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Life in Discovery

Groundbreaking RFUMS research into cocaine addiction published in foremost Nature science journal



North Chicago, IL – For almost 140 years, the British-based journal *Nature* has premiered some of the most significant papers in medicine and science, including Dr. Watson and Dr. Crick’s description of the structure of DNA – including Dr. Rosalind Franklin’s historic Photo 51 – the discovery of a hole in the ozone layer and the mapping of the human genome. Now, a research team under the direction of Dr. Marina Wolf, professor and chair of the Neuroscience Department at Rosalind Franklin University of Medicine and Science and faculty member in the Chicago Medical School, will have its work added to that impressive list of pioneering research.

The paper, “Formation of accumbens GluR2- lacking AMPA receptors mediates incubation of cocaine craving,” which first appeared on the *Nature* website on May 25, 2008, ahead of publication expected next month in the print addition, identifies a brain mechanism that helps to explain why craving for cocaine increases rather than decreases in the weeks and months after drug use has stopped.

The research was performed in the laboratories of Wolf, Michela Marinelli, Ph.D., and Kuei Y. Tseng, M.D., Ph.D., at Rosalind Franklin University, and the laboratory of Yavin Shaham, Ph.D., of the Intramural Research Program of the National Institute on Drug

Abuse (NIDA) in Baltimore, Maryland. The research was supported by NIDA, part of the National Institutes of Health (NIH).

Dr. Wolf's research used an animal model to study an important cause of relapse in abstinent cocaine users, namely craving triggered by environmental cues (people, places or things) that the user associates with cocaine. Such cues produce craving by increasing release of the neurotransmitter glutamate in a brain region known as the nucleus accumbens which is important for motivation and reward. Glutamate activates the nucleus accumbens neurons via AMPA-type glutamate receptors.

Dr. Shaham's lab showed previously that the ability of cues to trigger cocaine craving in rats progressively increases ("incubates") over the first 60 days of withdrawal. The findings published in *Nature* reveal that "incubation" of cue-elicited craving is due to the formation of new AMPA-type glutamate receptors in the nucleus accumbens. These new receptors enable stronger stimulation of nucleus accumbens neurons, resulting in more intense craving.

Perhaps most importantly, however, Dr. Wolf and her team have discovered that the newly formed AMPA receptors are atypical because they are missing a particular subunit (GluR2).

This raises the prospect of developing drugs that block the atypical AMPA receptors but do not interfere with functions mediated by normal AMPA receptors, which include learning and memory. Such drugs might be used to dampen craving during the first months of withdrawal when abstinent cocaine addicts are particularly prone to cue-induced relapse.

Dr. Wolf's interest in this area – understanding how glutamate mechanisms associated with learning and memory might contribute to long-lasting brain changes in addiction – began in the late 1980's. At that time, she recalls, research into addiction "was narrowly focused on the neurotransmitter dopamine."

Prompted by breakthroughs in understanding the cellular basis of learning, Dr. Wolf began reading about the role of glutamate in neuronal plasticity, or the ability of the brain to be "re-wired" by experience. As an addiction researcher, her interest in the field of neuronal plasticity was, she said, "relatively unique at that time."

"It was fascinating," said Wolf, "so I really dived in and ultimately built my research program around 'translating' learning and memory mechanisms to the addiction field. It seemed logical that the brain would use the same glutamate-based 'building blocks' to rewire the brain during normal learning and during the extremely strong habit learning that leads to compulsive behaviors in addicts."

It has been a long road from those initial forays to this latest study, with Wolf publishing numerous papers and earning many awards and honors, including a recent appointment to

NIH's Council of Councils. She is only one of two Chicagoland health science researchers who serve on the nationally distinguished advisory board.

However, Dr. Wolf also points out that the fruits of the Nature paper were due to the work of many dedicated researchers both outside and inside RFUMS. "It was a true collaboration in which scientists with diverse expertise came together to accomplish something none of them could have done alone," said Dr. Wolf. "I think it was a very inspiring and positive experience for all of us, and especially for the students involved in the project."

In addition to raising awareness of the university's pioneering work in the field of addiction, Dr. Wolf also believes the publication will help enhance the understanding that "addiction is a brain disease with cellular underpinnings, and, hopefully, we can treat it with a combination of drugs and behavioral therapy."

The level of recognition that publication in Nature will bring for Dr. Wolf and her colleagues has also extended beyond those in the medical field.

"It's tremendously exciting," said Dr. Wolf. "Even my daughters are impressed."

About Rosalind Franklin University of Medicine and Science

Rosalind Franklin University of Medicine and Science is a national leader in interprofessional medical and healthcare education, comprising the Chicago Medical School, College of Health Professions, Dr. William M. Scholl College of Podiatric Medicine and School of Graduate and Postdoctoral Studies.

Rosalind Franklin University recently received approval for its new doctoral program in Interprofessional Healthcare Studies – the first in Illinois – and will launch a new master in science program in Psychology Clinical Counseling in fall 2008.

There are more than 16,000 RFUMS graduates in the United States and worldwide.