

World Science News In Review

[Brain and Cognitive Sciences]

Key Stress Protein Linked to Parkinson's, Alzheimer's

Researchers at the Burnham Institute for Medical Research have discovered a mechanistic link between cellular stress caused by free radicals and an accumulation of misfolded proteins, which leads to nerve cell injury and death in neurodegenerative disorders such as Alzheimer's and Parkinson's Disease.

Protein Disulphide Isomerase (PDI) is a chaperone protein necessary for correct protein folding in times of cellular stress. Findings reveal that in patients with Alzheimer's and Parkinson's Disease, free radical overproduction, specifically nitric oxide (NO), causes PDI inhibition, which results in the protein misfolding. This new discovery provides the first molecular link between NO free radicals and protein misfolding.

Under normal circumstances, PDI levels increase in response to the accumulation of misfolded proteins, which result from cellular stress. PDI acts as a chaperone for aggregated proteins, rearranging their chemical bonds and refolding the proteins so that they can function normally. New research shows that molecules related to the free radical NO, which is present in elevated levels in neurodegenerative diseases, attacks PDI via a chemical S-nitrosylation reaction, altering PDI's structure and blocking its normal neuroprotective function, which leads to further protein misfolding, nerve cell injury and death. Results show that this altered form of PDI is present in elevated amounts in patients with Alzheimer's and Parkinson's Disease indicating that this altered PDI can be a potential marker for the disease as well as a potential therapeutic target.

—D. Zhang

Source: "Key Stress Protein Linked to Toxicities Responsible for Parkinson's, Alzheimer's." <http://www.newswise.com/articles/view/520701/>

Blocking Inflammatory Signals Protect Mice from MS

A group of researchers led by Brian Popko from the University of Chicago has shown that inflammatory attacks on myelin, the protective covering over nerves, can be prevented by blocking the response of myelin-producing cells to interferon-gamma. This discovery may lead to treatments of debilitating diseases such as multiple sclerosis.

Interferon-gamma, a chemical signal that activates the immune system, is not normally present in the nervous system but appears after inflammation. In Popko's experiments, transgenic mice were divided in two groups—one with a gene that produces interferon gamma in the nervous system, and one with a gene, SOCS1 (suppressor of cytokine signaling 1), which blocks the response of the myelin-producing cells to interferon-gamma. Most of the mice (18/20) with higher levels of interferon-gamma in the nervous system developed multiple symptoms of myelin loss, such as walking difficulty. Few mice (4/20) that had high interferon-gamma levels and expressed SOCS1 developed such symptoms. Physical examinations of the mice confirmed the decreased loss of myelin in those with the SOCS1 gene. These results not only validate the hypothesis that interferon-gamma is involved in demyelinating diseases, but also suggest a method to block it. A possible therapy for people with multiple sclerosis involves both SOCS1 and stem cells in repairing nerve damage.

—H. Zhou

Source: "Selectively Blocking Inflammatory Signals May Protect Mice From MS" <http://www.medicalnewstoday.com/medicalnews.php?newsid=43159>

Neural Stem Cell Gene's Role in Eye Development

Scientists at the University of North Carolina at Chapel Hill have demonstrated that the normal development of the eye requires that a specific amount of a stem cell gene be expressed at the right time and the right place. Neural stem cells are cells that can differentiate into different cell types in the nervous system. Retinal neural stem cells differentiate to form the neurons of the adult eye and the optic nerve.

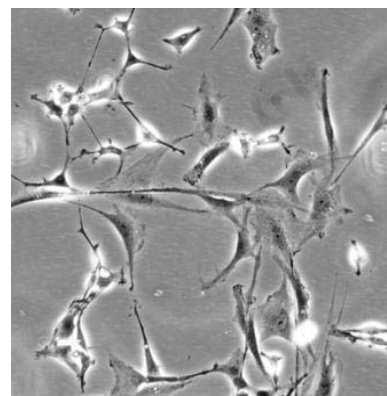
Dr. Larysa H. Pevny, assistant professor of genetics in the UNC School of Medicine, lead the team that has identified specific expression levels of the neural stem cell gene. SOX2 is a key gene in regulating the differentiation of neural stem/progenitor cells in the eye. Researchers have already discovered that, in mice, disruption of the SOX2 gene in neural retinal stem cells leads to a kind of abnormal development of the eye called microphthalmia, or small eye. Approximately 10 percent of all human cases of microphthalmia result from mutations in the SOX2 gene. Furthermore, the degree to which SOX2 gene is disrupted dictates the severity of microphthalmia.

Pevny believes the study indicates that normal development of the eye is contingent on the right amount of SOX2 being expressed at the right time and the right place. According to Pevny, "Too little SOX2 expression results in the neural stem cell pool to aberrantly differentiate into neurons during development. This disrupts the normal maintenance of the stem cell pool in the eye can disrupts the whole developmental process."

The complete loss of SOX2 expression in neural progenitor cells results in the loss of the cell's ability to either differentiate into neurons or to stay in the pluripotent state, and ultimately leads to a block in eye formation in mice. Loss of SOX2 also affects Notch1, a gene controlled by SOX2 that is expressed in several other stem cell/progenitor populations. Loss of Notch1 is partially responsible for abnormal development of the eye. Furthermore, SOX2 may play an important role in several other stem cell/progenitor populations as well.

—D. Zhang

Source: "Neural Stem Cell Gene Plays Crucial Role in Eye Development" <http://www.newswise.com/articles/view/520554/>



<http://www.iscr.ed.ac.uk/news/images/human%20NS%20cells%20live.jpg>

How Signals Travel Through Rats' Whiskers

Rats use their whiskers to sense objects in their environment. Chunxiu Yu and colleagues have suggested pathways for signaling to and from the brain, particularly through three regions in the thalamus, which modulates sensory signals between the cortex and the body. One of the signaling pathways conveys sensory information from whisker movement, one conveys sensory information from touch, and one conveys sensory information from a combination of both movement and touch. The authors believe that the three pathways work in parallel in order to apply different behaviors.

—H. Zhou

Source: "Scientists Reveal How Signals Travel Through Rats' Whiskers"

<http://www.physorg.com/news67082799.html>

Amphetamine Study Sheds Light on Addiction

Johns Hopkins University researchers have uncovered one possible explanation for why men are more likely than women to suffer from addictive disorders. In their experiment, described in the May 15 issue of "Biological Psychiatry," the researchers administered an amphetamine to 28 men and 15 women, and then used PET scans to measure the function of dopaminergic synapses. The researchers found that men generally experienced much larger dopamine release than women and also reported more of a "high," "rush." Contrastingly, women, as a group, reported more feelings of anxiety, dizziness, and distrust. This difference in neurological and psychological responses may explain the greater frequency of alcoholism, drug addiction, and schizophrenia among men.

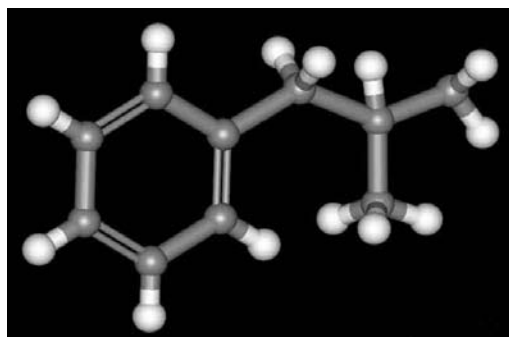
—M. Anahtar

Source: "Males on Speed"

<http://www.sciencemag.org/cgi/content/summary/312/5778/1287b>



Rats use their whiskers to engage in active sensing – a combination of movement and touch – when trying to figure out the location and identity of a certain object. But how the brain decodes the signals it receives from the whiskers is unclear.



Amphetamine

<http://www.urgence-pratique.com/2articles/medic/amphetamine.jpg>

Research Uncovers Signaling Paths in Brain-Immune System Links

A research group at the Children's Hospital of Philadelphia and the University of Pennsylvania, led by Steven D. Douglas, M.D., has discovered evidence of connections between the immune system and the central nervous system through research on signaling pathways in immune cells. The group analyzed neurokinin-1 receptors (NK-1R), docking sites for substance P, a common neurotransmitter with functions in both the immune and nervous systems. NK-1R is found on the surface of monocytes, immune cells that later develop into macrophages.

The team used two forms of NK-1R, differing in the size of the receptor, and added substance P to both cell cultures containing these receptors. The result was the same (increased calcium ions), but the signaling pathways were distinct. The shorter NK-1R used a different signaling molecule, a chemokine RANTES, to increase calcium levels. RANTES binds to another receptor CCR5, which allows some common strains of HIV to infect immune cells. With the addition of a drug aprepitant (commonly known as Emend) to both cell cultures, signaling in both forms of NK-1R was disrupted. This suggests that aprepitant helps prevent the virus from entering the immune cells and may be used to block HIV infection. Dr. Douglas hypothesizes that by blocking NK-1R, the CCR5 receptor is turned off for HIV, preventing the virus from entering immune cells. Understanding substance P's connection to distinct signaling pathways is important because it is the link between the nervous and the immune systems.

—H. Zhou

Source: "Research Uncovers Signaling Paths in Brain-Immune System Links"

<http://www.newswise.com/articles/view/520522/>

Pinpointing Autism's Genetic Roots

Researchers at the University of Texas Southwestern Medical Center have created mice that show deficits in social interaction, reminiscent of humans with autistic spectrum disorders. These mice also have physical abnormalities in the brain that mimic some cases of autism, showing the animals can be useful models in studying autism.



Steven Douglas, M.D.

<http://www.med.upenn.edu/camb/faculty/gt/douglas.html>

Research has focused on the gene Pten, which is known to suppress cancers in humans. Although some people with autism have mutations in Pten, it is unclear whether this abnormality is the cause of the disease. To test this hypothesis, Dr. Luis F. Parada, director of the Center for Developmental Biology and the Kent Waldrep Center for Basic Research on Nerve Growth and Regeneration, and his team of researchers deleted the gene in the front of the mouse brain and in areas of the hippocampus.

These mutant mice (now lacking the Pten gene) were found to be generally uninterested in unfamiliar mice while normal mice approached

physical manifestation most likely indicates the sensory overload that people with autism often experience.

Given these conclusions, the next step in this research is to treat these mice with drugs to investigate the possibility of reversing the condition.

—D. Zhang

Source: "New Findings Help Pinpoint Autism's Genetic Roots"
<http://www.newswise.com/articles/view/520087/>

Sight Restored to Chickens with Blinding Disease

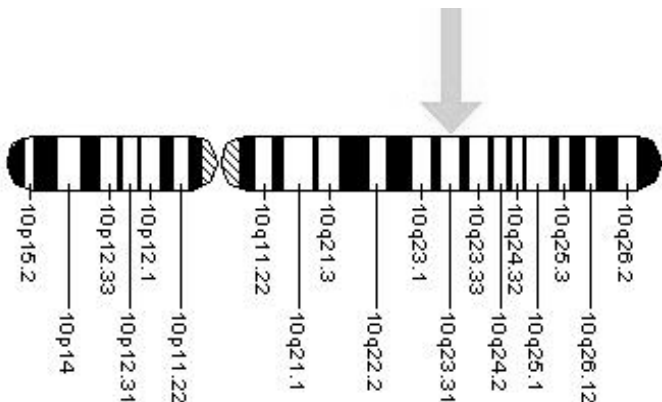
Scientists from the University of Florida have succeeded in restoring sight to chickens born with a genetic defect causing blindness. The defect, found in a type of Rhode Island Red chickens, causes malfunctions in the gene GC1, which prevent the production of an enzyme essential for sight. These scientists used a method that restored function to the photoreceptors in the retina by delivering the gene in a viral vector, which was injected through the eggshell into the developing nervous system. This method produced chickens that responded to visual stimuli, such as pecking at dots drawn on a piece of paper. With additional tests, 5 out of 7 treated chickens displayed what seemed like normal visual behavior. Furthermore, this finding may also provide insight into the treatment of Leber congenital amaurosis type 1 (LCA1), a similar genetic disease found in humans that is currently incurable. A possible treatment involves injecting the vector with the GC1 gene into the eyeballs of afflicted infants (diagnoses of LCA1 are not made until infants are several months old). However, more work must be done before this therapy can be used on humans.

—H. Zhou

Source: "UF scientists restore sight to chickens with blinding disease"
http://www.biologynews.net/archives/2006/05/23/uf_scientists_restore_sight_to_chickens_with_blinding_disease.html



<http://biology.clc.uc.edu/graphics/taxonomy/animals/aves/domestic%20chicken/JSC%200105%20Chicken%2001.JPG>




Location of the pten gene

<http://ghr.nlm.nih.gov/dynamicImages/chromomap/pten.jpeg>

the strangers. When they were exposed to both an inanimate object and another mouse, they showed equal interest in each—findings paralleling the way autistic children prefer toys to people—while normal mice preferred the other mouse. Mutant mice also ignored the raw material for nesting that they were given, while normal mice worked together to build nests. They were also hypersensitive to stressful stimuli, just as autistic individuals are overly sensitive to sensory stimuli.

The brains of mutant mice were also significantly altered in that their nerve cells were thicker than normal and had a higher-than-normal number of connections to other nerve cells in areas where the gene was deleted. This

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