Scientists Explore Function of 'Junk DNA'

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University of Iowa scientists have made a discovery that broadens understanding of a rapidly developing area of biology known as functional genomics and sheds more light on the mysterious, so-called "junk DNA" that makes up the majority of the human genome.

The team, led by Beverly Davidson, Ph.D., a Roy J. Carver Biomedical Research Chair in Internal Medicine and UI professor of internal medicine, physiology and biophysics, and neurology, have discovered a new mechanism for the expression of microRNAs -- short segments of RNA that do not give rise to a protein, but do play a role in regulating protein production. In their study, Davidson and colleagues not only discovered that microRNAs could be expressed in a different way than previously known, they also found that some of the junk DNA is not junk at all, but instead consists of sequences that can generate microRNAs.

Davidson and her colleagues, including Glen Borchert, a graduate student in her lab, investigated how a set of microRNAs in the human genome is turned on, or expressed. In contrast to original assertions, they discovered that the molecular machinery used to express these microRNAs is different than that used to express RNA that encodes proteins. Expression of the microRNAs required an enzyme called RNA Polymerase III (Pol III) rather than the RNA Polymerase II (Pol II), which mediates expression of RNA that encode proteins. The study is published in *Nature Structural and Molecular Biology Advance Online Publication* on Nov. 12.

"MicroRNAs are being shown to play roles in cancer and in normal development, so learning how these microRNAs are expressed may give us insight into these critical biological processes," said Borchert, who is lead author of the study. "Up to now it's been understood that one enzyme controls their expression, and we now show that in some cases it's a completely different one."

Genes that code for proteins make up only a tiny fraction of the human genome. The function of the remaining non-coding sequence is just beginning to be unraveled. In fact, until very recently, much of the non-coding sequence was dismissed as junk DNA. In 1998, scientists discovered that some DNA produced small pieces of non-coding RNA that could turn off, or silence, genes. This discovery won Andrew Fire and Craig Mello the 2006 Nobel Prize for medicine or physiology. Since their discovery, the field has exploded and small, non-coding RNAs have been shown to play an important role in development and disease in ways that scientists are only just beginning to understand.

"Not so many years ago our understanding was that DNA was transcribed to RNA, which was then translated to protein. Now we know that the levels of control are much more varied and that many RNAs don't make protein, but instead regulate the expression of proteins," Davidson explained. "Non-coding RNA like microRNAs represent a set of refined control switches, and understanding how microRNAs work and how they are themselves controlled is likely to be very important in many areas of biology and medicine."

Over 450 microRNAs have been identified in the human genome. Learning how they are turned on and in what cells and what they do, may allow scientists to turn that knowledge to their advantage as a medical tool.

Source: University of Iowa