The Evolving Definition of a Gene

KAREN HOPKIN

With the discovery that nearly all of the genome is transcribed, the definition of a "gene" needs another revision.

There was a time when a biologist could discover a new species by strolling into a field and saying, "What, ho! I've never seen one of those before!" Of course, by now biologists have seen it all—or at least all of the things that are easy to see. So a scientist who spies something seemingly new first needs to consider whether that creature belongs to a previously identified species.

> **gene\jēn*n*:** the unit of heredity that determines phenotype

But that's not as easy as it sounds. "There are people in the world of systematics who spend the entirety of their existence debating what is meant by the word 'species,'" says Laurence Hurst, of the University of Bath in the United Kingdom. "So, are two individuals members of the same or different species? It depends on how you define 'species.'"

Now the same seems to be happening with genes. "It's a slippery concept to define," says Chris Ponting, of the University of Oxford. "There's no one definition that encompasses all the objects that could be defined as being genes." In the past five years, numerous investigators using a variety of techniques have uncovered a cornucopia of ribonucleic acids (RNAs) that have excited great interest and called into question the way we think about "genes." Some RNAs, like microRNAs, regulate the expression of suites of genes. Some appear to influence the state of chromatin. Others may simply be the product of transcriptional noise—which may or may not play a role in keeping genes "readable." All lead us from our traditional genes-encode-proteins formulation of genome function.

"People have been discussing the meaning of the term 'gene' for many, many years," says Roderic Guigo, of the Center for Genome Regulation in Barcelona. "As we gain more knowledge about the molecular basis of genome activity, we should be able to more precisely define the concept of the gene. But actually it's the other way around. The more we learn, the less clear we are about what a gene is."

> **gene\jēn*n*:** the unit of heredity—located on chromosomes—that determines phenotype

Harvard's William Gelbart says, "The reality is that chromosomes are real biological objects that can be purified in a test tube.... And a 'gene' is a conceptual construct that helps us think about the individual units within that chromosome without quite knowing what they are. It's nice if people agree on the meanings of words so you know what you're talking about. But I don't think there will ever be an agreed-upon definition of a gene. I don't think there ever has been."

"When you speak with physicists, they're sometimes surprised we can use a concept that's so ill-defined," adds Laurent Duret, of the National Center for Scientific Research in France. "But in practice, when biologists talk about genes, they understand each other." What they don't yet understand, though, is what all these newly discovered transcripts are doing, and how they play into genome evolution and activity.

> **gene\jēn*n*:** the unit of heredity—located on chromosomes, that encodes one enzyme—that determines phenotype

Blame the biochemists

Genes were once defined in terms of heredity: A gene was essentially a heritable unit that produces a phenotype—the way an organism looks or behaves. "That's something we can measure," says Winston Hide, of the Harvard School of Public Health. "For example, a fungus can inherit the ability to metabolize leucine." And for population geneticists, that is definition enough: A gene conveys information about phenotype.

BioScience 59: 928–931. © Karen Hopkin. ISSN 0006-3568, electronic ISSN 1525-3244. All rights reserved. doi:10.1525/bio.2009.59.11.3