

# FINDING AN ALZHEIMER'S SWITCH

AN UNSUSPECTED PROTEIN REGULATES THE **PRODUCTION OF PLAQUE-FORMING PEPTIDES** 

by Paul Preuss, Lawrence Berkeley National Laboratory

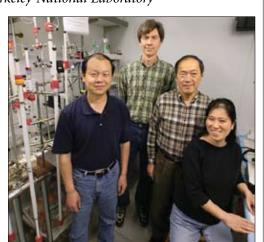
Researchers at the Department of Energy's Lawrence Berkeley National Laboratory (LBNL) have discovered an unsuspected subunit of the protein complex gammasecretase, which plays a central role in Alzheimer's disease. The researchers have shown that the newly discovered component, the protein CD147, regulates the production of the toxic peptides that cause amyloid plaques, the brain lesions that are the defining feature of Alzheimer's.

"Alzheimer's is worse than a disease — it takes the soul of a human being," said Bing Jap of LBNL's Life Sciences Division, in whose laboratory the new component was identified. "As the population of this country ages, the incidence of Alzheimer's is increasing, at a terrible increase in cost to society. Research leading to prevention or treatment is urgent."

The discovery and role of CD147 as a subunit of gammasecretase by Jap and his colleagues Shuxia Zhou, Hua Zhou, and Peter Walian is reported in Proceedings of the National Academy of Sciences, in an article in the online early edition of PNAS at www. pnas.org/cgi/content/abstract/ 0502768102v1?etoc.

#### How Alzheimer's Works

The most persuasive hypothesis of how Alzheimer's disease invades the brain is the so-called "amyloid beta protein cascade," in which a protein called APP is clipped into shorter pieces by enzymes known as secretases. (APP



The team that discovered CD147 in the gammasecretase native complex: Hua Zhou, Peter Walian, Bing Jap, and Shuxia Zhou.

stands for "amvloid precursor protein"; it is found in many tissues besides brain, but its functions are largely unknown.) If the portion of APP clipped by the beta form of secretase is further clipped by a third form, gamma secretase, the resulting fragments are amyloid beta peptides, A-beta 40 and A-beta 42. A-beta 42 in particular is toxic and causes the formation of amyloid plaques.

Unlike the majority of membrane proteins, gamma-secretase performs its proteolytic function neither inside nor outside the cell; instead, the crucial cut is made within the cell's thin membrane. In fact, all of the proteins and protein complexes involved — APP and the alpha, beta, and gamma secretases — are cell-membrane proteins, which penetrate the walls of the brain's neural cells.

Alzheimer's research would greatly benefit if the structures, particularly that of gammasecretase, could be established See Alzheimer's Switch, page 4

## Summer Interns Help Move Technologies to Market

In August 2004, eight MBA summer interns from Los Alamos National Laboratory's Technology (LANL) Transfer Division presented 11 projects to a panel of reviewers at the Los Alamos Technology Screening Initiative (LATSI) at the Los Alamos Research Park. The primary goal of this joint project between LANL's 2004 MBA Summer Internship Program and local

business developers, including Los Alamos Commerce and Development Corporation (LACDC) and Technology Ventures Corporation (TVC), was to give some commercial exposure and critical feedback to LANL inventors and to facilitate the process of technol-



<u>July</u> 2005

Michael Erikson (San Diego State University MBA candidate) presents his market opportunity assessment for LANL's "Quantum Dots Sunscreen Applications" to the Los Alamos Technology Screening Initiative panel.

ogy sourcing, screening, and portfolio development in northern New Mexico.

"The outcome of the presentations and review is a 'diagnostic' on each technology or idea, evaluating the future commercial po-See T<sup>2</sup> Interns, page 4

## Celebrating 15 Years of Transferring Ideas into INDEPENDENCE FOR Disabled Americans

by Dinah Cohen, Computer/Electronic Accommodations Program

On July 26, 1990, President George H. W. Bush signed into law the Americans with Disabilities Act (ADA), the largest civil rights legislation impacting an estimated 54 million Americans with disabilities. The law provides new opportunities for employment, communication, transportation and public access for people with disabilities. So often we think of this law and what is will do for "them" versus what it will do for "us." Having an accessible environment, free from discrimination, provides all of us the ability to be independent and participate in society as we get older and develop disabling conditions. As a U.S. Census Bureau report indicated, the implications of the baby-boomer population aging will have a dramatic impact on disability in America. By 2050, 25 to 30 percent of See Independence for Disabled Americans, page 2

ΕΝΤ S



# Government Invention of the Year

by Laurie Stauber, Technology Transfer & Partnership Office

Partnership Conference 2005 Enabling Naval Innovations to Win the Global War on Terrorism Washington, D.C. July 26-29, 2005

The Capitol Hill BioDefense Showcase Washington, D.C.

July 11, 2005

Naval-Industry R&D

N

SIDE

DOE's

Climate

Change

Tech

INL's

FLC

Joint

A C

In 1809, Humphry Davy,

an English chemist, invent-

*ed the first electric light.* 

Davy connected two wires

to a battery and attached

a charcoal strip betwween

the other ends of the wires.

The charged carbon glowed

making the first arc lamp.

In 1879, Thomas Alva Ed-

ison invented a carbon fila-

ment that burned for forty

hours. Edison placed his

filament in an oxygenless

bulb. (Edison evolved his

*designs for the lightbulb* 

based on the 1875 patent

he purchased from inven-

tors, Henry Woodward and

Matthew Evans.)

V

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Т

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Regional

Meeting

Remote

Robotics

FLC Midwest **Regional Meeting** Chicago, Ill. August 9-11, 2005

2005 Space and Missile **Defense** Conference Huntsville. Ala. August 15-18, 2005

FLC Mid-Continent/ Far West Regional Meeting Monterey, Calif. September 13-16, 2005 2005 Technology Transfer

Society Meeting Kansas City, Mo. Sept. 28-30, 2005 Federal Technology Watch

Increasing the size of grants awarded by federal agencies under the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs is being considered by the Small Business Administration (SBA).

Currently, 11 federal agencies participate in SBIR and 5 in the STTR program. SBA coordinates the programs.

"SBA has had discussions with the SBIR program managers about the 'possibility' of raising the SBIR/ STTR funding limits," SBA Assistant Administrator for Technology Edsel Brown confirmed. "The limits currently stand at \$100,000 for Phase I and \$750,000 for Phase II. The discussions have focused upon raising the levels to \$150,000 for Phase I and \$1,000,000 for Phase II. See DC on  $T^{2}$ , page 5

NASA's Inventions and Contributions Board (ICB) has announced that Dr. Bruce Steinetz and Patrick Dunlap, NASA Glenn Research Center (GRC) Mechanical Components Branch, have won the prestigious Government Invention of the Year Award for 2004 for their work developing a thermal barrier and solid rocket motor (SRM) joint design for the space shuttle. Their innovation is a unique, flexible, braided carbon-fiber thermal barrier designed to

withstand the extreme temperature environments in current and future solid rocket motors and other industrial equipment.

The revolutionary new thermal barrier solves the vexing problem of blocking 5500+°F rocket combustion gases from reaching temperature-sensitive O-rings while still



allowing 900-psi gases to position the O-rings in their grooves for proper sealing—a problem that has challenged rocket motor designers for decades. This innovation is recognized as a significant improvement over the current silicone joint-fill approach to safeguarding O-See Invention of the Year, page 5

## NewsLink

# FED LABS FLASH TECHNOLOGY TRANSFER NOTES

## Arnold Engineering **Reopens** Aerodynamics

Arnold Engineering Development Center (AEDC) has been tasked to reopen the National Full-Scale Aerodynamics Complex (NFAC) located at NASA's Ames Research Center near San Francisco to maintain a critical national aerodynamic test capability used primarily for rotorcraft.

The NFAC was built in 1944 to support research in aerodynamics, structural dynamics and acoustics. Investigations, using critical components (especially rotor blades) and, on occasion, full-size aircraft, focus on the aerodynamic characteristics of new configurations, with an emphasis on validating design estimates. The NFAC has two test sections. One, 40 feet high by 80 feet wide, is capable of obtaining velocities up to 250 knots; the other, 80 feet wide by 120 feet high, is capable of obtaining velocities up to 80 knots.

NASA closed the NFAC in 2003 because it had an inadequate source of funding to maintain the facility. However, the Department of Defense has an ongoing requirement for NFAC, and tasked the Air Force to reactivate the facility and return it to full operational capability in FY07.

## Albany Chemist A NACE Fellow

Bernard S. Covino, Jr., a Research Chemist at the Department of Energy's Albany Research Center, was inducted as a Fellow in NACE (National Association of Corrosion Engineers) International at the 60th Annual Conference and Exposition held in Houston, Texas, April 3-7, 2005. The NACE honor is for distinguished contributions in the field of corrosion and its prevention.

Mr. Covino has 35 years experience working for the federal government on corrosion and its effects on the U.S. transportation, energy, and environmental infrastructure. He has authored over 150 publications and presentations on atmospheric corrosion, bridge corrosion, geothermal analysis, high temperature corrosion, and corrosion sensors. He is currently editing the new edition of Volume 13: Corrosion, which is part of the ASM International series of handbooks.

## Volpe Betters Air Traffic Management



Volpe's ETMS 8.0 allows traffic managers to reroute air traffic around severe weather and to share that information with decision makers in the airspace user community.

Federal Aviation Administration (FAA) to support its Traffic Flow Management (TFM) system.

ETMS is used to track, predict, and plan air traffic flow, analyze effects of ground delays, and evaluate alternative routing strategies.

The Volpe Center is responsible for the development and daily operation of ETMS.

The ETMS deployment included a significant infrastructure modernization component where computers and telecommunications equipment at the Volpe Center's ETMS hub site and over 75 FAA field sites were successfully upgraded, resulting in a considerable increase in processing speed and capacity for handling air traffic information.

ETMS 8.0 contains new traffic flow management decision support tools that enhance the ability of traffic managers to reroute air traffic around severe weather.

In addition, this release provided several enhancements to ETMS's Traffic Situation Display—a tool that monitors the position of air traffic and helps to determine the traffic demand on airports and sectors. A common air traffic situational awareness makes possible collaborative decision-

and energy corrosion, cathodic protection, failure making between the FAA, air carriers, and military operations, which leads to improved aviation efficiency and safety.

## DOE Advances COMMERCIALIZATION OF CLIMATE CHANGE TECH

On June 6, Secretary of Energy Samuel Bodman, the Volpe Center completed in a speech before operational the Coal Council, deployment of announced that the De-Enhanced Traffic partment Energy (DOE)

ETMS 8.0.

The

National of will provide \$100 million to further develused by the op carbon sequestration technologies used

to capture and store greenhouse gases.

The research is part of President Bush's Global Climate Change Initiative, which is designed to reduce greenhouse gas intensity by 18 percent by 2012, in part through the development of significant sequestration technologies.

"DOE is working closely with the private sector and research universities to develop technologies to produce energy in a more efficient and environmentally responsible way, and carbon sequestration is at the cutting edge of these advances," said Secretary Bodman. "By moving carbon sequestration technology from the laboratory to the field with today's grants, we are another step closer to significantly reducing greenhouse gas emissions while maintaining the important role coal plays in America's energy mix."

The seven projects selected by the DOE are led by public-private sector consortiums of businesses, state agencies, and universities. The consortiums are part of a network of regional carbon sequestration partnerships created by the DOE to serve as the backbone of sequestration research network.

#### Disabled Americans, from page 1

the U.S. population will be over the age of 60 and "household disability" will become part of everyday experience for Americans.

In 1990, the Department of Defense (DoD) established the Computer/Electronic Accommodations Program (CAP) to address the challenges of employment in the changing electronic and computer environment. CAP is the centrally funded program in DoD to provide the assistive technology and accommodation services to employees with disabilities.

In October 2000, CAP was granted the authority to serve as the federal government's centrally funded program for assistive technology. Since its inception in 1990, CAP has filled over 40,000 requests for accommodations for DoD and 63 federal partner agencies. The accommodations are free to the requesting federal agency. The excuse that the cost of accommodation prohibits managers for hiring people with disabilities was removed. Assistive technology in 1990 was limited and its ability to interface with the standard computer environment caused a new set of barriers. Additional legislation was required to ensure interoperability in the Federal sector. Section 508 of the Rehabilitation Act, as amended, requires that all electronic and information technology that is purchased, developed and/or maintained in the Federal government (and now many state governments as well) must be accessible and useable by people with disabilities. Implemented on June 25, 2001, Section 508 began to bridge the gap between assistive technology

and mainstream information technology.

Over the years, the technology improved, interoperability was addressed via Section 508 and partnerships were developed with businesses and between government agencies to increase access and awareness. CAP, along with many other federal agencies, has worked with the Federal Laboratory Consortium (FLC) to review the needs of the disability community. In fact, much of the assistive technology available in the marketplace is a result of technology that has been developed in federal laboratories. Since the FLC identified assistive technology as a focus area in the mid 1990s, more attention has been placed on the importance of providing new technologies for people with disabilities. At CAP, there is a current push to focus on the specific employment needs for this population. If people with disabilities can work, then they too can be independent and able to engage in civil and economic systems. To achieve this goal, CAP is now researching its archives to analyze assistive technology trends and surveying its customers to identify their next generation of technology requirements to increase work independence and flexibility. Partnering with the Interagency Committee on Disability Research (ICDR), the Technology Administration at the Department of Commerce, and the Rehabilitation Engineering Research Center (RERC) on Technology Transfer, CAP seeks to identify the assistive technology needs of the future. This work will help prepare the federal government to recruit, place, promote and retain skilled workers, including the anticipated increase in workers with disabilities.

As we look at the next wave of assistive technology to meet the increasing demands of a growing population with increased expectations regarding access and independence, we need to look closely at the technology that is being developed for our defense, energy, and space programs. For example, each time we develop technology for a war fighter to access information while they are "hands-busy", we have also designed a product for a person with a dexterity disability. The same can be said for the technology we are developing to function in darkness - night vision goggles. This could be used for people with limited vision. As a nation, it is time to commit ourselves to move beyond a single population focus and begin to manage projects with all components of our society as possible customers. As we find new populations to serve, we must tailor our approaches. War fighters are familiar with the latest in technology when they are in theater. Now, many of them need technology for another reason. Our soldiers, sailors, airmen and marines are returning everyday from deployment in Operation Enduring Freedom and Operation Iraqi Freedom. Yet, many of them are not returning to their See Disabled Americans, page 5



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## NEWSLINK

# TECH WATCH | LABORATORY TECHS READY FOR TRANSFER

## AFRL'S AIRBORNE AND SUBTERRANEAN UHF ANTENNA

When conducting military operations, and particularly airborne operations, against an underground hardened target, it is often difficult to assess the degree of success achieved in neutralizing the target from further enemy use.

In addition to the difficulty arising from the underground and hardened nature of many present-day targets, gathering target damage assessment information is often accomplished from a distant and moving vantage point, i.e., from a moving aircraft, an aircraft that has not approached or has not remained in the target area because of concern for its own safety from ground fire or other hostile threats.

Moreover, such target damage assessment is often desired when neither the attacking nor the assessing aircraft has been within viewing distance of the target during the entire operation-but has remained over the horizon or at some safe distance from the target and its probable defenses during both the weapon launch and success assessment phases of the operation.

In any event, it is clearly not desirable to require the attack aircraft or any related aircraft to either remain in the target vicinity for assessment purposes or return to the target area for assessment purposes for a second neutralization attempt-particularly if such a second neutralization is not needed.

As a remedy for this success assessment difficulty, a pending patent has disclosed a system for collecting tangible objective target arrival experience data from the warhead device itself and making this data available at a remote mission analysis center, or to the pilot of the mission aircraft or to some other aircraft.

One of the more technically challenging aspects of this data collection sequence resides in the provision of an antenna apparatus capable of satisfactory electrical performance and physical endurance in the subterranean, as well as the airborne, phase

of a warhead delivery sequence.

In addition to the large deceleration forces expected when a warhead arrives at the desired detonation point within the interior of a hardened underground target, there are significant other environmental challenges to be tolerated by such an antenna.

The present invention is believed to provide an attractive resolution to these difficulties.

#### *Features*

Buried targets often do not show evidence of fuze function or damage at the surface.

Hopes of transmitting this information through the earth rely on matching the transmitter impedance to an antenna that can change its electrical length hundreds of percent if tightly coupled to surrounding earth and debris during penetration. As an alternative to losing efficiency in shortened antenna designs, or trying to fit frequency independent designs that are typically wavelengths in size, this approach uses heat-cured urethane to support, shorten, and control the impedance of the antenna element.

The material is similar to a shockresistant skate wheel and allows the longest penetrating wavelength to be radiated from a short cone monopole element.

When transmitting in air and down to multiple stories of buried high density polyethylene (HDPE) pipe, which has 2.5 percent carbon added for sun tolerance, the reflected power change was less than half of a standing wave unit.

#### Potential Applications

This invention is protected under patent number 6,380,906. Possible commercial application could include use with airborne deployment of seismic monitoring equipment over difficult faulted terrain, buried objects, or personnel retrieval.

More info: Jill Y. Barfield, 101 W. Eglin Blvd., Suite 143, Eglin AFB, FL 32542-6810, (850) 882-8591

## INL'S REMOTE Robotics

Idaho National Laboratory's (INL) Three-Dimensional Telepresence System for a Robotic Environment includes a camera pair remotely controlled by a control module affixed to an operator.

The camera pair provides three-dimensional viewing, and the control module, affixed to the operator, affords hands-free operation of the camera pair.

In one embodiment, the control module is affixed to the head of the operator and an initial position is established.

A triangulating device is provided to track the head movement of the operator relative to the initial position. A processor module receives input from the triangulating device to determine where the operator has moved relative to the initial position and moves the camera pair in response thereto.

The movement of the camera pair is predetermined by a software map that has a plurality of operation zones.

Each zone corresponds to a unique camera movement parameter such as speed of movement. Speed parameters include constant speed, or increasing or decreasing. Other parameters include pan, tilt, slide, raise or lower (the cameras).

Other user interface devices are provided to improve the three-dimensional control capabilities of an operator in a local operating environment.

Such other devices include a pair of visual display glasses, a microphone, and a remote actuator.

The pair of visual display glasses facilitates three-dimensional viewing, hence depth perception.

The microphone affords hands-free camera movement by using voice commands.

The actuator allows the operator to remotely control various robotic mechanisms in the remote operating environment.

More info: Gary Smith, (208) 526-3780

For more information,

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kwright@tamimail.com



This National Institutes of Health (NIH) technology relates to the identification of two highly conserved linear domains of Ebola or Marburg envelope glycoprotein (GP) and of amino acid residues within these regions critical for virus infection.

The identified domains could provide targets for rational design and development of broadly cross-protective antivirals and vaccines. There are currently no licensed vaccines against Ebola and Marburg.

The linear domains (or portions) could potentially be used as immunogens in a vaccine. Mutations containing these epitopes have been identified to result in the formation of noninfectious Ebola viral particles, which could be useful for developing vaccines against Ebola virus, a category A biodefense agent.

Vaccines utilizing these noninfectious particles may be safer than vaccines that use other common approaches, e.g., live-attenuated virus vaccines. This technology describes the polypeptides that form the noninfectious Ebola viral particles, the polynucleotide sequences encoding the polypeptides, vectors comprising the polynucleotides, host cells transformed with such vectors, vaccines and methods suitable for use in the prevention and/or treatment of hemorrhagic fever due to Ebola or Marburg, and a molecular decoy comprising the polynucleotides.

These additional materials could also form the basis of an Ebola vaccine or antiviral therapy.

Diagnostic applications involving the aforementioned materials are also described. Development of antiviral compounds and vaccines for treatment and prevention of Ebola and Marburg infections would be of tremendous benefit for biodefense and public health.

However, the current Ebola vaccine technologies, such as DNAbased vaccines and subunit vaccines, either have safety risks or lack broad cross-protectivity. Therefore, the present technology could provide a promising technology to make safe and broad cross-reactive antivirals or vaccines against Ebola and Marburg viruses.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.



Licensing contact: Susan Ano, (301) 435-5515, anos@mail.nih.gov



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#### *T*<sup>2</sup> *Interns, from page 1*

tential and providing specific next steps to further the development," said LACDC Executive Director Kevin Holsapple. "This project will contribute to forming a northern New Mexico 'deal pipeline' in support of technology business deal flow."

According to intern facilitator Marc Oettinger (2004 Babson College MBA), some projects represented dramatic technological advances. For example, in the future, a trip to the doctor's office could be like a walk in the park, thanks to technology under development at LANL. "A portable biosensor platform may eventually have the capability of detecting any pathogen or cancer marker in a per-

son's body through a painless saliva test," said Oettinger.

The review panel included venture capitalists, entrepreneurs, economic development professionals, and market experts.

The vSpring Capital group in Los Alamos, represented by Mike Connolly (a former member of LANL's Technology Transfer Division), participated in the project. "We were presented with outstanding innovative projects from the MBA students," Connolly said. "The program is something that benefits all of us, and we were glad to have an opportunity to participate." According to Holsapple, "This summer's activity is a prototype for potential future technology sourcing and screening not only of Laboratory technology, but other technologies developed outside the Lab as well."

#### *Recruiting and Retaining Talent*

According to a recent *Fortune* magazine article on what makes organizations great, "the single best predictor of overall excellence was a company's ability to attract, motivate and retain talented people." "Through our Technology Transfer Division's MBA Internship Program, we attract the best and the brightest future business leaders—the hardest people to hold onto. Ultimately, it's foolish to believe you can trap good people. However, by staying in touch and turning them into advocates, information resources, and business partners, Technology Transfer has created a robust alumni network that has turned into a trusted pipeline of new talent for our division," noted Belinda Padilla, the T<sup>2</sup> program manager responsible for developing and managing the MBA Internship Program.

Through this program, top-tier business school students evaluate LANL inventions for commercialization potential, helping the technical staff develop strategies to transfer these technologies to the private *See T<sup>2</sup> Interns, page 6* 

#### Alzheimer's Switch, from page 1

at high resolution by x-ray crystallography.

But membrane protein structures are particularly difficult to obtain. "Membrane protein complexes can be very difficult to purify in an intact form," said Jap. "Moreover, it's extremely difficult to get enough pure membrane protein to crystallize." Nevertheless, Jap's laboratory has earned a reputation for solving the structures of important membrane proteins.

As the first step to producing enough gamma-secretase to make crystals, Jap asked postdoctoral fellow Shuxia Zhou to lead the effort to characterize the native protein complex. Zhou is a biochemist with M.D. and Ph.D. degrees from Shanghai Medical University; before coming to LBNL she studied and taught in Shanghai, and at Oxford University and Kyoto University.

"Previous experiments establishing the role of gamma-secretase were genetic experiments done by causing its overexpression in cell lines and animal models," Zhou explained. "We wanted to isolate the native form and purify the whole gammasecretase complex."

#### An Unexpected Factor

Zhou and her colleagues isolated the native complex from cells of the HeLa line and separated its subunits by gel electrophoresis, which pulls the components apart according to their molecular weights.

"There were six strong bands in the gel, five of which we could identify because we expected to find them," said Zhou. The expected bands represented the four known subunits of gamma-secretase, the proteins named Nct (nicastrin), APH-1 (anterior pharynx defective 1), PEN-2 (presenilin enhancer protein 2), and Psn-1 (presinilin 1) — which is cleaved into

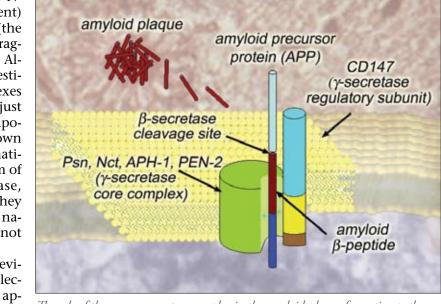
Psn-1 NTF (the Nterminal fragment) and Psn-1 CTF (the C-terminal fragment). In prior Alzheimer's investigations, complexes made up of just these four components were shown to be an enzymatically active form of gamma-secretase, but whether they constituted the native form was not known.

From the evidence of gel electrophoresis, apparently not. "In addition to these

Zhou said. "We brain. However, a newly discovered subunit of gamma-s didn't know what down-regulates the production of amyloid beta-peptides. it was." To find out, she and her colleagues clipped the band from the gel, extracted the protein, and sequenced its amino acids. But when CD147 was sil

The mystery protein turned out to be the membrane protein CD147. CD147 is expressed in many tissues and has many biological functions besides its role in tumor invasion, including reproduction, inflammation, protein transport and sorting within cells. It also has a role in neural function: when the CD147 gene is deleted in mice, the result is defective nervous system development, loss of working memory, spatial learning deficits, and disorientation — behaviors remarkably suggestive of Alzheimer's disease.

To investigate CD147's part in the activity of gamma-secretase, the researchers used targeted RNA to silence CD147 in cell cultures. The four



parently not. "In addition to these five bands we found an extra band," Zhou said. "We didn't know what

gamma-secretase complex, as well as the APP protein on which they operate, were unaffected by this silencing. But when CD147 was silenced, the production of amyloid beta peptides increased markedly.

The researchers established that the native form of gamma-secretase, incorporating CD147, appears in other cell lines, including kidney cells and neuronal cells, and is not unique to HeLa cells (which are derived from cervical cancer). CD147 itself is found in many contexts besides gamma-secretase, but only as a part of gamma-secretase does it regulate the production of A-beta peptides and thus amyloid plaques.

#### Goals for Further Research

Just how does CD147 do what appears to be its normal job of preventing excessive production of A-beta 42 peptides, and what causes it to fail? is a regulatory subunit of gamma-secretase, but we don't know how it works. As yet, we don't know its mode of action with respect to the other members of gamma-secretase and its substrates.

Determining this mode of action is a key goal of our future efforts."

About 25 amino-acid residues make up the length of CD147 that crosses through the cell membrane, one of which, glutamic acid, has net electrical charge. Such an unlikely placement for a charged residue suggests that this region of CD147 may seek to align with another protein's oppositely charged region, perhaps that of Psn-1. Disruption of this transmembrane teamwork could lead to in-

creased production of amyloid beta peptides which, in turn, may result in the amyloid beta plaque formation that is a hallmark of Alzheimer's disease.

"The answer to how the components of gamma-secretase components fit together inside the cell membrane has to wait for high-resolution structural work," said Zhou, "and for that we first have to make enough of the native complex to make crystals."

Bing Jap added, "Determining the atomic structure of the gamma-secretase complex, including CD147, is the next crucial step in understanding the molecular mechanisms by which the substrates are cleaved in various forms — and the next crucial step to designing Alzheimer's disease therapeutics."

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two parts in the mature complex, previously known components of the According to Zhou, "We know CD147 lbl.gov



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## FLC MID-CONTINENT/ FAR WEST MEETING TO EXPLORE NEW ENERGY



The joint FLC Mid-Continent/Far West regional meeting, "New Energy Economy: Roles and Opportunities for Federal Labs," will take place September 13-16, 2005, at the Portola Plaza, Monterey, Calif.

With gasoline prices over \$2.00 per gallon and rapidly diminishing oil reserves, this conference offers an intensive review of the technologies, funding and programs at federal laboratories, state-borne initiatives and incentives, and

mechanisms that hasten commercialization while buoying the economy.

Highlights include a marketing and commercialization training segment taught by Dr. Ken Dozier, Executive Director of both the USC Engineering Technology Transfer Center (ETTC) and the NASA Far West Regional Technology Transfer Center.

A special session, Market.com, will include invited guest Andrew Hamm of the Silicon Valley/ San Jose Business Journal. Other topics include Fairness of Opportunity, the Importance of Branding, Writing Collateral Material, etc.

Regional technology transfer awards will be celebrated. Special consideration will be given to alternative fuel technologies, programs and marketing plans. Nomination forms can be downloaded from the meeting website.

As a bonus, the world-famous Monterey Jazz Festival takes place September 16-18, 2005. For more information about the festival, visit <www. montereyjazzfestival.org.>

To register for the meeting, go to <www.flcfw.org/meeting>.

Invention of the Year, from page 1

rings, which may allow hot combustion gases to penetrate the joint.

#### As a case in point, Aerojet, manufacturer of the SRMs for the Lockheed-Martin Atlas V Evolved Expendable Launch Vehicle (EELV), used the GRC thermal barrier technology to quickly recover from a dramatic full-scale test stand failure. In this test, 5500+°F gases reached the Orings and flange in the original joint design, severing the nozzle from the SRM. After incorporating three GRC thermal barriers in its redesigned joint, Aerojet certified the new design to meet an aggressive schedule for launching a commercial satellite.

The breakthrough also promotes shuttle and astronaut safety, and allows nozzle joints to be assembled in one-sixth the time of previous approaches with much higher degrees of reproducibility.

NASA Senior Technologist Dr. Paul Curto, representing the ICB, affirmed, "This unique innovation is one of the best examples of how Glenn technology is critical to exploration, aerospace, and commercial activities all at once."

The new thermal barrier will enter service on Space Shuttle Mission STS-123, expected to launch in May 2007. The first Atlas V mission using the redesigned Aerojet SRMs launched the Rainbow direct-to-home digital TV satellite in June 2003. Subsequent flights launched the AMC-16 satellite providing DISH Network service (December 2004) and the Inmarsat 4-F1 satellite delivering broadband communications to 86 percent of the world (March 2005).

NASA will use Atlas V to launch the Pluto Horizons Spacecraft in 2006. The agency is also considering using Atlas V to launch payloads for the International Space Station, future Exploration Initiative missions, and versions of the Crew Exploration Vehicle.

The Invention of the Year Award warrants high respect by the ICB, according to NASA Chief Engineer Rex Geveden, who chairs ICB. "Our technical evaluation placed a present value on the (Glenn) invention at approximately \$25 billion dollars to America. Its use on the shuttle and Atlas V programs represents mission-critical successes."



#### Disabled Americans, from page 2

duty assignments, instead, they are recovering at various Military Treatment Facilities because of injuries they sustained in the Global War on Terror. CAP is committed to providing assistive technology and support to returning wounded service members. Accommodations are available for wounded service members with vision or hearing loss, upper extremity amputees as well as persons with communication and other disabilities to access the computer and telecommunication environment. CAP is available to provide accommodations to service members during recovery and rehabilitation, through transition and back to employment. As a nation, we must be committed to finding improved solutions that support their return to the theater as a disabled soldier, sailor, airmen, or marine. We must also discover new solutions to increase their independence in the stateside workforce. And, as our discoveries enable our wounded warriors to remain active, so to shall we improve the lives of millions of current and future Americans with disabilities.

On the 15th anniversary of the signing of the ADA, let's redouble our efforts to find the next wave of technology that will provide us all with new opportunities to be creative, innovated and support each other as we honor our wounded service members with new opportunities, increase employment opportunities for millions of Americans, and as we prepare for all of us to join the ever-growing population of people with disabilities.

## **JOB ANNOUNCEMENT!**

FLC Washington, DC Representative

The FLC is seeking a Washington, DC Representative. Responsibilities include providing coordination with federal agencies and Washington-based representatives of aligned communities (e.g., trade associations, nonfederal government associations, industry, etc.); promoting technology transfer to the private sector; and establishing dialogue and coordinating action on technology transfer issues with congressional committees.

Minimum qualifications are a bachelor's degree with a major in science, engineering, or business; a minimum of five years' experience in R&D, R&D program management, or technology transfer; and a working knowledge of the FLC's programs and organization. Skill in verbal and written communication; an ability to establish person-to-person relationships at all levels in the public and private sectors; and ability to work effectively as a member of a team are essential. A graduate degree and familiarity with the R&D-to-commercialization cycle are desirable but not required.

The position is a two-year assignment, but may be extended up to two additional years. Salary range is equivalent to SES, GS-13/14 grade level (approximately \$100,000 per year). Candidates for the position should submit a letter and resume by mail, fax, or e-mail to J. Susan Sprake, FLC Selection Committee, Federal Laboratory Consortium, 950 North Kings Highway, Suite 208, Cherry Hill, NJ 08034. E-mail (MS Word documents) applications to <flcmso@utrs.com> OR fax to (856) 667-8009. Applications must be received no later than July 25, 2005.

#### *DC on* $T^2$ *, from page* 1

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the June 14 Jacques Gansler chairs the SBIR study Established in 1982, federal agencies

justed."

Congressional staff seemed unaware of the discussions but sympathetic to the aims. "It's an excellent program and these adjustments are probably overdue," one aide told Federal Technology Watch (FTW).

Variations already exist in the size of Phase I and II awards made by different agencies. "We plan on having additional discussions on the issue," Brown said, "and will probably make a formal determination in the coming months."

The House Subcommittee on Environment. Technology. and Standards, chaired by Rep. Vernon Ehlers, R-Mich., is scheduled to hold a hearing this week on small business innovation and research and to examine the role of venture capital.

Witnesses at the June 28 hearing will be Acorda Technologies CEO Ron Cohen, Innovation Development In-

Gene Systems CEO Jonathan

Cohen. Earlier this month, the National Academies' Policy

and Global Affairs Division held a well-attended meeting on SBIR: the Phase III Challenge.

The transition from Phase II to Phase III is

#### an important

element in SBIR because Phase III is not federally funded and should represent the commercialization of R&D achieved during Phases I and II.

Speakers from several branches of the U.S. military provided insight at the mechanism.

A congressionally requested study of SBIR is being prepared by the National Academies.

Former Under Secretary of Defense for Acquisition and Technology

with annual R&D budgets that exceed Phase III as a \$100 million must set aside 2.5 perprocurement cent of their R&D grants and contractroute for ining funding for SBIR programs. novative These agencies must issue annual high-tech de-

lists of technical topics on which they seek R&D proposals from small businesses. Phase I is a feasibility study and can take six months, while Phase II often involves development of a prototype or demonstrator and can take up to two years.

The most recent Office of Management and Budget (OMB) statistics indicate \$2 billion was spent on federal SBIR programs last year, with the Department of Defense accounting for more than 50 percent of the total. OMB plans a cross-agency review of SBIR in FY06.

STTR is a sister program for small businesses and nonprofit research partners.

## NEWSLINK

## **55** Attend Seed Investing for Entrepreneurs

The FLC and the National Association of Seed and Venture Funds (NASVF) partnered on May 1, 2005, to offer "Swing for the Fences: Seed Investing for Entrepreneurs," an intensive one-day seminar covering the investment process stepby-step. The seminar was held in conjunction with the FLC 2005 annual meeting in Orlando, Fla.

Designed by the nation's leading seed investors, specialists, and seasoned professionals, the seminar provided a candid view of how true seed investors think, as well as how they choose their investments and work with the nation's best entrepreneurs. The 55 attendees included a diverse audience of FLC Agency and Laboratory Representatives, entrepreneurs, investors, academia, and industry.

Attendees mastered the finer points of the curriculum through an interactive workshop, roleplaying exercises, videotaped presentations, a practical "live" case study, and onsite coaching from a team of local experts. These experts included Barry Blass, CFO partner of Tatum Partners, with over 25 years' experience focused on entrepreneurial and middle-market companies in a broad range of businesses; Dan Rua, managing partner of Inflexion Partners, an experienced early-stage venture capital investor with a technology foundation and product design, development and management experience; Richard Fox, president, MetaTech Ventures, LLC, a serial entrepreneur who implements the methods and procedures he has developed over the years to assure the successful launch of new companies through MetaTech; Terry Brennan, attorney, Bogin, Munns & Munns, with more than 15 years' experience advising technology, multimedia, and entertainment companies and individuals in corporate, intellectual property, technology

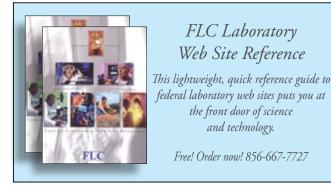
and entertainment transactions; and Kristie Chadwick, COO, University of Central Florida Venture Lab, with 19 years' experience in the high technology industry and who has worked for a variety of technology organizations, both large and small.

Each "Swing for the Fences" seminar focuses on the complete early-stage investment process for attracting angel capital; due diligence; valuing the enterprise; pricing the deal; the term sheet; negotiating the deal; and closing, mentoring and cashing out.

This focus provides attendees with the basics of pricing and structuring seed investments; networking opportunities to meet and collaborate with peers in the region and selected local professionals, advisors and seasoned investors; the experience of using team-based approaches to make and manage investments; and engaging and working with seed investors to accomplish their goals.

The NASVF is a national nonprofit organization committed to building local economies through investment and the facilitation of investment in entrepreneurial ventures. Visit the NASVF web site at <www.nasvf.org>.

If you or your organization is interested in hosting or attending an NASVF seminar, please contact Julie Evans, (609) 735-0797, or via e-mail at jevans@nasvf. org for more information.



#### $T^2$ Interns, from page 1

sector through licensing agreements and startup companies. The Technology Transfer Division has worked diligently to create a value proposition to encourage its MBA alumni to return to New Mexico.

Over the last couple of years, the Technology Transfer Division has begun to create the kinds of jobs talented MBAs want. In addition, New Mexico's relatively sparse population of seasoned management and savvy technology entrepreneurs offers rare opportunities for bigger challenges and greater responsibility at an earlier point in career development.

Since 1997, 15 of 55 MBA internship alumni have returned to New Mexico—an approximate 27% return rate. Six former interns have taken full-time positions at LANL, two at Sandia National Laboratories (Albuquerque), one at the University of New Mexico, and seven are entrepreneurs working for New Mexico startups, business development centers, or small high-tech companies.



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