weeks.

Ebola viruses are considered a dangerous threat to public health because of the high fatality rate of infected people, ability to transmit person-to-person, and low lethal infectious dose. Moreover, their potential to be developed into biological weapons causes grave concern. While some vaccines show protection in non-human primate studies, the strategies used may not be uniformly effective in the general human population due to pre-existing immunity to the virus-based vaccines.

Cancer Model

In an unexpected result, human cancer cells injected into a new animal model act in a manner similar to the way they do in humans, and may represent a new method for understanding and treating virtually all tumors. "It's a model for studying the mechanisms for how cancer cells evade the immune system, and for developing new diagnostic and therapeutic methods," says senior author John VandeBerg, Ph.D., SFBR's chief scientific officer.

The new animal model, the newborn opossum, represents an advance over other animals, such as the mouse, in which human cancers cannot survive unless the animal's immune system is totally absent. The new model is described in a paper appearing in the February 2009 issue of the *International Journal of Clinical and Experimental Pathology*. The research was supported by a grant from The Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation.

In the study, researchers injected human melanoma, colon cancer and prostate cancer cells into newborn opossums. The resulting tumors grew, invaded, spread and eventually regressed. Further studies found that as early as 11 days following injections with colon cancer cells, tumors grew and spread, and induced immune responses. The pattern showed how the cancerous cell first escapes the normal regulatory mechanisms by not appearing to be foreign to the immune system, and later is distinguished from normal cells, thus making the model capable of predicting activity in humans.

Typically, patients are administered several drugs which may appear to be effective but eventually decrease in efficacy. With a new testing tool, physicians might be able to gauge the efficacy of both standard and experimental cancer treatments before giving them to patients by injecting a patient's cancer cells into several groups of newborn opossums and comparing the efficacy of different treatments among groups. ■

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San Antonio, Texas 78245-0549

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PERMIT NO. 958

PROGRESS SPRING 2009

Progress is a publication of the Southwest Foundation for Biomedical Research. If you would like to be added to our mailing list or to update your mailing information, please contact Joseph Carey at jcarey@sfbr.org.

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