New study will examine link between head injuries, degenerative brain disorders

June 6 2016, by Kris B. Mamula, Pittsburgh Post-Gazette

Researchers at the University of Pittsburgh, UPMC and Carnegie Mellon University are putting together a study of degenerative brain disorders that have been linked to head injuries, the first project of its kind among the institutions and among the first in the country to use a novel tool in the search for treatments.

UPMC's Brain Trauma Research Center, Pitt's Department of Critical Care Medicine and Drug Discovery Institute, and CMU's Department of Mechanical Engineering are preparing to study treatments for traumatic brain injuries - including chronic traumatic encephalopathy, a degenerative brain disease that has been related to playing football and other contact sports.

The study is being undertaken for humanitarian reasons while a search for project funding continues, researchers said.

"One of the things that has been very challenging in head injuries is finding new therapies," said Patrick Kochanek, a physician and vice chairman of the critical care medicine department at Pitt. "The cool thing is bringing together all of the resources in Pittsburgh."

The study is in the "very early developmental stages," Dr. Kochanek said.

Dietary supplements, prescription antidepressants and hyperbaric oxygen are among a wide variety of remedies that are now used to treat head

injuries sustained while playing contact sports. But nothing has been proven to work for concussions, the common cold of head injuries, according to a search of the medical literature between 1955 and 2012 by the American Academy of Neurology.

The search was done for a summary of evidence-based concussion treatments by the Minneapolis-based trade association for doctors who specialize in the treatment of brain and nervous systems disorders.

CTE is a progressively debilitating disease first identified in Pittsburgh in 2002 by forensic pathologist Bennet Omalu during an autopsy of former Steelers center Mike Webster, who played professional football from 1974 to 1990.

Omalu, who is now chief medical examiner at San Joaquin County, Calif., linked the repetitive hits to the head that Webster and other players experience during football with the development of CTE, although some have questioned the connection.

Pitt brings to the project a new approach in understanding disease and drug development, which combines storehouses of medical data and analytic models to mimic complex cellular workings in the search for new treatments for disease. Historic drug discovery was like firing a shotgun in the hope of hitting a therapy target, which compares to the sharpshooter capability of the new Pitt tool.

The approach is called quantitative systems pharmacology and Pitt is among only a half a dozen or so academic centers nationwide using it, according to Anton Simeonov, scientific director at the National Center for Advancing Translational Sciences, an institute within the National Institutes of Health in Bethesda, Md.

Historically, scientists isolated compounds from soil or other materials,

then screened them for effects in the body. The process was "pretty unscientific," but resulted in some drug breakthroughs, said Charles Craik, director of the Quantitative Biosciences Consortium at the University of California, San Francisco.

By the 1980s, researchers were identifying molecular switches inside cells that could be turned off or on with compounds to achieve a certain effect.

"There were all these good things happening, but what was missing was a model - some visualization about how things were working," said Craik.

D. Lansing Taylor, director of Pitt's Drug Discovery Institute, who is also involved in the study of brain injury therapeutics, said lower drug development costs and less time needed to bring new therapies to market are part of the new system's promise, he said. "This will change the face of how we do this," Taylor said.

For the Pitt-CMU study, researchers will expose a matrix of cells to the kinds of forces that football players with head injuries experience, then test the effectiveness of various drugs in restoring normal cellular function or protecting cells from injury, Kochanek said.

The Department of Defense and the Pennsylvania tobacco lawsuit settlement fund are among the sources that will be solicited to finance the project, researchers said. The National Football League also funds head injury research and UPMC has had NFL funding in the past, which could be another potential source of support.