A repression of gene activity in the brain appears to be an early event affecting people with Alzheimer’s disease, researchers funded by NIH have found. In mouse models of Alzheimer’s disease, this epigenetic blockade and its effects on memory were treatable.

“These findings provide a glimpse of the brain shutting down the ability to form new memories gene by gene in Alzheimer’s disease, and offer hope that we may be able to counteract this process,” said Dr. Roderick Corriveau.

Dr. Li-Huei Tsai and her team found that a protein called histone deacetylase 2 (HDAC2) accumulates in the brain early in the course of Alzheimer’s disease in mouse models and in people with the disease. HDAC2 is known to tighten up spools of DNA, effectively locking down the genes within and reducing their activity, or expression. In the mice, the increase in HDAC2 appears to produce a blockade of genes involved in learning and memory. Preventing the build-up of HDAC2 protected the mice from memory loss.

Dr. Tsai and her team examined two mouse models of Alzheimer’s around the time that the mice begin to show signs of brain cell degeneration. They found that the mice had higher levels of HDAC2, but not other related HDAC proteins, specifically in the parts of the brain involved in learning and memory. This increase in HDAC2 was associated with a decrease in the expression of neuronal genes that HDAC2 regulates.

Use of a gene therapy approach to reduce the levels of HDAC2 prevented the blockade of gene expression. The treatment also prevented learning and memory impairments in the mice. It did not prevent neuronal death, but it did enhance neuroplasticity.

Dr. Tsai and her team also examined HDAC2 levels in autopsied brain tissue from 19 people with Alzheimer’s at different stages of the disease, and from seven unaffected individuals. Even in its earliest stages, the disease was associated with higher HDAC2 levels in the learning & memory regions of the brain.

“We think that the blockade of gene expression plays a very important role in the cognitive decline associated with Alzheimer's disease,” said Dr. Tsai. “The good news is that the blockade is potentially reversible.”

Dr. Tsai theorizes that HDAC2 is brought into play by beta-amyloid. Indeed, she and her team found that exposing mouse neurons to beta-amyloid caused them to produce more HDAC2.

For more information on this research, click here.
**NINDS FUNDING ANNOUNCEMENTS**

RFA-NS-13-001, Limited Competition for Continuation of the NIH Exploratory Trials in Parkinson's Disease (NET-PD): Coordinating and Statistical Centers (U01) – April 17, 2012

RFA-NS-12-007, Stroke Prevention/Intervention Research Program (SPIRP) (U54) – April 3, 2012

RFA-MH-13-030, Eradication of HIV-1 from CNS Reservoirs: Implications for Therapeutics (R01) – September 12, 2012

RFA-NS-12-010, Exploratory Laboratory and Analysis Projects in Parkinson’s Disease Biomarkers (U18) – May 23, 2012

RFA-NS-12-011, Studies in Parkinson’s Disease Biomarkers Discovery (U01) – May 23, 2012

PAR-12-097, Ancillary Studies in PREDICT-HD (U01) – April 25, 2012

PAR-12-032, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Etiology, Diagnosis, Pathophysiology, and Treatment (R01) – June 22, 2012

RFA-OD-12-003, Small Business Alzheimer’s Disease Research (SBIR[R43/R44]) – April 30, 2012

PAR-11-319, Scalable Assays for Unbiased In Vitro Analysis of Neurobiological Function (R21/R33) – June 5, 2012

PA-11-014, HIV Infection of the Central Nervous System (R01) – May 7, 2012

PAS-10-183, Validation of Novel Therapeutic Targets for Huntington’s Disease (R01) – June 5, 2012

PAR-09-263, Ancillary Studies in Clinical Trials of CNS/PNS Disorders NINDS Accelerated Awards Program (R01) – April 16, 2012

PA-11-085, Genetic Susceptibility & Variability of Human Structural Birth Defects (R01) – June 5, 2012

PAR-11-045, Outcome Measures for Use in Treatment Trials for Individuals with Intellectual and Developmental Disabilities (R01) – June 5, 2012

PA-10-258, Neurobiology of Migraine (R01) – June 5, 2012

For more information or to find more funding opportunities, please click [here](#).

**PATIENT ORGANIZATION EVENTS**

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Click [here](#) for more details.

**Upcoming FDA Peripheral and Central Nervous System Drugs Advisory Committee Meeting**

May 24, 2012
Intrathecal (IT) Administration of Rituximab to Treat Multiple Sclerosis (MS)

The pathology of MS is characterized by an abnormal immune response directed against the central nervous system. In particular, T-lymphocytes are activated against the myelin sheath of the neurons of the central nervous system causing demyelination. SP-MS is the chronic phase of MS. The majority of people who have relapsing-remitting MS eventually develop SP-MS. There are currently no effective treatments for SP-MS patients who do not have evidence for focal brain inflammation measured by contrast enhancing lesions (CEL) on brain MRI. NIH investigators have proposed that intrathecal administration of Rituximab, a monoclonal antibody (Ab) that depletes B cells and effectively decreases CEL in relapsing-remitting MS (RR-MS) but does not affect progression of disability in progressive MS, may deplete B cells from the intrathecal compartment leading to inhibition of T cell activation within intrathecal compartment, and thereby provide a novel therapeutic approach to treat SP-MS.

Use of Marrow-Derived Glial Progenitor Cells as Gene Delivery Vehicles into the Central Nervous System

The present disclosure relates to a method of treating Parkinson's disease by transfecting bone marrow cells with glial cell line-derived neurotrophic factor (GDNF) using a retroviral vector, and then administering the transfected cells intravenously to a mammal. The results reported confirm that cells derived from bone marrow can migrate into the brains of adult mice. The detection of marrow-derived cells in brains of adult mice within days of transplantation provides a method in which genetically altered hematopoietic cells could be used to treat acute diseases of the brain.

Novel Small Molecules to Treat Alzheimer's Disease: Amyloid Beta Channel Blockers with Anti-inflammatory Properties

Alzheimer's Disease is thought to be due to the neurotoxic effect of the Amyloid beta (Abeta) peptide. The inventors discovered that Abeta has intrinsic calcium channel activity, and that entry of calcium into neurons through this channel leads to neuronal cell death, playing a role in Alzheimer's pathology. Consistently, Abeta channel blocking drugs act as a “cork” to save neurons from Abeta-dependent cell death. Two potent and efficacious candidate drugs, MRS2481 and its enantiomer species MRS2485, have been discovered. Both block the Abeta channel with similar potency (ca. 500 nM) and efficacy (100%). However, inhibition by MRS2481 is easily reversible, while inhibition by MRS2485 is virtually irreversible.

To view full descriptions of these technologies and to find more available for licensing, please click [here](#).
FDA REFORM LEGISLATION

BIO supports two pieces of legislation that would reform and modernize the FDA to speed life-saving treatments and breakthrough medicines to patients living with debilitating diseases. BIO CEO Jim Greenwood issued statements praising both the TREAT Act and the FAST Act. BIO has also testified on the Hill in support of the proposed reforms.

S. 2113 – Transforming the Regulatory Environment to Accelerate Access to Treatments (TREAT) Act
This bill would reform the FDA by advancing regulatory science and innovation, elevating FDA and empowering operational excellence, and enabling modernized patient-centric clinical development. Specific proposed reforms include updating FDA’s mission statement, enhancing the agency’s access to external scientific experts, and strengthening the Accelerated Approval pathway.

Sponsor: Sen. Kay Hagan (NC)
Status: Referred to the Senate HELP Committee

H.R. 4132 – Faster Access to Specialized Treatments (FAST) Act
This bill would reform the Accelerated Approval pathway at the FDA to expedite the approval of drugs for serious life-threatening diseases or conditions while maintaining important safety standards.

Sponsors: Rep. Cliff Stearns (FL-6) and Rep. Edolphus Towns (NY-10)
Status: Referred to the House Committee on Energy and Commerce

NEUROLOGY/CNS-FOCUSED LEGISLATION

H.R. 1897 – Alzheimer’s Breakthrough Act
This bill would require the NIH Director to establish a strategic Alzheimer’s research plan to expedite therapeutic outcomes for individuals with or at risk for Alzheimer’s.

Sponsor: Rep. Christopher Smith (NJ-4)
Status: Referred to the House Committee on Energy and Commerce

H.R. 1970 – National Childhood Brain Tumor Prevention Network Act
This bill would establish a National Childhood Brain Tumor Prevention Network to provide grants for research on the causes of and risk factors associated with childhood brain tumors.

Sponsor: Rep. Barbara Lee (CA-9)
Status: Referred to the House Committee on Energy and Commerce

H.R. 2600 – National Pediatric Acquired Brain Injury Plan Act
This bill would require the Secretary of HHS to make a payment for each fiscal year from FY2012-FY2018 to the State Lead Center in each state for implementation of the National Acquired Brain Injury Plan, as developed by the International Advisory Board of the Sarah Jane Brain Foundation.

Sponsor: Rep. Lance Leonard (NJ-7)
Status: Referred to the House Committee on Energy and Commerce

H.R. 1988 – Qualifying Therapeutic Discovery Project Tax Credit Extension Act
This bill would extend the Therapeutic Discovery Project through the year 2017 and fund it at $1 billion per year. Qualifying investments in years 2011 through 2015 would qualify for the credit or grant.

Status: Referred to the House Committee on Energy and Commerce

H.R. 942 – American Research and Competitiveness Act
This bill would extend and make permanent the R&D tax credit. It would also increase the ASC rate to 20%.

Sponsor: Rep. Kevin Brady (TX-8)
Status: Referred to the House Committee on Ways and Means
HOUSE OF REPRESENTATIVES HEARINGS ON BIOTECHNOLOGY

House Energy and Commerce Committee, Subcommittee on Health

At this hearing, the Health Subcommittee heard from a variety of industries that are regulated by the FDA and depending on the User Fee Acts being reauthorized. For the biopharmaceutical industry, the committee focused on the FDA Accelerated Approval process. BIO Board Member John Maraganore testified on the importance of the Accelerated Approval pathway and in support of the FAST Act, which would enhance Accelerated Approval at FDA.

House Appropriations Committee, Subcommittee on Labor, HHS, Education, & Related Agencies

This hearing focused on the newly-established National Center for Advancing Translational Sciences (NCATS) at NIH. NIH Director Collins and NCATS Acting Director Insel testified on the process of getting NCATS up and running and the expectations they have for the Center. Industry representatives, including BIO Board Member Scott Koenig, testified on the importance of NCATS and the key role it will play in advancing translational research.

House Committee on Science, Space, and Technology, Subcommittee on Technology and Innovation
“Fostering the U.S. Competitive Edge” — March 27, 2012

The Technology and Innovation Subcommittee held this hearing to better understand how federal policies and regulations affect competition, innovation, and job growth. BIO Board Chairman Ron Cohen testified on several steps that Congress has already taken to spur innovation, including SBIR, TDP, and patent reform. He also spoke in favor of reforms to the Accelerated Approval pathway at FDA.

SENATE HEARINGS ON BIOTECHNOLOGY

Senate Committee on Banking, Housing, and Urban Affairs
“Spurring Job Growth Through Capital Formation While Protecting Investors, Part II” — March 6, 2012

The Senate Banking Committee held this hearing to discuss several proposals on how to ease capital formation for emerging companies. The bills under consideration included an on-ramp to the public market for emerging growth companies and reforms to SEC Regulation A, SEC Regulation D, and the SEC private shareholder limit. OncoMed Pharmaceuticals CFO Will Waddill testified on how these policies would affect growing biotech companies and stimulate innovation and job growth. The legislation that BIO supported at the hearing was later combined into one bill and passed as the JOBS Act.

Senate Committee on Health, Education, Labor, and Pensions
“Strengthening FDA and the Medical Products Industry for the Benefit of Patients” — March 29, 2012

The Senate HELP Committee held this hearing to discuss the upcoming reauthorization of PDUFA and how FDA and its regulated industries can speed treatments and therapies to patients. Sara Radcliffe, Executive Vice President of Health, testified on behalf of BIO; she was joined by other industry representatives as well as Janet Woodcock (CDER) and Jeffrey Shuren (CDRH) from the FDA.
On December 31, 2011, President Obama signed into law the National Defense Authorization Act, which reauthorized the SBIR program through 2017. Included in the reauthorization was an end to the eligibility ban on venture-backed companies. Now, venture-backed companies will be able to compete for 25% of SBIR funds at NIH, NSF, and the Department of Energy and 15% of funds at all other agencies. Additionally, research agencies with SBIR programs will increase the set aside from 2.5% to 3.2% by 2017. BIO is in the process of reaching out to SBA, which will propose rules on affiliation in the upcoming months.

BIO has been advocating Congress for an extension and expansion of the Therapeutic Discovery Project (TDP) tax credit program. The TDP was enacted in 2010 and awarded $1 billion in tax credits and grants to breakthrough biotechnology companies with fewer than 250 employees. To support extension and expansion of this important program, BIO produced three video vignettes which give policymakers a view of what TDP has done for biotech companies already. The videos highlight companies that received awards through the program and emphasize the positive effect that the funding had on job creation, the development of treatments, and U.S. competitiveness. To view these videos, please click here, here, and here.