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UNIVERSITY OF NEBRASKA MEDICAL CENTER



Governor Heineman speaks on Bioterrorism Preparedness



Governor Heineman

Lectureships are amongst the premiere events of an academic institution, and we are privileged this year to have had an outstanding individual presenting at this year's Harry W. McFadden, Jr., M.D. Lectureship on April 14, 2005, the Honorable Dave Heineman, Governor of the State of Nebraska.

Governor Heineman was sworn in as Nebraska's 39th Governor on Friday, January 21, 2005. Prior to becoming Governor, he served more than three years as Lieutenant Governor. As Nebraska's director of homeland security, chairman of the Nebraska Information Technology Commission (NITC), and the presiding officer of the Nebraska Legislature.

Governor Heineman's lecture on "Building on the Nebraska Model for Bioterrorism Preparedness" focused on the extraordinary job Nebraska has done relative to bioterrorism preparedness. This all began in 1997 with the move of the Nebraska public health lab to UNMC.

Governor Heineman praised UNMC's role in advancing the Nebraska Model, "an integrated, coordinated and comprehensive" preparedness plan that spans everything from information technology and transportation to agriculture and academia.

The Harry W. McFadden, Jr., M.D. Lectureship was established in 1985 upon his retirement as Chairman of the Department of Medical Microbiology. Dr. McFadden was a graduate of the Nebraska College of Medicine in 1943. After completing his training in pathology, he became a faculty member at UNMC where he rose to the rank of full professor and became Chairman of the Department of Medical Microbiology in 1956. He held that position for nearly 30 years until his retirement in 1985, at which time the department was merged with Department of Pathology and Laboratory Medicine to become the current Department of Pathology and Microbiology. At that time, the pathologists of the department contributed an endowment to establish this lectureship. Dr. McFadden has had numerous awards and recognitions for his many contributions to microbiology, pathology, and most notably to medical education. It is for his contributions as an outstanding educator of medical students. The alumni of the Class of 1964, on their 25th reunion, decided to further endow the McFadden Lectureship, making it a premier event at UNMC.

A few of the distinguished guests at the celebration dinner the evening before were, Governor Heineman and his wife, Sally Ganem; Senator Abbie Cornett and her husband, Mark Stranglen; Senator Gwen Howard and her daughter, Carrie; Senator Pam Brown; Senator Lowen Kruse and his wife, Ruth; Dr. Dick Raymond, Chief Medical Officer for the State of Nebraska; Dr. Steve Hinrichs, director of the University's Biosecurity program and his wife, Deb; Regent Dr. Drew Miller and his wife, Annabeth; Regent Dr. Randy Ferlic; Alumni of the Class of 1964 Nebraska College of Medicine; Dr. Chet Thompson and his wife, Barbara; Dr. Vale Sorensen and his wife, Peggy; and Dr. Cleve Trimble.



L to R: Chancellor Maurer, Dr. Harry McFadden, Governor Heineman, Dr. Samuel Cohen



Dr. Steve Hinrichs and Governor Heineman



L to R: Tony Sambol, Governor Heineman, Ann Fruhling, Rhonda Noel (front)

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Letter from the Chairman



Samuel M. Cohen,
M.D., Ph.D.

Another academic year is about to begin, with the conclusion of an exciting year in our department and on campus. Important events have occurred in our department involving all our missions, including education, research, and clinical service.

A significant effort in the past several months has revolved around planning for a new Bioterrorism Preparedness Laboratory, including new laboratories for research, and planning for a new clinical laboratory. The efforts of numerous individuals are involved in this process as it continues. This project will follow on the soon-to-be completed opening of the Center of Excellence Building, which will include a new, modern and expanded operating room suite and a new gross and frozen section room for pathology.

The clinical laboratory also recently completed a successful CAP inspection. Congratulations to all those involved with this major effort.

As always, the end of an academic year brings the departure of some of our residents and fellows, but the arrival of others. Dr. Jean Thomsen has gone to Virginia Commonwealth University Medical Center for completion of her residency and a fellowship in surgical pathology and cytopathology. In addition, Dr. Ken Young completing his 2-year hematopathology fellowship and will be taking a faculty position at the University of Wisconsin, my old alma mater. We wish them both great success in their future careers.

We would like to welcome two new residents, Dr. Kyle Perry from the University of Florida and Dr. Neil Rawlinson from Boston University, who will start their residency programs in pathology on July 1, 2005. We also are excited about the return of Dr. Hina Nashaud who will be rejoining our department as a hematopathology fellow. We are also welcoming four new faculty: Dr. Mavis Fletcher from the University of Iowa who joined our department May 1, 2005. Drs. Ken Bayles, Kelly Rice and Jong-Sam Ahn, will join us July 1, 2005 from the University of Idaho.

This past year has had numerous successes for our department. We look to the coming year for yet even more exciting and greater achievements by our faculty and other members of our department.

"This project will follow on the soon-to-be completed opening of the Center of Excellence Building, which will include a new, modern and expanded operating room suite and a new gross and frozen section room for pathology."

Promotions(*) and New Hires

Tricia Aden		Lab Assistant	Molly Hartmann		Lab Assistant
Burak Aksu, PhD		Visiting Researcher	Wendy Jamison		Graduate Assistant
Brandi Babcock		Lab Assistant	Toru Kanno, PhD, DVM		Visiting Researcher
*Leslie Bruch, M.D.		Associate Professor	Kayla Kapels		Lab Assistant
Laurie Bruck		Administrative Assistant	Stephanie Kelly		Clinical Services Manager
Nicole Clark		Research Technologist II	Teresa Kottwitz	MARP	Industrial Engineer
Sarah Clayton		Client Service Representative	Kristin Landis		Research/Ed. Services Manager
Uğur Coşkun, M.D.		Visiting Researcher	Anthony Militti	MARP	Mechanical Engineer
Alicia Dafferner		Research Technologist I	Mary Newcomb	MARP	Project Director
Jeff Engel	MARP	Systems Analyst III	Takamasa Onishi, M.D. PhD		Post Doc Research Associate
Maria Erickson		Secretarial Specialist	Kim Plath		Lab Assistant
Zhong Feng Liu, M.D.		Visiting Researcher	Doreen Potter		Client Services Representative
Paul Fey, PhD		Associate Professor	Ramona Repaczki	MARP	Systems Analyst III
*Catherine Gebhart, PhD		Assistant Professor	Agnes Figuieredo, PhD		Visiting Researcher
*Timothy Greiner, M.D.		Professor	Shawn Slater		Research Technologist II
Amber Grimes	MARP	Medical Technologist	David Smith, PhD		Instructor
Lloyd Halsell, III		DNA Analyst			

Faculty & Staff Service

Marjorie Boyden	35 Years of Service	Shirene Seina	10 Years of Service	Yuri Persidsky	Tenure
Patricia Koso	20 Years of Service	Frances Aguilera	5 Years of Service	Samuel Pirruccello	Tenure
David Varga	20 Years of Service	Susan Anson	5 Years of Service	Rakesh Singh	Tenure
Karen Hansen	15 Years of Service	Michael Arington	5 Years of Service	Deborah Perry	Volunteer of month, January
Jeanette Beda	10 Years of Service	Christine Glaser	5 Years of Service		
Dalton Johnson	10 Years of Service	Cynthia Hardesty	5 Years of Service		
Scott Kurz	10 Years of Service	Randi Nelson	5 Years of Service		

Biocontainment Unit Unveiled



Julie Gerberding, M.D.

On March 7, 2005, Julie Gerberding, M.D., director of the Centers for Disease Control and Prevention (CDC), unveiled Nebraska's new Biocontainment Unit at The Nebraska Medical Center. "Nebraska is leading the way (in bioterrorism preparedness) and the biocontainment unit is one stellar example of that kind of preparedness," Dr. Gerberding said. The 10-bed unit, set up to handle highly contagious and deadly infectious conditions, is the first-of-its-kind in the nation. "We do not have any other

capacity like this in the nation," Dr. Gerberding said. "Part of the beauty of this particular facility is that it would serve not only for Nebraska, but for the other states that are engaged in the Midwest Alliance." The unit is equipped with special air-handling systems to ensure that germs do not spread beyond the patients rooms. Ultraviolet light, a dunk tank for lab specimens and sterilizer for items to be taken out of the unit are just some of the safety features designed to keep germs inside the unit and protect people on the outside. The unit also has two videophones that would give families and friends a connection to loved ones inside the unit. The videophones also will make consultations easier and safer.

The unit is set up to handle a wide variety of contagious and deadly infectious conditions, including the following hazardous diseases: small pox, anthrax, tularemia, the plague, botulism, SARS, monkey pox, avian flu, vancomycin-resistant staph infection, viral hemorrhagic fevers, and antibiotic-resistant tuberculosis.

There are only two other biocontainment patient care units in the country. The U.S. Army Medical Research Institute of Infectious Diseases houses a two-bed special Biosafety patient care suite at Fort Detrick, Maryland, for military members and investigators who may be exposed to infectious agents, and the CDC has a two-bed unit at Emory University Hospital in Atlanta.

"Nebraska is leading the way (in bioterrorism preparedness) and the Biocontainment unit is one stellar example of that kind of preparedness"

Dr. Gerberding praised the leadership of Nebraska, which is recognized nationally for its collaboration on bioterrorism preparedness issues, calling it a model for the nation. Governor Dave Heineman says, "Nebraska is a leader in bioterrorism preparedness and this collaborative effort is another shining example of what can be accomplished by working together." The funding comes from federal bioterrorism preparedness dollars allocated to Nebraska, along with contributions from The Nebraska Medical Center and UNMC. Each state received funds to plan and develop bioterrorism projects.

Nebraska's success, Gerberding said, has evolved from established priorities, phenomenal performance and leadership, vision and passion of state leaders to execute the job. Steve Hinrichs, M.D., professor of Pathology and Microbiology and director of the University of Nebraska Center for Biosecurity, says having the Biocontainment Unit and the Nebraska Public Health Laboratory located in the same area is an important benefit to the state. "The Nebraska Public Health Laboratory brings state and university expertise and resources together in a collaborative effort," Dr. Hinrichs says. "The laboratory's nearby location provides state-of-the-art services and enhances our overall preparedness for the threat of bioterrorism and infectious disease threats."

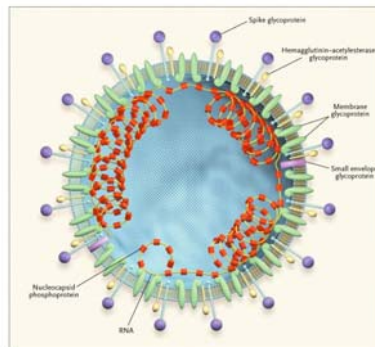
Philip Smith, M.D., medical director of the biocontainment unit, says, "The unit is a valuable regional and potentially national resource that is unique because of its 10-bed size and because it is a health department initiate project with collaboration between public health, a university and a hospital."

"This unit gives testimony to what can happen through collaboration," Glenn Fosdick, President and Chief Executive Officer of The Nebraska Medical Center, said. "A hospital alone cannot do what we've done here. A state medical school or health department alone cannot do what we have done. It takes all of us working together with our eyes on the future and our focus on preparedness."

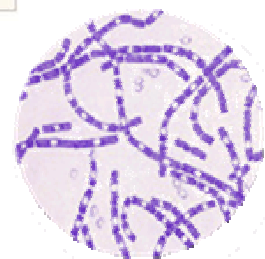
Dr. Gerberding praised the "health protection heroes" who volunteered and trained to work in the new biocontainment unit, which creates the "safest possible environment." Fosdick, too, praised the 15 registered nurses, seven respiratory therapists and seven technicians who have been selected and specially trained to staff the unit, should it be needed. "(We) see before us a group of protectors – individuals who volunteered to work in a unit where they will wage a bedside battle with the most contagious and deadly disease in the world. I want you to see the faces of courage – the people who've come to us and said, "I want this job".

"Since 2002, the four campuses of the University of Nebraska have worked together on terrorism research through a Center for Biosecurity administered by the University of Nebraska Medical Center," Governor Heineman said. "UNMC has earned praise over and over again for its caliber of research. It leads the way in developing technology to detect and react to a biological attack. State government's unique collaboration with UNMC and other partners makes very, very good sense."

"The laboratory's nearby location provides state-of-the-art services and enhances our overall preparedness for the threat of bioterrorism and infectious disease threats"



SARS Corona



Bacillus Anthracis

Department of Defense funds Research project



MARP Team

The Microbiology Automations Research Project (MARP), directed by Dr. Rod Markin received funding from the Department of Defense (DoD) in October 2004. The objective of the MARP is to develop a broad microbiology (including bacteriology, mycology, and virology) automation platform that will allow for and support the

creation of an automated microbiology technology that can be used by the Army in the clinical laboratory. It can also be used for non-clinical microbiology applications, potentially including bioterrorism testing.

The project will evaluate certain types of known microbiology specimen container systems for automation. At the conclusion of the grant, MARP should be able to dramatically improve how microbiology specimens are processed and cultured.

There are tangible and intangible benefits of the Project. The tangible benefits include a reduction in DoD healthcare costs, 24-hour/7-day-a-week operations and production, extremely quick turn-around times (critical in field settings), decreased errors and increased quality through repetitive and standardized processes. This means more troops can be processed more quickly, more ambient air samples can be tested, and more work can be done on site, all with less training than might otherwise be needed. Intangible benefits include advancing systems engineering for other applications and gradually standardizing specimen handling and processing.

The four goals of the MARP are:

1. To identify issues needed to commence work on a full-scale automation prototype;
2. To determine which specimen collection devices/systems should be "standardized" using optimal, high-priority modeling;
3. To build/develop a component prototype "Specimen Collection Vehicle" (SCV), based on data gathered from a market survey, which can be easily incorporated as an integral component to a full-scale automation prototype; and
4. To develop functional and technical specifications for a MARP prototype.

Currently, the project staff has completed six surveys and has 12 more scheduled in upcoming months. Hospitals throughout Omaha will participate, as well as such prestigious institutions as the Mayo Clinic.



Robotics



Update

Additional laboratory working space for the Special Pathogens and Biosecurity Laboratory sections of the Nebraska Public Health Laboratory (NPHL) in Wittson Hall was completed and officially opened on January 20, 2005. In addition to the Biosecurity and Special Pathogens Laboratory sections, the Chemical Terrorism Preparedness Laboratory (CTPL) is also located here. The new space gives these NPHL laboratory sections substantially more area to continue developing the capability and capacity necessary for public health related testing. This capacity has been developed to provide testing in a variety of situations, from suspected biological or chemical terrorism events to West Nile virus testing.

The Biosecurity and Special Pathogens Laboratory sections of the NPHL have the capacity and capability to test for a variety of bacterial agents by culture, DNA detection by polymerase chain reaction, or by detection of whole bacteria or biotoxins by an enzyme-linked immunoassay (ELISA) test known as time-resolved fluorescence (TRF). (See Table 1). As new assays are developed and released by the Centers for Disease Control and Prevention, the NPHL will continue to receive the testing kits and diagnostic reagents needed to perform the assays.

Classification	Agent
Bacterial	<i>Bacillus anthracis</i> , <i>Yersinia pestis</i> , <i>Francisella tularensis</i> , <i>Brucella</i> spp., <i>Burkholderia</i> spp., <i>Salmonella</i> spp., <i>Shigella</i> spp., <i>E. coli</i> O157:H7, <i>Vibrio cholerae</i> , <i>Coxiella burnetti</i> , <i>Chlamydia psittaci</i> , and <i>M. tuberculosis</i> (multi-drug resistant)
Viral	SARS-associated Coronavirus, Variola virus (Smallpox virus), Monkeypox virus, Vaccinia virus, Varicella-Zoster virus, and Western and Venezuelan Equine Encephalitis viruses.
Parasitic	Cryptosporidium
Toxin	Ricin, <i>Staphylococcus</i> enterotoxin B, and <i>Clostridium botulinum</i> toxin.

Table 1.

Reagents and test parameters are currently available to test for the following special pathogens and select agents.

The CTPL continues to develop the capability to rapidly detect the presence of chemical agents in human specimens such as blood, urine, and tissue. Two types of mass spectrometers, an Inductively-Coupled Plasma-Mass Spectrometer (ICP-MS) and a Gas Chromatography-Mass Spectrometer (GC-MS), will be utilized. Currently, the NPHL can test for cyanide and 13 elements including arsenic, and has recently received another GC-MS to be used for nerve agent analysis in urine specimens once training and validation is complete. Anticipated date for this is June 2005.

Researchers Discover Unknown Bacteria



Nebraskense

After four cancer patients in five years contracted the same mysterious, life-threatening lung infection, a UNMC cancer physician wanted to know exactly what bacteria was causing the infection. Knowing would give him a better idea of how to more effectively treat the infection.

Employing molecular diagnostics to solve the mystery, UNMC microbiologists and laboratory specialists at The Nebraska Medical Center accomplished something prestigious in the world of microbiology. They identified a previously unknown organism and named it Nebraskense (pronounced neh-brah-SKEN-see) after the state.

"This may not be equivalent to discovering a new planet, but for biologists, it's very exciting," said Steven Hinrichs, M.D., UNMC professor of Pathology and Microbiology and director of The Nebraska Medical Center microbiology and virology laboratories. "This bacterium wasn't just created. It's just that it hasn't been recognized before. It's probably been around for a long time."

The organism, called Mycobacterium Nebraskense, is in a family called Mycobacterium, which include diseases like tuberculosis and leprosy. Nebraskense, a new bacterium species commonly found in soil and water, is slow growing and is known to cause chronic lung infection, including pneumonia.

The UNMC discovery will allow laboratory specialists around the world to identify the organism faster and earlier, enabling health professionals to use the most appropriate treatment. Dr. Hinrichs says treatment is the key because the organism is almost impossible to avoid.

Gail Woods, M.D., professor of pathology at the University of Utah, and a scientist with Associated Regional and University Pathologists, Inc., said the Nebraska discovery solved a mystery for her laboratory. "We had the isolate but couldn't identify it," Dr. Woods said. "We didn't know what it was. Once we had the information, we added it to our database. The discovery will allow scientists to learn more about the disease it causes."

"Within each organism's DNA, there are signature sequences areas that are unique to the organism," Peter Iwen, Ph.D., associate professor in the UNMC Department of Pathology and Microbiology said. "There are multiple signature sequences that can be used for identification purposes. The signatures we have identified are somewhat unique and found to be reliable for identification purposes. A test we've developed allows us to look at the unique sequence in the genetic material of an organism and identify the species."

The team is also working on developing the ability to "direct test" patient specimens – making identification available between a matter of hours and a couple of days, instead of taking a month or longer as currently required. In addition, scientists also are looking to develop tests to determine the resistance of bacteria to certain drugs.

"Health professionals routinely prescribe treatments before they know the organism causing the disease," Dr. Iwen said. "They don't always know what's wrong. Some ask, why worry about obscure organisms that are difficult to identify?" The answer is: because frequently, they require different treatments."

From their work on the project, researchers have patented a molecular diagnostic test kit and are applying for patents on others they're developing. The kits enable more rapid and accurate ways to diagnose disease. Laboratories performing diagnostic testing for micro-organisms, including human and animal, are potential users of the test kits.

"Our capability in virology and molecular diagnostics is probably only exceeded by places like Mayo Clinic, Baylor, and a couple of national laboratories," Dr. Hinrichs said. "Most labs don't employ these methods. We're just beginning to see the vast potential of this technology. It's faster and more accurate and has the ability to reveal aspects of bacteria such as whether it has antibiotic resistance. It will revolutionize microbiology."

Rodney Markin, M.D., Ph.D.



Rodney Markin, M.D., Ph.D.



David T. Purtilo, M.D.

On January 8, 2005, the department celebrated the naming of Dr. Rodney S. Markin as the David T. Purtilo Chair of Pathology. The Chair is in honor of Dr. David T. Purtilo, Chairman of the Department of Pathology and Microbiology at UNMC from 1981 to his untimely death in 1992 at the age of 53. David had the wisdom and foresight to establish a major program funded by contributions from the faculty members of the department establishing insurance policies on themselves for future endowments. Ultimately, this program will endow 14 chairs or professorships for the department.

Dr. Markin was recruited as a resident by Dr. Purtilo in the department and ultimately as a faculty member. It was one of many outstanding recruitments by Dr. Purtilo in changing the department from a clinical and teaching entity to a major academic department with significant extramural research funding for clinical and basic research.

Dr. Markin has an unusual combination of backgrounds including a Ph.D. in chemistry, board certification in anatomic and clinical pathology, and special expertise in hematopathology in anatomic pathology and clinical chemistry, laboratory automation, and laboratory information systems in clinical pathology. His research has involved all of these areas, but he is best known for his development for laboratory automation systems, including his recent endeavors in automating processes for microbiology testing, particularly as it could be related to bioterrorism preparedness.

At the celebration dinner at Happy Hollow Country Club, he was joined by his wife, Annette, his two sons, Nicholas and Christopher, his father and other family members, friends and faculty colleagues.

Dr. Rod Markin epitomizes the vision of excellence in academic pathology anticipated and expected by Dr. Purtilo, and it is a pleasure and honor to name him as the David T. Purtilo Chair in Pathology.

Schenken Award Goes to Three Recipients

Three UNMC students received the 2005 J. R. Schenken M.D. Outstanding Achievement in Pathology and Microbiology Award during the honors convocation on May 12, 2005. The Schenken Award is presented to outstanding medical students in honor of Dr. Jerald R. Schenken, a nationally recognized pathologist. The award is presented to those medical students who best exemplify scholarship and professionalism in Pathology and Microbiology during their medical school careers.

Dr. Schenken, who practiced pathology at Methodist Hospital in Omaha, was involved with UNMC from 1965 until his death in 2001. This award recognizes Dr. Schenken's contributions to the education of future physicians and medical technologists and to the continuing education of health professionals. Since Dr. Schenken was involved in medical education broadly, the awards are not limited to individuals going into pathology. The winners this year and their residency plans are:

- Michael Feilmeier: Ophthalmology
University of Miami/Bascom Palmer Eye Institute, Miami, FL
- Stephen Schinker: Internal Medicine
University of Texas Health Science Center, San Antonio, TX
- Nicole Sherman: Obstetrics & Gynecology
University of Iowa Hospitals & Clinics, Iowa City, IA

Congratulations to these three outstanding young physicians.



Department Has Strong Presence at USCAP

The largest meeting of anatomic pathologists in the United States was held in San Antonio, Texas during the first week of March. Historically, the United States and Canadian Academy of Pathology (USCAP) has been a favorite venue for the UNMC Department of Pathology & Microbiology. This year was no exception. The department was recognized as one of the top 20 departments, out of two hundred twenty departments, for the number of posters and presentations by our residents, fellows and faculty at the meeting. Our strong presence at this meeting reflects the diverse research endeavors of our department.

Pathology Residents Corner

The past six months have been a very busy and productive time for our residency program. The largest project was preparation for the ACGME residency accreditation site visit which took place on February 23, 2005. We would like to extend a big thank you to all the faculty, residents and staff who worked so hard in preparation for this day. At this time, we do not anticipate receiving feedback on our residency program until next fall. Until then we will diligently continue working on several goals including re-designing the residency web site, rewriting the residency manual, and residency recruitment will be our major focus for 2005.

It is with pleasure that we announce Dr. John Gentry has agreed to serve as the Chief Resident for the 2005-2006 academic year. We would like to thank our current Chief, Dr. Rachel Stevens for a job well done. Her work and ideas this past year have been integral to many improvements in the program. In addition, Dr. Kurt Mathews also deserves a thank you for his involvement as Chief during Rachel's maternity leave this past fall.

Match Day took place on March 17th. Our residency program had two positions available and filled both. As of July 1, 2005 Drs. Kyle Perry, University of Florida and Neil Rawlinson, Boston University will join our program as first-year residents. We look forward to welcoming them both to Nebraska and our department.


Dr. Neil Rawlinson



Dr. Kyle Perry

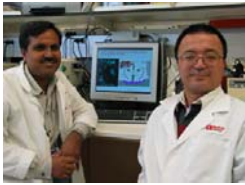


Congratulations to...

- **Dr. John Gentry** on his publication: Klinger ET, Bernal K, Paustian F, Schafer D, Hoagbin J, Gentry J, Swindells S. A 48-year-old HIV positive man with chronic intermittent diarrhea. Clin Infect Dis 39 (8):1174, 1239-40, 2004. 
- **Dr. Kurt Mathews** on his publication: Mathews K, Gulizia J. Young woman with abdominal pain and fullness. Consultant 44:12:1514-1520, 2004.
- **Dr. Rachel Stevens'** accomplishments, not the least of which was the birth of her second child, Owen Stevens, on October 13, 2004. Rachel also had a poster presentation entitled, "Analysis of HER-2 Gene Amplification Using an Automated FISH Signal Enumeration System" at the March 2005 USCAP meeting in San Antonio.
- **Dr. Jean Thomsen** for securing fellowships in surgical pathology and cytopathology at Virginia Commonwealth University Medical Center in Richmond, Virginia, where she will begin her training in July 2005. Dr. Thomsen was also appointed as a resident representative on the CAP/ACGME Cytogenetics Committee this past year as well as being selected to participate in the Council of Scientific Affairs (CSA) Leadership meeting in March 2005.

This only scratches the surface of the accomplishments our residents have had in the past 6 months. We look forward to reporting even more exciting resident activities and accomplishments in the months to come.

UNMC Research May Help Fight Prostate Cancer



Rakesh Singh, Ph.D. left and Mitsuru Futakuchi, Ph.D. right

Researchers at UNMC have reported the findings of a new study that sheds light on a mechanism involved in the pathological destruction of bone caused by metastatic prostate cancer.

The findings provide critical insight into the process of prostate cancer-driven bone destruction and identify a treatment that may interrupt bone disease caused by the spread of

prostate cancer. The research is published in the cover story in the May 2005 issue of *Cancer Cell*, a premier scientific journal.

The spread of cancer to other body regions is the primary cause of death from prostate cancer. The most common place for prostate cancer to metastasize is bone, causing intense pain, pathological fracture, and immobility. At the current time, treatment options for patients with bone metastases are limited.

Rakesh Singh, Ph.D., associate professor of pathology and microbiology, and Mitsuru Futakuchi, Ph.D., a post doctoral research fellow, headed the collaborative study between UNMC, Vanderbilt University and Nagoya City University in Nagoya, Japan. Dr. Singh is the principal investigator. Dr. Futakuchi is a visiting postdoctoral fellow from Japan. Lynn Matrisian, Ph.D., chair of the department of cancer biology at Vanderbilt University, also was a key participant in the study.

The study, which has been ongoing for the past five years, used a new rodent model that mimics the changes to bone that occur following prostate cancer metastasis.

Transplantation of prostate tumor tissue onto bone surfaces provided a histological picture similar to human prostate cancers growing in the bone. The goal of the study was to look for mechanisms that drive the behavior of this disease, with the hope of discovering new therapeutic targets.

"Bone remodeling is always going on in the body. It's a natural process," said Dr. Singh. "What we found is that for the metastatic tumor to grow in the bone, it must exploit the normal bone remodeling process by using the same pathway."

Dr. Futakuchi said: "Bone is not a very fun place for cancer to grow. For tumor cells to grow in the bone, a vicious cycle must occur involving bone destruction and the release of growth factors necessary for tumor cell growth. The destruction must occur, because the tumor needs the space to grow."

The researchers identified genes that are expressed in the tumor-bone interface but not in the tumor alone. Several genes that play a role in bone physiology were abnormally regulated, including the gene for MMP-7.

Cells called osteoclasts at the tumor-bone interface were observed to secrete MMP-7. Osteoclasts break down bone as part of normal bone remodeling, but are overactive in cancerous bone, leading to excessive bone destruction.

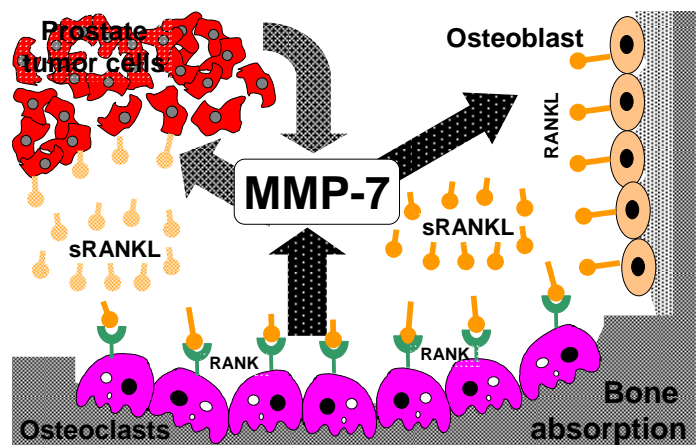
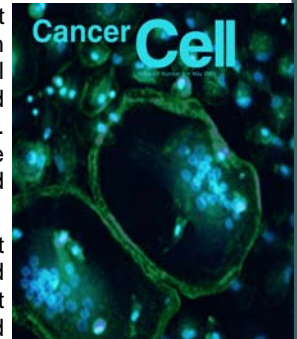
MMP-7 is an enzyme that regulates communication between the tumor and surrounding normal tissue by processing cytokines and growth factors to active forms. MMP-7 has been shown to be involved in the invasion and spread of several cancers.

The researchers found that MMP-7 cleaved a molecule called RANKL into a soluble form that promoted osteoclast activation and bone degradation. Mice deficient in MMP-7 had little to no soluble RANKL and exhibited substantially reduced prostate cancer-induced bone degradation compared to control mice expressing MMP-7.

The researchers conclude that MMP-7 plays a major role in prostate cancer-driven osteolysis and that the mechanism of MMP-7 action involves cleavage of RANKL to a soluble form that promotes osteoclast activation and pathological bone breakdown. "Our results make MMP-7 an attractive therapeutic target for the control of prostate cancer-induced bone osteolysis," Dr. Futakuchi said.

Dr. Singh said the next step will be for researchers to extend the study to breast cancer. He said prostate and breast cancer are most likely to spread to the bones. In approximately 60 percent of patients with metastatic prostate or breast cancer, the metastasis occurs in the bone.

"This is all about quality of life," Dr. Singh said. "Bone cancer is very painful and treatment options are lacking. We now need to look at these regulators of bone metastasis and try to develop targeted therapeutics that will prevent the bone metastasis from occurring."



MMP-7 promotes prostate cancer-induced osteolysis via the solubilization of RANKL. *Cancer Cell*, 7: 485-496, 2005

"This is all about quality of life, bone cancer is very painful and treatment options are lacking. We now need to look at these regulators of bone metastasis and try to develop targeted therapeutics that will prevent the bone metastasis from occurring."

Mary Haven to Retire



When Mary Haven was named associate dean of UNMC's School of Allied Health Professions in 1995, she had an idea of how long she'd stay in the position. She thought 10 years would be a good time to be associate dean and see things through, then time for new ideas.

"Haven joined UNMC on March 1, 1968, as a clinical chemist in pathology/microbiology and medical technology. "Mary Haven has been a part of the gyroscope that has kept our department, the clinical laboratory and the Allied Health programs on course during her tenure at UNMC. We have all been educated through one venue or another by Mary. I have personally enjoyed working with her both in the department and the College of Medicine over the years," says vice-chairman Dr. Rodney Markin. When accepting the associate dean position, she succeeded Reba Benschofer, Ph.D., who also spent 10 years in the role.

During Haven's tenure, she has expanded the distance learning programs beyond that of most allied health schools and colleges. By this fall, SAHP will have four programs offered by distance learning: medical technology, radiation therapy, radiography and cytotechnology. She became nationally recognized for her work and research in clinical chemistry and her contributions to education. "She is one of the most remarkable individuals I have known," declared department chair Dr. Sam Cohen.

Upon retiring, Haven and her husband, UNMC ophthalmologist Gerald Christensen, M.D., plan to travel. She also intends to stay involved with international programs at the medical center.



Grants Funded



- Julia Bridge – IRSG Studies of Alveolar Rhabdomyosarcoma Gene Fusion – 2/1/05—1/31/06 - Awarded by: NIH through University of Pennsylvania School of Medicine- \$69,050.
- Julia Bridge – A Validation Study of the ThinPrep UroCyte Collection and Slide Preparation Systems with UroVysion – 12/07/04—2/06/05 – Awarded by: Abbott Laboratories- \$50,000.
- Wing Chan – Molecular Signatures to Improve Diagnosis and Outcome Prediction in NHL– 6/01/05—4/30/10– Awarded by: DHHS/NIH/NCI- \$1,714,885.
- Nora Chapman– Inhibiting Demyelination By Immunization Using Coxsackievirus Vectors– 4/01/05—3/31/06– Awarded by: NIH through Creighton University- \$39,247.
- Samuel Cohen– Six-Month Oral Investigative Urinary Bladder Reversibility Study in Male Rats 2/22/05—2/21/06– Awarded by: Bristol-Myers Squibb Company- \$175,292.
- Samuel Cohen– Three-Month Oral Investigative Study of Urine Composition in Male Rats– 4/07/05—4/06/06– Awarded by: Bristol-Myers Squibb Company- \$80,848.
- Paul Dunman– Develop Methods for Monitoring Bacterial Gene Expression Using Affymetrix Gene Chips– 6/01/05—5/31/06– Awarded by: Merck & Co, Inc.- \$77,037.
- Paul Dunman– Role of the Staphylococcus Aureus Accessory Regulator SarA in Post-transcriptional Virulence Factor Regulation– Awarded by: American Heart Association (National)- \$65,000.
- James Gulizia– Educational Support-Awarded by: Educational Support office.
- Steve Hinrichs– Department of Homeland Security– LETPP– 4/01/05—3/31/07- Awarded by: NEMA-\$109,500.
- Steve Hinrichs– Department of Homeland Security– SHSG– 4/01/05—3/31/07– Awarded by: NEMA- \$152,468.
- James Talmadge– UNMC Eppley Cancer Center Support Grant– 9/20/04—7/31/05– Awarded by: DHHS/NIH/NCI- \$250,000.
- James Talmadge– Novel Technologies for Non-Invasive Detection, Diagnosis and Treatment of Cancer– 11/30/04—11/29/05– Awarded by: Alnis Biosciences, Inc.- \$55,587.
- James Talmadge– Analysis of the Antigenicity of KSA Vaccines– 3/24/05—6/23/05– Awarded by: Immuno– Designed Molecules, Inc.- \$5,846.
- Steven Tracy– Coxsackievirus Modulation of T1D Outcome in NOD Mice– 3/01/05—2/28/06– Awarded by: Juvenile Diabetes Research Foundation International- \$155,295.
- Dennis Weisenburger– Lymphoma Defined Cytogenetically for Epidemiologic Study– 4/01/05—3/31/06– Awarded by: NIH through Northwestern University-Chicago- \$124,119.

Path/Micro Baby Party



Path/Micro family

The Department's Annual Baby Party was held on
March 16th, 2005.
Many families attended and fun was had by all!



Sean Vollmer (grandson to Dr. Cohen)



Samantha, Danielle, & Tatum Holmstrom
(daughters to Jessie, Cytology lab)



Danielle Koch (daughter to
Melissa, Rapid Response Lab)



Shonia, Joseph, & Kaitlyn Struck

Special Announcements

Weddings:



- Jamie (Parman) Bass to Wayne Bass:
January 14, 2005
- Michelle Faron to John Gasko:
June 18, 2005
- Jeff Annin to Amanda Finch:
July 30, 2005

Babies:



- Sabrina, age 9 & Ashley, age 6 adoption by Julie Moreno
- Madeline Sophia Fontana, 7-9-04, to Jennifer Fontana
- Joeli Nicole Benson, 7-28-04, to Jeremy Benson
- Bryson Michael Tracy, 12-01-04, grandson to Kathy Salerno
- Kaitlyn Rose Struck, 12-10-04, to Shonia Struck

Upcoming events:



- Department Zoo Picnic—July 10th

Recognitions:



- Stephanie Lavoie, daughter of Beverly Lavoie, was selected for a foreign exchange program to study for one semester in Melbourne, Australia. She is a senior at Kansas State University.
- Christian Johansson, son of Dr. Sonny Johansson, was recently promoted to CEO of the Baltimore Economic Alliance where he has been Vice President since August 2003.

Graduates:



- Mark Gregory, son of Marcy Gregory, graduated May 14, 05 from Iowa Western Community College with a degree in Electronic Communications Media.
- Stuart Bridge, son of Dr. Bridge, graduated May 05 from the School of Engineering in Physics and Math at Washington University in St. Louis. He will be a first year med student at UNMC in August 05.
- Benjamin Iwen, son of Dr. Iwen, graduated from North Dakota State University, Fargo with a BS in Environmental Science and a BLA in Landscape Architecture.
- Edward Matthews, brother of Katrina Matthews, graduated from Bellevue University with a MA in Business Management.
- Sara Salerno, daughter of Kathy Salerno, graduated from UNO with a degree in Marketing in December.
- Andrea Felber, daughter to Glenda Felber, graduated from Creighton with a BSEMS in May.
- Emily Holbrook, daughter of Maureen Holbrook, graduated from Papillion LaVista High School. Emily is going to UNO, wants to work with geriatrics, probably in physical therapy.
- Joseph Graser, son of Karen Graser, graduated from Bryan High School. He will be attending Peru State College.
- Clark Kephart, son of Lynne Owen, graduated from Millard North. He will be attending Metro Tech as part of the Passport Program.
- Jared Plath, son of Kim Plath, graduated from Burke High School and will be attending UNO.
- Steven Timko, son of Denise Timko, graduated from Omaha North and will be attending UNO.

Newsletter Team

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With a special thanks to Kristin Landis for getting us off on the right foot.

Continued article suggestions are appreciated!