Rett Syndrome hope

LI researchers report on possible drug for developmental disorder

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Long Island scientists have moved a tantalizing step forward in efforts to better understand — and alleviate — some of the devastating symptoms of Rett Syndrome, a rare, incurable, neurodevelopmental condition that primarily strikes girls.

The syndrome shares key symptoms associated with autism spectrum disorders but has many symptoms that are unique, including, an underlying genetic mutation, said biochemist Peter Tonks of Cold Spring Harbor Laboratory.

Writing in the current issue of the Journal of Clinical Investigation, Tonks and colleagues report on a possible — but still distant — drug intervention.

"When you do classical academic research that has the opportunity to help real patients, it's a reason to get out of bed in the morning," Tonks said. "It's a very exciting time."

Tonks and research associate Navasona Krishnan have found that their so-called small-molecule — an experimental drug candidate — extends life expectancy in mouse models bred to develop Rett Syndrome. Tonks hopes eventually to move forward with human clinical trials of the approach. Currently, there are no drugs available to address symptoms associated with the neurodevelopmental disorder.

Tonks' strategy involves inhibiting the activity of an enzyme called PTP1B, which he discovered a 25 years ago. The enzyme goes awry in Rett Syndrome, as it does in certain cancers and some metabolic disorders. Controlling it, he and his team found, relieved syndrome-related symptoms in the humanized mice.

"Tonks and colleagues found, for example, that PTP1B levels are extremely high in the afflicted mice. But when the enzyme was inhibited, cell communication processes flowed normally. Now, he wants to know whether inhibition with his candidate molecule will do the same in people and is collaborating with scientists at Case Western Reserve University in Cleveland.

Rett Syndrome usually appears in toddlers after a normal period of development during infancy. Scientists have found that mutations in the MECP2 gene, which resides on the X chromosome, cause the condition. Because males with Rett Syndrome have only one X chromosome, they usually die as infants. Females with the syndrome, however, can survive into middle age, experts say.

But afflicted girls and women have a constellation of problems: breathing difficulties, Parkinson-like tremors, small head size, mental retardation, poor muscle development and an inability to speak. People with Rett Syndrome require lifelong, round-the-clock care.

Advocates for children and adults with the syndrome call it the most physically disabling of disorders linked to the autism spectrum.

"Historically it was considered an autism spectrum disorder," said Monica Coenraads, executive director of the Rett Syndrome Research Trust in Connecticut and the mother of an 18-year-old daughter with the syndrome.

"Now that there is a gene associated with it, it's no longer included in the DSM IV,\" Coenraads said of the Diagnostic and Statistical Manual, Fifth Edition. The volume is considered the bible of psychiatry.

Nevertheless, she added, many people still refer to Rett Syndrome as an autism spectrum disorder. An estimated 16,000 people are affected in this country, with 350,000 worldwide.

Dr. David Katz, professor of neuropsychology and psychiatry in the School of Medicine at Case Western, said the work at Cold Spring Harbor Laboratory is on an intriguing track. "These are promising results, encouraging results,\" Katz said, who has studied Rett Syndrome for years.

"This is what we call early stage findings where there are encouraging results in a mouse model."

Murder charge for college cop

CINCINNATI — A University of Cincinnati security officer who shot a motorist during a traffic stop over a missing front license plate was indicted yesterday on a murder charge, with a prosecutor saying the officer "purposely killed him" and "should never have been a police officer."

The case comes amid months of national scrutiny of police dealings with African-Americans, especially those killed by officers. The motorist, Samuel DuBose, was black.

The officer, Ray Tensing, is white, although authorities haven't indicated that race was a factor in this case.

Hamilton County Prosecutor Joe Deters announced the indictment in the July 19 shooting at a news conference.

Authorities have said Tensing saw that a car driven by DuBose, 43, was missing the front plate, which is required by Ohio law. They say Tensing stopped the car and a struggle ensued after DuBose refused to provide a driver's license and to get out of the car.

Tensing has said he was dragged by the car and forced to shoot at DuBose. He fired one shot, striking DuBose in the head.

But Deters dismissed Tensing's claim that he was dragged by the car and suggested he shouldn't have pulled DuBose over to begin with.

"He fell backward after he shot [DuBose] in the head,\" Deters said, adding that it was a "chicken crap" traffic stop.

Tensing is 25, according to the Cincinnati Enquirer. On video from his body camera shown yesterday, he is heard asking for DuBose's driver's license several times with DuBose at one point saying he had one. Later, DuBose said, "But I don't think I have it on me."

Tensing asked DuBose to unbuckle his seat belt. About that time, Tensing appears to be trying to open the door, and DuBose puts his hand on the door and leans away. The video becomes shaky, but a gunshot can be heard and DuBose appears to be slumped in the seat before the car moves away.

Tensing turned himself in at the Hamilton County Justice Center yesterday and was processed on charges of murder and voluntary manslaughter.