Nanotechnology Identifies Peptide "Fingerprint" in Both Forms of ALS

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A nanospray emitter developed by chemist Troy Wood has identified a common molecular signature in familial and sporadic forms of Lou Gehrig&acutes disease.

A nanotechnology developed by a University at Buffalo professor has enabled researchers to identify a molecular signature common to both familial and sporadic cases of amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease.

It is the first time that a common molecular signature has been found in patients with both familial and sporadic cases, where no other family members have the disease, of ALS.

The finding, published in July in the *Proceedings of the National Academy of Sciences*, reveals that a peptide found in a gene in spinal cord fluid is common to patients with the disease.

The work was done through a collaboration of UB chemists with scientists studying ALS at California Pacific Medical Center Research Institute, The Johns Hopkins University, University of California at San Diego and University of Pittsburgh.

Troy Wood, Ph.D., associate professor of chemistry in UB's College of Arts and Sciences and a co-author on the PNAS paper, began working with the ALS researchers following a talk given in 2005 at UB's New York State Center of Excellence in Bioinformatics and Life Sciences by Vishwanath R. Lingappa, Ph.D., a research institute scientist from California Pacific.

At the suggestion of Bruce A. Holm, Ph.D., senior vice provost and executive director of the Center of Excellence, Wood began working with Lingappa to identify an unknown protein species he and his team had found in nanogram quantities (billionth of a gram) in spinal cord fluid samples from ALS patients.

At such low quantities, Wood explained, the standard analytical chemistry technologies are of no use.

"Only nanotechnology is capable of identifying a species in these amounts," he said. "Because of the minute amounts of analyte that are present in some samples, nanospray technologies, in particular, which reveal what we call a peptide's mass 'fingerprint,' have emerged as one of the most important tools in the field of proteomics."

In the ALS research, the UB researchers used trypsin, an enzyme, to digest or break down the unknown analyte into small peptide pieces that constitute the "fingerprint," which, in turn, allows researchers to identify the species through mass spectrometry.

"The nanospray emitter allows you to handle very low fluid volumes so you need just a few microliters of sample," said Wood. "Without this technology, you would need milliliters -- from a hundred to a thousand times more sample."

Once the trypsin digestion process is complete, the fluid is then injected by syringe into the nanoelectrospray emitter.

The nanospray emitter that Wood developed and patented, called "NiagaraFlow," then ionizes the fluid, turning it into a very fine mist. Those ions can then be identified by mass spectrometry, an analytical chemistry technique that identifies analytes by their mass.

When an electrical potential is applied, the peptide is emitted as a fine mist of extremely small droplets, each of which is smaller than a micron, a millionth of a meter.

"Because the spray is emitted at such a low rate, 10 nanoliters per minute, we had around a hundred minutes during which the mass spectrometer could collect data before the sample was exhausted," said Wood.

The UB researchers identified that this unique, cross-linked species contains superoxide dismutase, a protein that had been previously linked to only the familial form of ALS.

"These results say that the mechanism in ALS involving superoxide dismutase is even more general," said Wood. "But without the nanospray technology, we couldn't have identified it."

The peptide provides researchers with an important piece of information as to where to focus future research.

In addition to Wood and Lingappa, other co-authors on the paper are William L. Wood, who recently earned his doctorate in chemistry from UB; Evgenia Alpert, Don Cleveland, Arie Gruzman, Jian Liu, the lead author, Robert G. Miller and M. Dharma Prasad of the California Pacific Medical Center Research Institute; Jeffrey D. Rothstein of The Johns Hopkins University, and Robert Bowser and Ronald Hamilton of the University of Pittsburgh.

Source: University at Buffalo