


**NEWS
RELEASES
1996**
Latest Research Improves Gene Therapy Techniques

INDIANAPOLIS--A major breakthrough in improving the efficiency of gene therapy is reported in the August issue of Nature Medicine. Researchers from the Howard Hughes Medical Institute at the Indiana University Medical Center and Takara Shuzo Co., Ltd., a biotechnology firm in Otsu, Shiga, Japan, propose that their findings have significant implications for future human gene therapy trials. Funding for this research was provided by the National Institutes of Health.

The research team reports that the human protein fibronectin, which already was known to have adhesion properties, also can act as an adhesive for retroviral particles that are used to transport genes into cells in gene therapy protocols.

David Williams, M.D., principal investigator on the study and member of the Herman B Wells Center for Pediatric Research at the Indiana University Medical Center, and a Howard Hughes Medical Institute Investigator, explained, "In essence, think of fibronectin as Velcro and retroviral particles and stem cells as balls. Envision that, like Velcro, the fibronectin allows attachment of the retroviral particles and stem cells, or balls, immediately adjacent to each other. This then permits genes to pass easily from the retroviral ball to the stem cell ball."

Williams also said that the findings answer some of the unknown questions that have eluded gene therapy researchers and therefore allowed only slow, limited progress in this area of research. He noted that the findings have significant implications for gene therapy trials, and may have implications on the development of new strategies for the treatment of retroviral infections such as HIV. In gene transfer, retroviral particles are used to carry normal genes into cells of the body in order to correct defective genes. Gene therapy trials have had limited success, in part because of low gene transfer efficiency. Earlier research has shown that fibronectin is abundant in bone marrow and is responsible in part for the adherence in bone marrow of hematopoietic stem cells, the source of all other blood cells. This new research showed that retroviral particles also bind to the same area of fibronectin. By using cloned fibronectin fragments, researchers discovered a dramatic improvement in gene transfer from the retroviral particles to the target stem cells.

Williams and other researchers at Indiana University Medical Center are awaiting approval from the FDA to begin the first human gene therapy trial using this new technology in the treatment of children and adults with brain cancers. The Indiana University Medical Center is comprised of the IU School of Medicine, The James Whitcomb Riley Hospital for Children, and University Hospital & Outpatient Center on the Indiana University-Purdue University campus in Indianapolis.

Takara Shuzo Co., Ltd., a leading biotechnology company in Japan specializing in genetic engineering, owns the worldwide patents for cloned fibronectin fragments.

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**August 5,
1996**
Gene Therapy

July 2, 1996
IUMC

Achieves
Certification
from
Commission
on Cancer

July 10, 1996
IU

Researcher
Developes
Model of
Blood Vessel
Growth

July 3, 1996
IUSM

Recognized
For
Graduating
High Number
of Family
Practice
Residents

July 3, 1996
IUMC

Receives
\$500,000
Unrestricted
Grant

Rep. Crosby
Honored at
IU Medical
Center

May 16, 1996
Cochlear
Implants

Knee

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Replacement
Technique

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For Immediate Release
July 2, 1996



IU MEDICAL CENTER ACHIEVES CERTIFICATION FROM COMMISSION ON CANCER

INDIANAPOLIS-- Indiana University Medical Center has received a three-year Cancer Program Approval status granted by the American College of Surgeons Commission on Cancer. Only 22 percent of health care facilities in the U. S. have earned the certification and these institutions annually provide care in 80 percent of the nation's cancer cases.

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The approval was based on requirements focusing on key program components including the Cancer Committee, cancer conferences, patient care evaluation and the Cancer Registry.

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The authorization was awarded after IUMC demonstrated that these elements are in place and functioning, providing educational, multidisciplinary exchanges on cancer patient management and quality control, and monitoring the success from primary treatment through long term follow-up.

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The certification benefits patients, the institution and the community by encouraging a true multidisciplinary focus for improved cancer-related care. The new standards set by the Commission on Cancer will enable the I.U. Medical Center to better evaluate and enhance efforts to achieve a more patient-oriented and outcome-driven cancer program.

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IU Researcher Develops Model of Blood Vessel Growth

INDIANAPOLIS-- Ophthalmologists like Ronald P. Danis, M.D. director of the retina service in the department of ophthalmology at Indiana University Medical Center, are studying ways to stop blood vessels from overgrowing in the eyes of patients with diseases such as diabetes, sickle cell anemia and macular degeneration.

In his efforts to understand why these blood vessels grow so abundantly in the eye, Danis has successfully developed a model of new blood vessel growth. The model will be used to explore the mechanisms responsible for abnormal vessel production in eye diseases. These blood vessels are stimulated to grow naturally as part of the healing response, but their growth can cause problems, disrupting the function of tiny retinal structures such as photoreceptors, associated nerves and communicating tissues. Blood vessel overgrowth eventually results in varying degrees of blindness.

Danis said the project can have far-reaching implications, not only to people with various eye diseases but also to individuals with other illnesses.

Blood vessel growth factors have been successfully identified, synthesized and applied in other areas of medicine, such as wound healing, and are currently being developed for applications in cardiology and cancer therapy. Inhibition of growth factors is of interest to cancer researchers and others, since blood vessel growth retardation would be an effective means of interrupting tumor growth.

Danis' model, which was unveiled during the 1996 annual meeting of the Association for Research in Vision and Ophthalmology, is inexpensive and consistently reproducible in other laboratories. The development of the model has taken several years; it is hoped it will aid scientists in comparing research results and hasten the discovery of a drug to intervene in blood vessel growth.

Danis was assisted in this research by Yishuang Yang, M.D., an ophthalmology resident at IU, and David P. Bingaman, D.V.M., a research veterinarian at Purdue University.

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For Immediate Release
June 3, 1996



IU SCHOOL OF MEDICINE RECOGNIZED FOR GRADUATING HIGH NUMBER OF FAMILY PRACTICE RESIDENTS

INDIANAPOLIS--The Indiana University School of Medicine has been recognized by the American Academy of Family Physicians for its high number of graduates selecting family practice medicine as their area of specialization.

The Academy presented Family Practice Percentage Awards to medical schools during the recent conference of the Society of Teachers of Family Medicine in San Francisco.

This year's awards, presented May 20, recognize medical schools with the highest three-year average of graduates entering family practice residency training programs during the period from 1993- 1995. Nearly 24 percent (23.6 percent) of the graduates at IUSOM chose family practice residency training programs.

The AAFP initiated the award program in 1992 to honor medical schools for their efforts in motivating and educating students about the role of family physicians. Family physicians continue to be in high demand throughout the country since they serve as primary care physicians for the majority of medical problems for people of all ages.

Topping the list of schools graduating the highest percentage of doctors entering family practice residency programs was the University of Washington School of Medicine, Seattle, with 29 percent. Marshall University School of Medicine, Huntington, W. Va., was second with 27.9 percent and the University of Minnesota Medical School was third with 26.8 percent. IUSOM had the 10th highest percentage in the nation of graduates entering family practice residency programs.

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For Immediate Release
June 3, 1996



IU MEDICAL CENTER RECEIVES \$500,000 UNRESTRICTED GRANT

INDIANAPOLIS-- An Indiana University Medical Center researcher is closer to reaching his goal of eliminating the need for heart transplantation and improving the quality of life for persons stricken with heart disease with receipt of a \$500,000 Bristol-Myers Squibb Unrestricted Cardiovascular/Metabolic Diseases Research Grant.

Loren J. Field, Ph.D., associate professor of medicine at the IU School of Medicine and a senior scientist at IU's Krannert Institute of Cardiology, will supervise the five-year, no strings attached grant. The funding began in April 1996.

Dr. Field joined the IU School of Medicine in 1990. Dr. Field, who is a professor in the departments of medicine, physiology and biophysics, is leading a team of researchers in developing strategies to repair heart damage. This research is particularly significant because heart muscle cannot regenerate itself after it has been damaged. Consequently, millions of people who have suffered from heart attacks or from diseases that kill heart muscle are left in a weakened state. These individuals are often in need of an organ transplant as their disease progresses.

Research at the IU Medical Center is focused on increasing the number of healthy muscle cells in diseased hearts. It is hoped that this can be accomplished by coaxing the surviving muscle cells to grow or proliferate. The research relies on the identification and isolation of key genes which might serve as therapeutic targets to promote heart muscle growth.

Using an alternative repair strategy, the Field group has recently shown that healthy donor muscle cells can be directly grafted into adult hearts. These latter experiments are particularly encouraging, as the donor muscle cells are able to form stable grafts which are indistinguishable for host muscle by a number of criteria.

Dr. Field said the Bristol-Myers Squibb grant will be a boon to his research. "The support provided by Bristol-Myers Squibb will enable us to expand our research program and, hopefully, will allow us to more rapidly determine the therapeutic potential of our experiments," Dr. Field said. "Philanthropic support like the Bristol-Myers Squibb grant program is important for biomedical research and we are extremely grateful to have been selected."

In announcing the grant, Dr. William A. Scott, senior vice president, Exploratory & Drug Discovery Research at Bristol-Myers Squibb, said: "Dr. Field's work with genetically altered cells to increase the number of healthy cardiac myocytes shows great promise for improving cardiac function in a failing heart. We are excited about this opportunity to join him in his search for a viable alternative to heart transplantation for end-stage heart disease."

This is the third unrestricted biomedical research grant the university has received

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from Bristol-Myers Squibb this decade. Last year, Lawrence H. Einhorn, M.D., who developed the cure for testicular cancer at the IU School of Medicine, received a \$500,000 Cancer Research Grant to further his work in "translational" research which bridge's the gap between the laboratory and the clinic to bring novel therapies to the bedside. Dr. Einhorn is a distinguished professor of medicine at IU.

In 1990, James A. Lemons, M.D., who developed new formulas to support fetal and newborn nutrition and growth, received a five-year, \$250,000 Bristol-Myers Squibb/ Mead Johnson Unrestricted Nutrition Research Grant. Dr. Lemon is the Hugh McK. Landon Professor of Pediatrics and director of the Section of Neonatology/ Perinatology in the Department of Pediatrics at the IU School of Medicine.

The cardiovascular/metabolic diseases grants program is one of six biomedical research grants programs funded by the Bristol-Myers Squibb Foundation. The others support research in cancer, infectious disease, the neurosciences, nutrition and orthopaedics. More than \$63 million has been committed to these programs to date.

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For Immediate Release
June 3, 1996



REP. CROSBY HONORED AT IU MEDICAL CENTER

INDIANAPOLIS-- Rep. Susan Crosby, D-Roachdale, has been honored by the Department of Psychiatry at the Indiana University School of Medicine for her long-term advocacy for the advancement of mental health services and research in Indiana.

Rep. Crosby chairs an external advisory board established by the Department of Psychiatry. Its purpose is to assist Hugh Hendrie, M.B.Ch.B., department chairman, in responding to challenges presented by the changing health care marketplace while strengthening the department's unique teaching and research roles. The advisory board will advise the department in communications with advocacy organizations and other community groups to build greater visibility and support for the department's three-part mission of teaching, research and clinical care.

Rep. Crosby received a plaque to recognize her work during a department reception May 31.

"Rep. Crosby is an extraordinary individual with a deep commitment to improving mental health care and research for the citizens of Indiana," said Dr. Hendrie. "Her great personal attributes and considerable political skills have been of inestimable value in advancing the academic and research mission of the department of psychiatry during the past 20 years."

Rep. Crosby is the only state legislator to have twice received the Legislator of the Year Award for support of mental health services in Indiana.

She is a member of the board of directors of the National Mental Health Association and the National Alliance for Research on Schizophrenia and Depression. She is a past president of the board of directors of the Mental Health Association in Indiana, Inc.

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For Immediate Release
May 16, 1996



RESEARCHERS SAY DATA INDICATES EARLY IMPLANTATION AN ASSET TO LANGUAGE DEVELOPMENT AND UNDERSTANDING

INDIANAPOLIS-- Indiana University Medical Center researchers Thursday (May 16) presented new data collected from children who received cochlear implants at the 131st Meeting of the Acoustical Society of America at Indianapolis.

One of the presenters, Karen Iler Kirk, Ph.D., said that information on children who were implanted at a young age is limited because it was only recently that children as young as 2 years of age have routinely received cochlear implants.

"Preliminary findings suggest that early implantation (by the age of 5 years) produces better word recognition performance in young prelingually deafened children," Kirk said. "Children in the early cochlear implant group had higher average word recognition scores and were better at identifying lexically difficult words than children who received their implant after the age of 5 years."

A second IU Medical Center researcher, Mario Svirsky, Ph.D., will report results which indicate that children who receive cochlear implants improve their expressive language ability at the same rate as children with normal hearing. Svirsky said that the data being presented at this week's national meeting is considered preliminary because it is the first study to investigate language development up to 2.5 years after implantation.

Testing of speech understanding and language development was done with standard testing devices, along with the Lexical Neighborhood Test and the Multisyllabic Lexical Neighborhood Test, which were developed at the IU Medical Center in 1995.

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NEW KNEE REPLACEMENT TECHNIQUE USED AT IUMC

INDIANAPOLIS-- Thousands of knee replacement surgeries are performed each year in the United States, but a new technology may simplify the procedure and make it safer, according to an Indiana University Medical Center orthopaedic surgeon.

Edward J. Hellman, M.D., an assistant professor at the IU School of Medicine, has incorporated a new procedure, known as the Insight Knee Instrumentation System, into the operating room. The device is made by Osteonics Corp.

Hellman said he believes the procedure, which is being used by only a handful of surgeons nationwide, could speed recovery time. His primary interest in the system, though, is that he believes it is potentially safer.

Under standard procedures, the surgeon performing the knee replacement surgery drills a tunnel into the femur and places a rod in the tunnel to align the knee replacement component with the hip.

"That technique releases fats and bone marrow into the blood stream," Hellman said. "The fats and marrow could lodge in the lungs causing pulmonary problems."

The new procedure eliminates the need to drill into the femur, thus significantly reducing the release of bone marrow and fats into the blood stream.

Hellman said that the amount of foreign substances coursing through the heart during the standard surgery, and at the time the tourniquet is released, is amazing. The amount of bone marrow and fats entering the heart is appreciably reduced using the new procedure, he said.

The Insight method is a two part system. Insight uses a pneumatically powered arm to hold the knee during the surgery and a tension-based alignment system with an electronic leveling device to indicate when the knee and hip are properly aligned. Once ideal alignment is determined, the knee prosthesis is correctly positioned in the leg.

Additionally, Hellman noted that the prosthesis does not cover the hole drilled in the femur in the standard procedure. "The bone has a good blood supply so there's bleeding into the knee," he said.

Hellman said that the same knee implants are used in the Insight method, all that has changed is the technique.

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