

FINDINGS

Spring/Summer 2012 • omrf.org



PANDEMIC

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Honor your loved ones by celebrating an anniversary, wedding or graduation with a donation to OMRF.

Our scientists are dedicated to understanding and developing more effective diagnostics and treatments for Alzheimer's, cancer, lupus, multiple sclerosis and heart disease.

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FINDINGS



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Chartered in 1946, OMRF is an independent, nonprofit biomedical research institute dedicated to understanding and developing more effective treatments for human disease. Its scientists focus on such critical research areas as Alzheimer's disease, cancer, lupus and cardiovascular disease.



A United Way Partner Agency



12 **COULD IT HAPPEN AGAIN?** The flu outbreak of 1918 claimed millions of lives worldwide. OMRF's Drs. Judith James and Linda Thompson are working to make sure the next pandemic never comes.

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COVER STORY



In 1977, Kim Winton got her first look at research as a Fleming Scholar in Dr. Jordan Tang's lab at OMRF. Our story about Tang's Alzheimer's disease research in the last issue of Findings prompted her to reach out to her former mentor:

Dear Dr. Tang,
When I read the recent article about your Alzheimer's research in the fall 2011 *Findings* magazine, I noticed that the building blocks for this research date back to some of your original stomach enzyme research from 20 or so years ago. I was one of the Fleming Scholars working in your lab in 1977. **I want to thank you for that experience.** It was a tremendous starting block for my career. I am very proud to be a small part of the legacy that you will leave to mankind. My own grandmother is 93 and has suffered from the effects of Alzheimer's and dementia for many years, so I know the profound effects that it has on the patient and the family. After reading the article, **it made me feel like I may have made some tiny contribution to the cure for such a devastating disease.**

Dr. Kim Winton

Director, USGS Oklahoma Water Science Center
U.S. Geological Survey
Oklahoma City

P.S. I still have my autographed lab coat!

Dear Kim,
Thank you for your email and kind words of encouragement. You are right. **The thread of our research does go back to the pepsin structure we studied when you were in my lab.** Pepsin turned out to be the grandfather of a family of proteases that function in different diseases such as hypertension, AIDS, Alzheimer's and infectious diseases. I feel fortunate to have been in a great place at the right time. Looking back, it has been quite a scientific journey and one I hope has a ways to go.

I am glad to know that the time you spent in our lab had a positive influence in your later career development. I am also pleased to know that you are working to keep our natural resources and environment in good shape.

Thank you again for writing, and best wishes.

Dr. Jordan Tang

J.G. Puterbaugh Chair in Medical Research
OMRF

My sister died 11 years ago as a result of lupus.

I know your scientists and doctors are working on eradicating that disease as well as others. Although it's too late to help my sister, I just want to say thank you and keep up the good work.

Jason Headen

Norman via Facebook

Congratulations on the fine article on Jordan Tang

and the efforts to bring a discovery to a drug. I saved the article and shared it with my wife to explain the uphill difficulties in medical research. She, a published author herself, read it on the plane and said, "This was fantastic – so well written. Thanks for sharing it with me."

Lee Ginsburg

Santa Rosa, CA

Wow! Just finished reading this issue of Findings.

The journey to discovery is amazing. One of my dear friends is on hold for a lifesaving cancer treatment because her medication isn't available. OMRF scientists are working hard for ways to save lives, but I never imagined a situation where a patient couldn't fight for their own life because of a drug shortage.

Teresa Dillon

Tulsa via Facebook

Please hurry to find a cure for Alzheimer's.

My mother and sister both died of it, and now I am concerned for my own health. I know it costs money and that FDA approval can take a long time, but we see so many Alzheimer's cases now. I can't give a lot of money, but I know every gift helps. Hopefully we'll see some help for it soon.

Linda Wasson

Cushing, OK

WRITE TO US!

Send us an email at findings@omrf.org or mail your letters to *Findings*, 825 Northeast 13th Street, Oklahoma City, OK 73104. Please include your name and address, and you'll receive an OMRF T-shirt if we publish your letter.

FOLLOW US ONLINE!  

Can You Prevent Alzheimer's?

We've all heard about the crossword puzzles. You know, the ones that could keep you from developing Alzheimer's disease.

A 20-year survey of 469 elderly people living in the Bronx, NY, showed that those who kept mentally active through pursuits such as reading, playing board games and doing crossword puzzles had a lower incidence of Alzheimer's or other forms of dementia than their counterparts who didn't engage in these activities. And the more you did, the better your chances of avoiding Alzheimer's. For example, those who did crossword puzzles four days a week had a 47 percent lower risk of dementia than those who did but a single puzzle a week.

It sounds like a pretty compelling argument for the curative powers of word games. Until you dig a little deeper. "It's a classic causation versus correlation problem," says OMRF President Stephen Prescott. "Are these mental activities keeping Alzheimer's at bay? Or is this just a case of folks who've been dealt a good genetic hand?"

Unfortunately, the jury is still out on this—and on the larger question of whether there's anything at all you can do to stave off Alzheimer's disease. In 2010, a National Institutes of Health panel of experts concluded that "no evidence of even moderate scientific quality exists to support the association of any modifiable factor . . . with reduced risk of Alzheimer's disease."

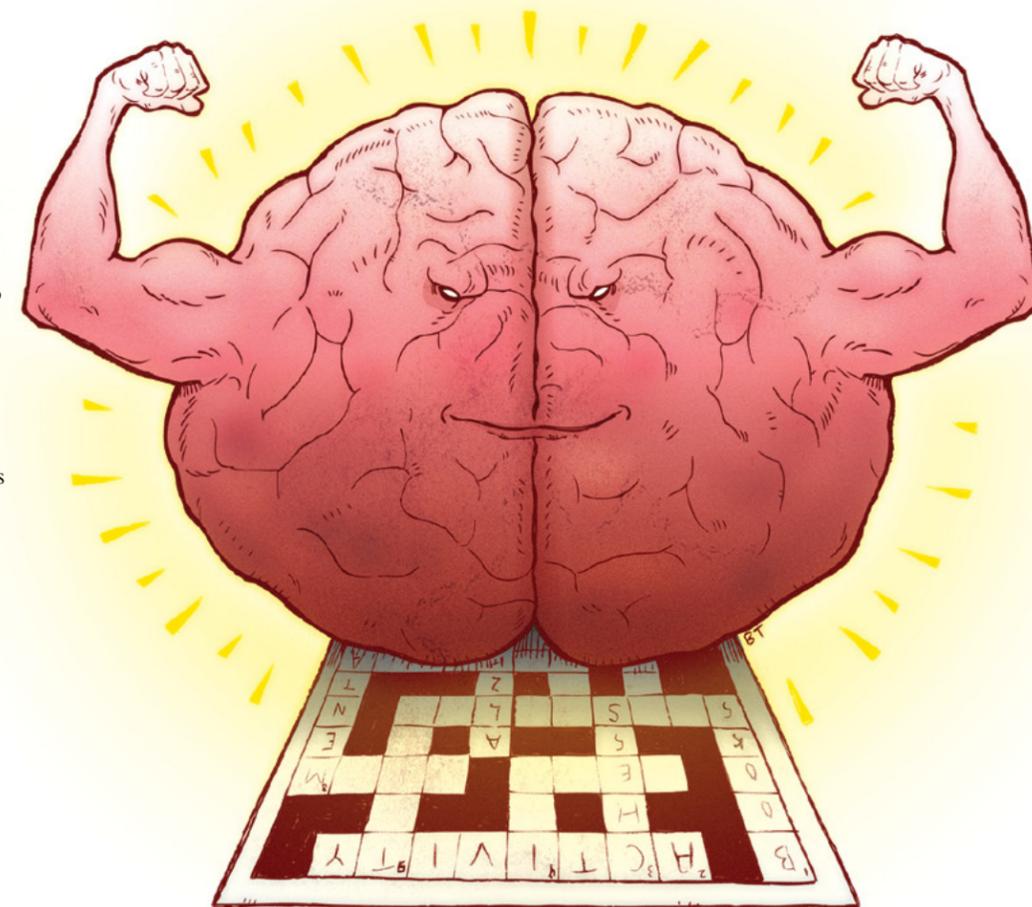
In a world where we have 34 million cases of Alzheimer's and no effective treatments, prevention would seem to be the name of the game. Indeed, there have been studies establishing a link between the disease and a laundry list of modifiable behaviors and conditions: physical inactivity, smoking, depression, low education, hypertension, obesity and diabetes. At the 2011 Alzheimer's Association International Conference, researchers used a mathematical model to estimate that these behaviors and conditions could be responsible for about half of the world's Alzheimer's cases.

The key word here is "could."

"There's evidence that all of these are risk factors, but the extensive studies necessary to establish that they cause Alzheimer's have not been done," says Dr. Jordan Tang, who has researched Alzheimer's disease at OMRF for more than a decade. Still, he says, it makes good sense to do all that you can to minimize your risk for Alzheimer's.

"Research already shows that being physically active, not smoking and controlling your weight and blood pressure can reduce your risk of heart disease and other illnesses," he says. "So why not do all of these things now?" One day soon we may find out that those same healthy habits also protect us from Alzheimer's.

By 2050, more than 100 million people are projected to be living with Alzheimer's.



Ask Dr. P

OMRF President Stephen Prescott answers your health questions

Still Going Strong

I just turned 82. For an old guy, I'm in excellent health. Despite the usual (cancer, hypertension, knee replacement) and unusual (cracked vertebrae, fractured heel and antibiotic resistant infection caused by a rock-climbing accident at age 74) array of health-related hurdles I've experienced in life, I still play tennis, go climbing and work out at the gym every week. My parents both lived to the age of 96. At this point, can I just throw away the standard instruction manual and do what I want?

Mike Cohen, Wynnewood, PA

What a great problem to have! That said, I have a little good news/bad news on the life expectancy front. Your parents were outliers, meaning they lived well beyond the average lifespan. When that happens, statistics show that the next generation, while still expected to live longer than most, will likely have a shorter lifespan than mom and dad. On the other hand, the fact that you've already passed the 80 mark puts you in rarified statistical company, predicting a big cake with 90-plus candles in your future.

At this stage of the game, I do think you can tear out a few chapters of the health manual. For example, in colon cancer, it takes about 15 years from initial cellular changes until the development of fully invasive cancer. At some moment, and that point could be now, you might decide, if I'm not going to get colon cancer for at least another 15 years, enough with those colonoscopies. You might make similar decisions with regard to other preventative procedures and medications where the short-term detriment now outweighs the long-term benefits.

On the dietary front, I'd still recommend that you eat a balanced diet and strive to maintain a healthy body mass index. But if you want to have an extra serving of dessert or two, go for it. Similarly, while I'm not advocating over-indulgence, studies have repeatedly shown that regular consumption of modest amounts of alcohol is associated with longer life and better health outcomes.

If you don't smoke, don't start now. Even if you eliminate the long-term risks, there are simply too many short-term health issues associated with tobacco use to risk it.

Finally, and probably most importantly, stay active. The biggest health risk for seniors is falls, which cause fractures, immobility and, ultimately, life-threatening infections. By staying active, you maintain muscle mass, bone density, flexibility and balance.

So keep up that gym membership and Tuesday tennis game; there's no reason to abandon the fitness regimen that has helped take you so far in life. Heck, I guess that goes for climbing, too. Just do me a favor and wear a harness, okay?

Send your health questions to Dr. Stephen Prescott at askDrP@omrf.org.

Fat Mice Teach Value of Exercise

Contrary to popular belief, running may actually protect against arthritis

New research from OMRF and Duke University has found that even without weight loss or a change in diet, exercise reduces symptoms of arthritis in obese mice. "This suggests that weight loss alone isn't the only way that exercise can protect against osteoarthritis," says OMRF's Dr. Tim Griffin, the lead author on the study, which appeared in the journal *Arthritis and Rheumatism*.

The researchers fed mice a high-fat diet, and the animals gained weight. After eight weeks, they gave half of the mice exercise wheels. Researchers then compared the arthritis symptoms in these animals, which ran an average of about 3½ miles per day for four weeks, with the sedentary mice.

The mice that ran experienced fewer arthritis-related problems, despite the fact that they shed no weight and continued on the same high-fat diet as the sedentary mice.

"In some areas of the joints, exercise provided protection against osteoarthritis," says Griffin. "The active mice also had improved blood markers associated with inflammation and diabetes, factors that may contribute to arthritis progression."

Osteoarthritis is the most common joint disorder. Its symptoms, pain and stiffness, typically begin in middle age. Often, its causes are unknown, but obesity is a significant risk factor, and one of the major questions in the field is whether exercise will help or harm obese patients.

"Some believe that the increased impact on the joint during exercise causes further harm," says Griffin. "But these results suggest the opposite."

Indeed, a 2008 study from Dr. Eliza Chakravarty, now a scientist at OMRF, and colleagues at Stanford University found that runners over the age of 50 suffered fewer disabilities than their non-running counterparts. The researchers also found that running was not associated with greater risk of arthritis. "We'd anticipated that the runners were going to have more osteoarthritis and wear-and-tear injuries, and we were very surprised when that was not the case," she says.

At OMRF, Griffin is conducting more studies to examine the long-term effects of exercise on osteoarthritis. "It's a horrible disease to live with and one that significantly decreases the quality of life for those who have it," he says. "Hopefully, we'll be able to use this research to find ways to mitigate and reverse that pain."



“For arthritis symptoms, running appears to counteract some effects of obesity and high-fat diets.”

-Dr. Tim Griffin



An OMRF Emmy

When seven OMRF scientists signed on for a musical “boot camp” with Chickasaw composer Jerod Tate, they knew they were in for something completely different. But they never imagined the experience would lead to an Emmy award.

In only 10 days, they each composed a piece of classical music for string quartet—even though none of the researchers had any experience with stringed instruments or composing music. OETA filmed the entire process, capturing footage as the scientists learned music theory, terminology and writing, struggled through the composition process and, finally, listened to a string quartet from the Oklahoma City Philharmonic perform their work before a live audience.

At the 2011 Heartland Regional Emmy Awards, “The Science of Composing,” OETA’s documentary about the project, won the prize for best cultural documentary.

“The process of learning to compose music reinvigorated me, both as a person and as a scientist,” says Dr. Courtney Montgomery, who took part in the project. “The Emmy just added an exclamation point to a great experience.”

Survey Says...

The *Scientist* magazine has compiled the results from its 2012 analysis of the best places to work for postdoctoral fellows, and OMRF has come up a big winner—again. The survey results ranked OMRF 5th for 2012, up from 6th position in 2011. Scores ranked institutions’ quality of training and mentoring, facilities, compensation packages and career development opportunities for young scientists.

Postdoctoral fellows are typically junior scientists who have recently completed their doctoral degrees. They spend 3 to 5 years at a research institution gaining experience and training under the guidance of senior scientists before moving on to lead laboratories, work in the biotechnology industry or pursue other careers in the biological sciences.

“We place a strong emphasis on scientific training at OMRF, and this survey tells us that we’re more than holding our own against the nation’s research powerhouses,” says OMRF President Stephen Prescott. “The work our postdocs do has a major impact on the quality of our science, so we focus on giving them everything they need to thrive.”



What makes OMRF a great place to work? Three scientists weigh in



“I like working at OMRF because it’s a nice, friendly place with a very collaborative environment. Just yesterday, somebody from another lab came by to teach me a new technique.”

Dr. Mandi Wiley



“The foundation has really excelled with core facilities. We have invested well in equipment.”

Dr. Mark Coggeshall



“What makes OMRF a great place to work is the people. We get support from every department—from our librarian Beth Mikkola to the receiving dock.”

Dr. Hui-Ying Lim

Grants Awarded - 2011

Dr. José Alberola-Ila, Hematopoietic Stem Cell Senescence; Regulation of NKT Cell Development and Function by *c-Myb*

Dr. Rita Issa, Biomedical Regulation of Oxidative Homeostasis in Articular Cartilage

Dr. Marta Alarcón-Riquelme, Analysis of the Novel SLE Gene BANK1 on B-Cell Function; Dissecting a Novel Molecular Genetic B-Cell Pathway in Lupus

Dr. Jana Barlic-Dicen, Roles of the Chemokine Receptor CXCR4 in Adipogenic Progenitor Cell Mediated Hyperplasia; The Role of the Chemokine Receptor CXCR4 in Obesity

Dr. Hong Chen, A Novel Regulator in Prostate Cancer Progression and Metastasis; Epsin in Angiogenesis and Vascular Remodeling; Inhibiting Epsin: A New Anti-Cancer Strategy

Dr. K. Mark Coggeshall, Molecular and Immunologic Analysis of the Pathobiology of Human Anthrax

Dr. Dean Dawson, Meiotic Centromere Behavior in Yeast; Meiotic Functions of *Mps1*

Dr. Yunzhou Dong, Drug Development for Prostate Cancer

Dr. Michael Dresser, Mechanics and Regulation of Chromosome Dynamics in Meiotic Prophase

Dr. Darise Farris, T Cell Tolerance and Autoimmunity to Nuclear Antigen *La*

Dr. Jianxin Fu, Role of O-Glycoprotein Podoplanin in Postnatal Lymphangiogenesis

Dr. Patrick Gaffney, Molecular Mechanisms and Genetics of Autoimmunity TNEAIP3 (*A20*) and

Susceptibility to Systemic Lupus Erythematosus

Dr. Gary Gorbsky, Chromosome Movement in Prometaphase

Dr. Courtney Griffin, Epigenetic Regulation of uPA During Vascular Development

Dr. Timothy Griffin, Independence of Body Weight and Leptin in Osteoarthritis; Stimulating Endogenous Cartilage Antioxidant Capacity

Dr. Kenneth Humphries, Mitochondrial Dysfunction in Amyotrophic Lateral Sclerosis; Mitochondria in Cardiac Ischemic Preconditioning

Dr. Judith James, Science in a Culture of Mentoring; Oklahoma Rheumatic Disease Research Core Centers; Oklahoma Autoimmunity Center of Excellence

Dr. Paul Kincade, Hematopoietic Stem Cell Senescence; Early Events in Mammalian B-Cell Differentiation

Dr. Kristi Koelsch, A Novel Approach to Gene Discovery in Juvenile Arthritis

Dr. Susan Kovats, Estrogen Receptor - IRF4 Interactions in DC Development; Regulation of Dendritic Cells by Estrogen Receptors During Influenza Infection

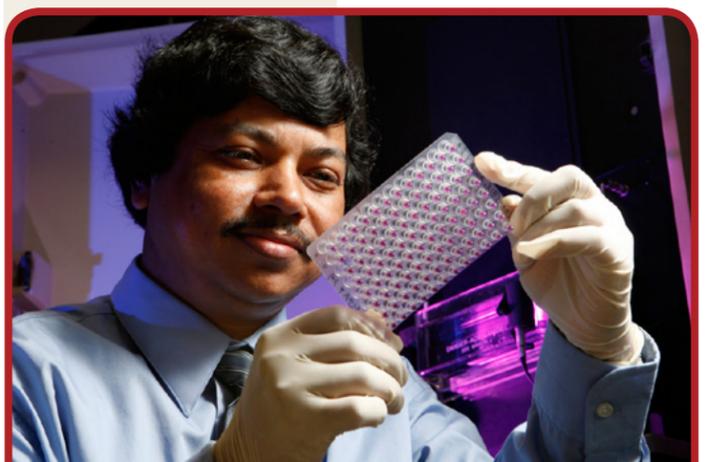
Dr. Florea Lupu, Complement Inhibition as Sepsis Therapy

Dr. Rodger McEver, Interdisciplinary Research in Vascular Biology; Cellular Regulation of Selectin-Ligand Interactions, Mechanisms for Blood Cell Adhesion Under Flow, Protein-Glycan Interactions in the Vascular System

Dr. Ken Miller, Forward Genetic Analysis of the Synaptic GS Pathway

Dr. Kevin Moore, Identification of Tyrosine-Sulfated Proteins in the Male Genital Tract

Dr. Kathy Moser, A Sjögren’s Syndrome Diagnostic; Oklahoma Sjögren’s Syndrome Center of Research Translation; Genetic Basis of Human Sjögren’s Syndrome



Dr. Swapan Nath, Identification of Lupus Predisposing Variants by Comparing Multiple Populations; SLE Susceptibility and Clinical Significance at 2q22-44 Across Multiple Ethnicities

Dr. Gabriel Pardo, MS Center of Excellence

Dr. Roberto Pezza, MND1 and HOP2 in Homologous Recombination

Dr. Scott Plafker, Control Redox Regulators by the Ubiquitin System

Dr. James Rand, Regulated Splicing of the Cholinergic Gene Locus; Synaptic Mutations and Oxidative Stress; Neuroigin, Oxidative Stress and Autism

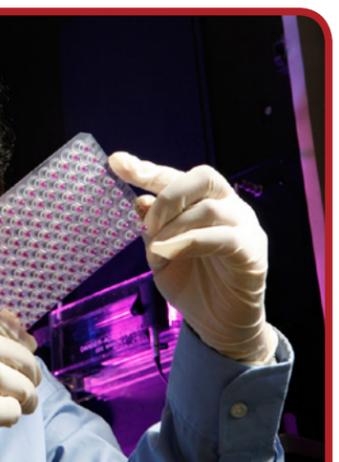
Dr. Susannah Rankin, Sororin Sister Chromatid Cohesion and Cell Cycle Control

Dr. William Rodgers, Cytoskeletal Regulation of Raf1 Structure and Function

Dr. Christopher Sansam, The Role of TICRR in the Human DNA Damage Response

Dr. Xiao-Hong Sun Notch-Induced Protein Degradation in Lymphopoiesis; Role of *Id1* in Bone Marrow Niche and Mesenchymal Stem Cell Differentiation

Dr. Jordan Tang, Beta Secretase Inhibition for Treating Alzheimer’s Disease



Dr. Linda Thompson, The Regulation of Inflammatory Responses by CD73

Dr. Weidong Wang, Small Molecules that Replace OCT4 During Induction of Human iPS Cells

Dr. Carol Webb, Role of the Transcription Factor ARID3a in Lupus; ARID3a and Induction of Pluripotency in Human Cells

Dr. Lijun Xia, Role of Mucin-Type O-Glycans in Intestinal Inflammation; Glycoengineering of Endothelial Progenitor Cells for Therapeutic Neovascularization in Ischemic Stroke

TOWER OF POWER

In March, OMRF put the finishing touches on the top floor of its new research tower. With the completion of the McCasland Foundation Conference Center and the Masonic Foundation of Oklahoma Laboratory, OMRF wrapped up the largest campus expansion in the foundation's 66-year history.

Even before it was finished, the tower garnered national support and recognition for OMRF. In 2010, the National Institutes of Health awarded OMRF a major construction grant to support the project. The grant followed a nationwide competition involving more than 1,200 universities and medical research institutes, only a tiny fraction of which received awards.

With its green features, the building was named as one of 25 finalists for the 2010 Renewable Energy World North America Award. It is now in the final stages of earning a gold certification in Leadership in Energy and Environmental Design (LEED), making it one of but a handful in the state to earn this prestigious seal of sustainability from the U.S. Green Building Council. And earlier this year, it was nominated for R&D Magazine's 2012 Lab of the Year.

Most importantly, the tower has served as a magnet for bringing some of the world's most talented young scientists to Oklahoma. As OMRF moves forward, this facility will continue to play a key role in attracting new talent to Oklahoma and improving medical research and care in our state and beyond.



TAKE A
LOOK
INSIDE

TOWER OF POWER

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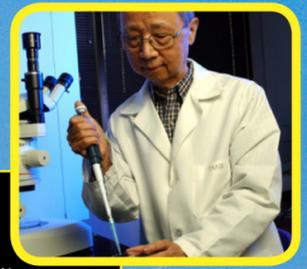
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When they're installed this summer, 18 wind turbines will spin atop the tower, generating electricity to help power the building.



After more than 50 years in the same building, Dr. Jordan Tang now continues his innovative research in the new Alzheimer's Disease Center.

In the Samuel Roberts Noble Cardiovascular Institute, OMRF's cardiovascular biologists study processes that are crucial to heart diseases, blood disorders and cancer.



The highlight of this floor is a new 3,400-square-foot cryostorage facility. This repository, one of the largest in the U.S., will hold and protect more than 150,000 biological samples at a temperature of -80°C.

Now empty, these floors will allow for future expansion.

OMRF's largest research team, the Arthritis & Clinical Immunology Program, is headquartered on this floor.



The Multiple Sclerosis Center of Excellence provides comprehensive care for more than 2,000 MS patients.



Here, MS patients receive physical therapy in a dedicated area equipped with special features tailored to their needs. This floor also houses the imaging core facility.

TAKE A LOOK INSIDE

PANDEMIC

by Adam Cohen

BETH DOESN'T
FEEL WELL

Flu. With its ability to mutate and spread at lightning speed, a devastating global outbreak may be just a matter of time. And if that happens, it will begin with a single sick person.



STOOD NEXT TO
BETH AT THE GATE

SAT ACROSS FROM
BETH ON THE PLANE

TOUCHED A
DOOR HANDLE
AFTER BETH

FLIPPED THROUGH A
MAGAZINE BETH LEFT
IN HER SEAT

DAY 1

Beth Emhoff has a cough. Not a particularly loud or violent one. Just a cough.

Nothing to worry about, right?

DAY 2

Beth isn't feeling so well. She's the one who started coughing yesterday. And today, she's doing more of it.

Right now, she's at Chicago's O'Hare International Airport, awaiting her connecting flight from Hong Kong back to her home in Minneapolis. But before she arrives, she'll dip her fingers into a bowl of peanuts. She'll hand her credit card to the bartender. She'll grip countless door handles, rails and other objects that will then be touched by other travelers.

Those people will, on average, bring their hands to their faces 2,000 to 3,000 times a day. So for most of them, whatever microorganisms come in contact with their fingers will soon end up in their bodies. If any of those tiny bugs are viruses, their hosts may soon become carriers. Which would mean an ever-growing army spreading disease with every touch, breath, sneeze, kiss, cough, hug and handshake.

DAY 4

Beth is dead.

She collapsed in her kitchen. Although paramedics rushed her to a nearby hospital, doctors were unable to save her. Truth be told, they don't know what, exactly, caused a previously healthy woman in her late 30s to die suddenly.

Perhaps an autopsy will tell more.

DAY 5

Beth died of influenza.

But this type of flu is unlike any the world has seen before. It began when the virus jumped from an infected pig to a human. Unlike most other strains that have moved from animals to humans, though, this one passes easily from one human to another. And it carries a mortality rate of 25 to 30 percent.

DAY 135
FOURTEEN MILLION
PEOPLE ARE DEAD.

As viruses learn to outsmart the drugs we've developed to fight them, the likelihood of a widespread epidemic increases.

Fortunately, Beth Emhoff isn't real. She's a character in *Contagion*, a 2011 film that imagined the rapid, worldwide spread of a deadly new virus. But the threat of a pandemic flu that claims millions of lives is no fiction.

"It happened in 1918," says OMRF immunologist Dr. Linda Thompson. "And it could happen again."

Thompson should know. With fellow OMRF immunologist Dr. Judith James, she's spent the past six years heading a National Institutes of Health project studying influenza. The researchers' specific focus is understanding why vaccines do not protect certain people from the flu.

Like all flu researchers, Thompson is acutely aware of the pandemic virus that emerged in 1918, just as World War I was coming to a close. Scientists now believe this virus, dubbed Spanish flu, began in birds, but genetic changes enabled it to spread to humans. And when it jumped to people, the illness packed a deadly one-two punch. Not only was it highly contagious, but it carried a death rate of two percent. This may not sound like much, but it's roughly 200 times more lethal than typical seasonal flu. Hard statistics are difficult to come by, but experts now estimate that by the time the 1918 outbreak came to an end, it had killed about 50 million people worldwide.

"What makes flu viruses so dangerous is that they mutate rapidly and spread easily," says Thompson, who holds the Putnam City Schools Distinguished Chair

in Cancer Research at OMRF. "Even with proper medical treatment, a newly emergent strain could claim many, many lives."

In 2009, a highly contagious strain of influenza emerged from southeast Asia. While most new forms of influenza come from this region of the world, researchers were particularly worried because this virus initially originated in another species—pigs—which meant the human body's immune system might lack the tools to form an effective response. With easy transmissibility and potential lethality, the so-called swine flu seemed to possess the two key ingredients for a pandemic. So health authorities sprang to action.

At OMRF, Thompson, James and Dr. Ken Smith assisted the U.S. Centers for Disease Control in Atlanta as CDC scientists scrambled to develop ways to diagnose, treat and prevent the virus. The OMRF researchers sent the CDC 67 antibodies they had produced against different strains of the flu. The hope was that the antibodies would bind to the newly emergent form of the virus, paving the way for the creation of rapid diagnostic tests and front-line therapeutics for health-care workers as they treated the sick.

The CDC's efforts paid off. Researchers succeeded in developing a vaccine that was produced in large quantities and administered in clinics, doctor's offices, pharmacies and shopping malls around the country. But that process took the better part of a year. In the meantime the

virus infected an estimated 50 million Americans. And while swine flu ultimately proved much less deadly than initially feared, killing only 1 in 2,000 people it infected, the virus nevertheless claimed 10,000 lives in the U.S. alone.

Still, Thompson says, the outbreak taught valuable lessons. "This was a dress rehearsal. It set in motion an international collaboration to get the virus isolated and sequenced, to get that information disseminated, and to get a vaccine produced rapidly." That infrastructure, she says, is still in place today. And it's just waiting to kick into gear when the next potential strain of deadly pandemic flu emerges.

Thompson and James' laboratories are part of the global flu-fighting infrastructure. Teaming with Dr. Gillian Air at the University of Oklahoma Health Sciences Center, their research focuses on why people with compromised immune systems fail to make effective immune responses to flu. Specifically, they've studied a subcategory of immunocompromised individuals: patients with the disease lupus. "Although we've restricted our project to lupus patients, we hope that what we learn will have broader implications," says James, who holds the Lou C. Kerr Chair in Biomedical Research at OMRF.

Every fall for six years, the OMRF researchers immunized 30 lupus patients and 30 healthy people with the seasonal flu vaccine. They drew small amounts of blood

from each group of volunteers at regular intervals—the day of immunization, then 2, 6 and 12 weeks later—and studied the samples to find out what happened in each group.

Typically, immunization should trigger the production of antibodies and T cells, two of the body's disease fighters. James and Thompson found that the lupus patients who were vaccinated produced normal amounts of both. But the quality of the antibodies paled in comparison to those of the healthy subjects.

James and Thompson published a number of scientific papers that detailed these and other findings they made. For example, the researchers identified certain sub-groups of lupus patients who responded just as well as healthy people to vaccinations. They also found other sub-groups who made poor responses and were much more likely to experience adverse reactions.

One of their most intriguing findings involved swine flu. In a small sub-study, the researchers administered a seasonal flu vaccine, which did not contain swine flu strains, to 10 healthy people. As expected, all of those who received the vaccine produced antibodies to the strains of flu contained in the vaccine. But half of those who received the shot also made antibodies to swine flu. "It was a small test group, but the results were clear: Even if a new strain of virus comes along, the regular vaccine may provide some protection," says Thompson.

Immunologists have always considered seasonal flu shots an important way to protect people from the virus. But, says Thompson, "It turns out they may be even more helpful than we thought."

Going forward, the OMRF researchers still have many questions they'd like to answer. Chief among them, says James, is "How can we take somebody who usually makes a bad response to the flu vaccine and turn that person into a good responder?" They're also exploring ways to harness a technology developed at OMRF to produce antibodies that could protect first responders in the event of a newly emergent strain of the virus.

Although the antibodies would not provide permanent protection, they could be used to temporarily bolster the immune systems of nurses, doctors and other health-care workers, allowing them to attend to the sick without risk of infection. This

could help buy researchers crucial time to develop a vaccine that could be widely distributed. Still, that process could take as long as a year. In the meantime, millions could die.

While the OMRF researchers continue their search for answers, James says the prospect of a deadly outbreak doesn't keep her up at night. "There's so much monitoring and surveillance that we should be able to catch things early enough to avert a major, catastrophic outbreak."

Plus, she says, health care has improved significantly since the 1918 outbreak. "We

know much more about the virus and about the immune system. Now we have antiviral drugs. Now we have intensive care units."

Still, she admits, "surprises can happen." After all, viruses constantly evolve. The task for researchers like James and Thompson is to keep up with those changes—and to anticipate the next mutation, whatever it may be.

The end of 2011 and the first months of 2012 passed without significant upticks in seasonal flu activity. With each quiet week, the chance for a pandemic dropped. At least for another year, *Contagion* was just a movie. ■

OMRF's Drs. Judith James and Linda Thompson were part of the CDC team that helped fight the swine flu outbreak of 2009.





Dr. Scott Plafker

Dr. Scott Plafker joined OMRF in 2011. But it wasn't a giant leap. He'd spent the previous eight years at the University of Oklahoma Health Sciences Center, developing a research focus on age-related macular degeneration, or AMD. At OMRF, he's continuing that work, and last fall received a five-year grant from the National Institutes of Health. That award will allow him to work toward a deeper understanding—and, he hopes, new treatment strategies—for a disease that robs millions of elderly people of their sight.

“I rarely miss a spin class. Exercise helps me think.”

I run home from work every day. We live three miles away, but I take a loop through downtown to make it a five-mile run.

I'm usually reading 3-4 books at once. I like Jeffrey Deaver thrillers but also non-fiction authors like Wendell Berry and David Foster Wallace.

Twice a month, I volunteer as a reading partner at our neighborhood elementary school. I did it when I was in graduate school, too.

I always wanted to go skydiving, but my wife says I should have done that before we got married. It's too late now.

My hero is probably Sherlock Holmes for his impressive powers of deduction.

My only regret is not taking up for kids who were made fun of at school. I didn't mistreat them, but I failed to defend them. Looking back, I really wish I had done that.





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Meet our scientists

WHEN DR. HAL SCOFIELD ISN'T STUDYING AND TREATING AUTOIMMUNE DISEASES, HE TRADES HIS STETHOSCOPE FOR A WHISTLE TO REFEREE SOCCER GAMES. A BROKEN ANKLE IN 2006 NEARLY SENT HIM INTO RETIREMENT, BUT HIS LOVE OF THE GAME HAS HIM BACK ON THE FIELD AGAIN.

