New research adds additional layer of complexity to human protein landscape

February 26 2016

New VIB/UGent research adds an extra dimension to the known set of human proteins. Genes can shift their expression towards alternative protein versions (proteoforms) that rival their full length counterparts in stability. For that reason, the diversity of human proteins seems to be fundamentally underestimated. Professors Petra Van Damme and Kris Gevaert report these results in the journal *Molecular Systems Biology* this month.

In 2001, the entire human genome was decoded in an ambitious, collaborative project called the Human Genome Project. Computer programs were used to predict the boundaries of genes in the raw DNA sequence and the detection of gene transcripts served as validation of this annotation process. Of course, the real proof of a gene being protein coding is to catch the actual protein.

To do exactly that, Van Damme and her team make use of modern mass spectrometry and ribosome profiling technologies. Previously, they and others exposed alternative translation start codons in up to 20% of the human protein-coding genes, which had simply been overlooked by prediction algorithms scanning the human DNA code. PhD student Daria Gawron (VIB/UGent) comments, "A cell might thus –depending on the situation- decide to express a smaller or larger version of a certain protein."

"In the past, researchers who observed shorter versions of certain proteins, quickly shelved them as non-functional byproducts of protein

degradation", Van Damme (VIB/UGent) says. "Our work shows that these protein variants are generally conserved. Not only are these proteoforms coded for in the genome, they are also tightly regulated and often display altered stability."

These findings might have important implications for a new and quickly developing science field: gene editing. "To knock out a gene, a point mutation in its DNA sequence can be very accurately introduced with modern gene editing techniques. However, scientists should be aware that by doing so, they might actually induce the formation of a truncated, more stable version of the protein, provoking the exact opposite effect than desired," Gawron explains.

More information: D. Gawron et al. Positional proteomics reveals differences in N-terminal proteoform stability, *Molecular Systems Biology* (2016). DOI: 10.15252/msb.20156662

Provided by VIB (the Flanders Institute for Biotechnology)