3Qs: New clues to unlocking the genome

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Last week, *Nature* Magazine, *Genome Research* and *Genome Biology* published 30 papers on breakthrough research that will change the face of genetics. After nearly a decade of searching, the Encyclopedia of DNA Elements (ENCODE) Consortium has assigned biochemical functions to 80 percent of the genome. Previously considered "junk," the development adds significant insight into the importance of the non-coding regions of DNA. We asked Veronica Godoy-Carter, assistant

professor of biology, to explain.

What is noncoding DNA and why has it been called "junk"?

The genetic material present in all living organisms is DNA. It is understood that "coding" DNA can be "read" by the cellular machinery, as we read a page in a book, mostly as proteins (e.g., your hair and nails are made up of proteins). However, there are sections of the DNA in metazoans (e.g., humans) and in some unicellular organisms known to have no readable code, that is, noncoding DNA. The word "junk" was used in the 14th century to denote an old or inferior rope. Today it is used to characterize useless articles or those of little value. Thus, when researchers started to decipher the linear sequence of the DNA, it became obvious that a large fraction of it is noncoding. Therefore, the word "junk" was used to describe such noncoding regions.

We've known for a while that noncoding DNA actually has very important physiological functions. How does this new research change or add to that understanding?

ENCODE has shown that, contrary to previous views, most of the sequences of the human genome are not useless. Though it was previously known than noncoding regions were important for regulation, this project has demonstrated that noncoding sequences serve as a roadmap for regulatory DNA binding proteins that effect expression of coding regions. Previous to this large-scale analysis, no one knew about the extent of regulatory regions that existed in "junk" DNA, now referred to as "dark matter." For example, there are many sites that are specifically chemically modified, permitting inhibition or induction of the DNA coding regions. Remarkably, the regulation of expression does not only occur in coding regions that are adjacent to regulatory elements, as pre-

viously thought. In some cases, regulation is long range and seems to occur only when the regulatory elements are near coding regions in the three-dimensional space!

How will this new understanding of noncoding DNA change the face of genetic research?

The long-range regulation of coding regions in the DNA is such an exciting finding because it will permit us to start understanding the effect of known changes in the DNA sequence (i.e., mutations) between, say, healthy and cancer tissues. As it turns out, many mutations associated with disease are in noncoding regions, which previously made little sense. Now it will be possible to map mutations on this roadmap and importantly it will be possible to understand how mutations far away in the linear DNA change the regulatory landscape of cells.

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