

Fall 2010
Semiannual Newsletter
Neuroscience Training Program

BRAIN WAVES



GENE REGULATING HUMAN BRAIN DEVELOPMENT IDENTIFIED

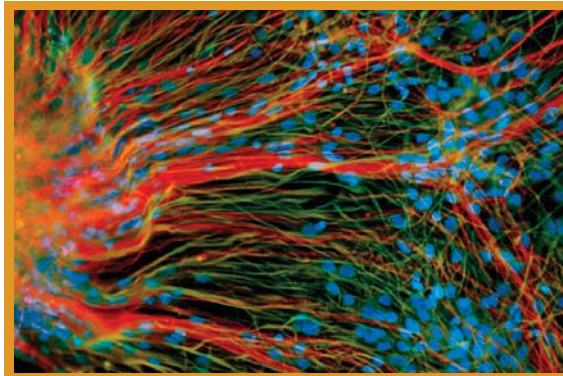
By: Terry Devitt

University Communications

July 1st, 2010

MADISON - With more than 100 billion neurons and billions of other specialized cells, the human brain is a marvel of nature. It is the organ that makes people unique.

Now, writing in the journal *Cell Stem Cell* (July 1, 2010), a team of scientists from the University of Wisconsin-Madison has identified a single gene that seems to be a master regulator of human brain development, guiding undifferentiated stem cells down tightly defined pathways to becoming all of the many types of cells that make up the brain.



The new finding is important because it reveals the main genetic factor responsible for instructing cells at the earliest stages of embryonic development to become the cells of the brain and spinal cord. Identifying the gene - known as Pax6 - is a first critical step toward routinely forging customized brain cells in the lab.

What's more, the work contrasts with findings from animal models such as the mouse and zebrafish, pillars of developmental biology, and thus helps cement the importance of the models being developed from human embryonic stem cells.

The new work, conducted in the Waisman Center laboratory of UW-Madison neuroscientist Su-Chun Zhang, reveals the pervasive influence of Pax6 on the neuroectoderm, a structure that arises early in embryonic development and that churns out the two primary forms of brain cells - neurons and glial cells - and the hundreds of cell subtypes that make up the human brain.

"This is a well-known gene," says Zhang, a professor of anatomy in the UW School of Medicine and Public Health. "It's been known for a long time from work in mice and other animals, but what Pax6 does in human development isn't very well known."

In animals, the gene is known to play a role in the development of the eye and is seen in some neural cells. In the human cells used in the new Wisconsin study, Pax6 was observed in virtually all of the cells of the neuroectoderm. "The fact that Pax6 is uniformly expressed in all human neuroectoderm cells was a surprise," Zhang explains. "This is a phenomenon that is a departure from what we see in animals. It seems that in the earliest stages of development, human cells are regulated by different processes."

The finding may help explain why the human brain is larger and, in many respects, more advanced than what is observed in other species. In the laboratory dish, human brain stem cells are chock full of Pax6 and produce a large volume of cortical cells, notes Xiaoging Zhang (no relation to Su-Chun Zhang), a UW-Madison neuroscientist and the lead author of the *Cell Stem Cell* paper.

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Welcome New Faculty!

Barbara Bendlin, Medicine
Ph.D. University of Arizona
Aging; Alzheimer's disease

Rasmus Birn, Psychiatry
Ph.D. Medical College of Wisconsin
Functions of Sleep Using Molecular and
Genetic Approaches

Michelle Ciucci, Communicative Disorders
Ph.D. University of Arizona, Tucson
Functions of Sleep Using Molecular and
Genetic Approaches

Jon Levine, Director of Primate Center
and Physiology
Ph.D. University of Illinois
Steroid Hormone Actions in the Brain

Robert Thorne, Pharmacy
Ph.D. University of Minnesota
CNS Drug Delivery and Distribution

Welcome New Students!

Ewa Bomba

B.S. University of Illinois – Chicago
Major Professor: Rotating

Yun Ding

B.S. University of Science & Technology of China
Major Professor: Luigi Puglielli

Sharon DuBois

B.S. University of Waterloo
Major Professor: Jon Levine

C.P. Frost

B.A. Dartmouth College
Major Professor: Rotating

Erik Hoel

B.S. Hampshire College
Major Professor: Rotating

Kyunghee Kim

B.S. Sookmyung Women's University
M.S. Korean Advanced Institute of Science and
Technology

M.S. Kansas State University

Major Professor: Robert Fettiplace

Josh LaRocque

B.S. University of North Carolina at Chapel Hill
Major Professor: Brad Postle

Tristan Lee

B.S. St. Louis University
Major Professor: Rotating

Martina Ly

B.A. Scripps College
Major Professor: Rotating

Angela Navarrete Opazo

B.S. Universidad de Concepción
M.S. Universidad de Chile

Major Professor: Gordon Mitchell

Maia Pujara

B.S. Furman University
Major Professor: Rotating

Ryan Selleck

B.S. University of Michigan at Ann Arbor
Major Professor: Rotating

Awards and Achievements

Dr. Rao Adibhatla - Awarded a NIH RO1 Grant

Michelle Edelman - NTP Travel Award

Kimberly Farbota - Institute on Aging T-32 Pre-Doctoral Training Grant

Eugenia Friedman - NIH NRSA Predoctoral Fellowship

Patrick Hernandez - N&PP Internship with Government Accountability Office

Jesus Mena - New Investigator Travel Award by the Society for the Study of
Ingestive Behavior & NIH NRSA Fellowship

Elliott Merriam - NIH NRSA Fellowship

Lindsay Pascal - N&PP Internship with AAAS in Scientific Freedom, Responsibility,
and Law Program

Miguel Santiago-Medina - Invited by Okinawa Institute of Science and Technology
to participate in Developmental Neurobiology Course

Chelsey Smith - NTP Travel Award & NSF Pre-Doctoral Fellowship

Michael Zorniak - invited to speak at Lake Forest College's 10th Annual Neuro-
Frontiers Workshop

GENE REGULATING HUMAN BRAIN DEVELOPMENT IDENTIFIED (cont'd.)

"In human brain development, this plays a really important role," says Xiaoqing Zhang. "In humans, the cortex is a major part of the brain. In the mouse, the cortex is a much smaller part of the brain."

Adds Su-Chun Zhang, "In a way, it makes sense that the human brain is regulated in a different way. The brain distinguishes the human as a unique species."

In practical terms, the new finding will help scientists refine and improve techniques for making specific types of neural cells. Such cells will be critical for future research, developing new models for disease, and may one day be used in clinical settings to repair the damaged cells that cause such conditions as Parkinson's disease and amyotrophic lateral sclerosis or Lou Gehrig's disease.

"This gives us a precise and efficient way to guide stem cells to specific types of neural cells," says Xiaoqing Zhang. "We can activate this factor and convert stem cells to a particular fate."

The discovery of the new role of Pax6, says Su-Chun Zhang, is the first time researchers have discovered a single genetic factor in human cells that is responsible for shepherding blank slate stem cells to become a particular tissue stem cell type. "Until now, for any organ or tissues, we didn't know any determinant factors. This is the first," he says.

There are certainly other genes at play in the cells of the developing brain, says Su-Chun Zhang: "You may need additional genes, but they're in a supporting role. Pax6 is the key."

The National Institutes of Neurological Diseases and Stroke, part of the National Institutes of Health, supported the new study.

Brain Responds Same to Acute and Chronic Sleep Loss

University of Wisconsin - Madison
August 9th, 2010

Burning the candle at both ends for a week may take an even bigger toll than you thought.

Researchers at the University of Wisconsin-Madison have found that five nights of restricted sleep - four hours a night - affect the brain in a way similar to that seen after acute total sleep deprivation.

The new study in rats, appearing in the current online edition of the Proceedings of the National Academy of Sciences, adds to the growing evidence scientists are accumulating about the negative effects of restricted sleep for both the brain and the body.

"There's a huge amount of interest in sleep restriction in the field today," says Dr. Chiara Cirelli, associate professor of psychiatry at the School of Medicine and Public Health, who led the research.

Many people are sleep restricted, either because they have to or because they choose to be, she says.

"Instead of going to bed when they are tired, like they should, people watch TV and want to have an active social life," she says. "People count on catching up on their sleep on the weekends, but it may not be enough."

This "casual" lack of sleep can be harmful.

"Even relatively mild sleep restriction for several nights can affect an individual's ability to perform cognitive tasks," Cirelli says. "For instance, recent studies in humans have shown that five days with only four hours of sleep/night result in cumulative deficits in vigilance and cognition, and these deficits do not fully recover after one night of sleep, even if 10 hours in bed are allowed. Sleep restriction can also increase resistance to insulin, leading to a risk of diabetes."

Cirelli and her team kept rats awake 20 hours a day over five days while continuously recording the animals' brain waves with a sophisticated EEG as they were asleep and awake. The EEGs measured slow wave activity (SWA), the best marker of an individual's need to sleep as well as the intensity of sleep that follows a period of wakefulness.

"Slow-wave activity reflects the fact that sleep is regulated by homeostasis: in general, the longer we stay awake, the higher is SWA in the subsequent sleep. We knew that this was true after acute total sleep deprivation (for instance when we stay up all night); now we found that this is also true after chronic sleep restriction." Cirelli notes.

According to the rat cumulative SWA measures, the sleep restriction produced intense recovery sleep following each wake cycle, with both longer and deeper sleep. The more effective the researchers were in keeping the animals awake during those 20 hours, the larger the sleep rebound they saw during the following four hours.

"It was an indirect but powerful indication of how sleepy the animals actually were," Cirelli says.

Even when the animals seemed awake and were moving around, heightened SWA was evident in their "wake" EEG.

"Monitoring SWA levels during waking time is very important in understanding the whole picture," she says. "High SWA levels during periods of both sleeping and waking signal that you need to go to sleep."

The researchers also found that SWA levels were different in different areas of the brain, and they speculate that this may depend on what parts of the brain had been used during the waking period.

Knowing that sleep restriction evokes the same brain response as sleep deprivation will help scientists better understand the harmful effects of sleep disturbances, says Cirelli.

"Scientists have learned much from 40 years of studies on total sleep deprivation, she says. "Now we know we can apply the lessons we learned from acute sleep deprivation to chronic sleep restriction, which is very relevant to people's lives today."

Co-authors include Susan Leemburg, Vladyslav V. Vyazovkiy, Umberto Olcese, Claudio L Bassetti and Giulio Tononi.

<http://www.med.wisc.edu/news-events/news/brain-responds-same-to-acute-and-chronic-sleep-loss/28612>

Congratulations Spring & Summer Graduates

Chuenchanok Khodthong graduated from Thomas F. Martin's lab and will be working in a job in industry.

Li Li graduated from Katherine Kalil's lab and will be a postdoc at Pfizer, Inc. studying Parkinson's Disease

Donald McLaren graduated from Sterling C. Johnson's lab and will be a postdoc at Harvard University.

Michael Murphy graduated from Giulio Tononi's lab and will be returning to Medical School.

Joseph Wildenberg graduated from Beth Meyerand's lab and will be returning to Medical school.

CONTRIBUTIONS TO THE PROGRAM

Funds given to the program are used to support recruiting activities, guest speakers, the undergraduate award in neurobiology research and the annual program picnic. For additional information, please contact the program office at (608)262-4932. To contribute, please contact the UW Foundation at: www.uwfoundation.wisc.edu

Thank you to all those who have contributed and continue to support the Neuroscience Training Program and its students.

Congratulations to
the students who
have passed their
pre-liminary
examinations!

Nima Ghitani
Ellen Guller
Miguel Santiago-Medina
Michael Zorniak

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Fall 2010 Events

Monday, Aug. 30th

Neuroscience Research Symposium

Saturday, Sept. 11th

Annual NTP Fall Picnic - Mary Behan's Farm, All Neuroscience students, faculty, staff, alumni, family and friends are invited

Thursday, Sept. 30th

Mark Mayford, Department of Cell Biology, The Scripps Research Institute

Thursday, Oct. 21st

Mar Sanchez, Department of Psychiatry and Behavioral Sciences, Emory University

Neuroscience and Public Policy Seminar Series

Friday, September 10th

David Eagleman, Department of Neuroscience, Baylor College of Medicine
Neuroscience and the Law

Friday, October 8th

Alan Leshner, CEO, AAAS
Title to be announced

Friday, November 12th

Roger Pielke, University of Colorado, Boulder
Making Sense of Science in Policy and Politics

Friday, December 3rd

David Jentsch, UCLA
Animal Research and Animal Rights

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