

Our Winged Relatives

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Knowing the full sequence of the chicken genome will not only help us to breed more productive and healthier birds and to keep avian-borne diseases, such as bird flu, under control. By comparing the human and chicken genomes, we will also gain a better understanding of our own biology

Apart from being one of the most economically important farm animals in history, the chicken is also a major model system for laboratory work. Chicken embryos have been especially useful in research on animal development, due to the ease of experimentation using chicken eggs. Furthermore, a lot of basic discoveries in virology and oncogenesis have been made while working with the chicken model. The laboratory culture of chicken lymphocytes B (a cell line dubbed DT40) is also one of the most important laboratory systems in immunology. DNA can be exceptionally easily modified in these cells, thus the DT40 cell line is likely to become an important model in other fields of molecular biology as well.

Interpreting chicken genome

Scientists have succeeded in determining the DNA sequence of a single hen, now more than seven years old, living at a research facility in Michigan. The hen is a Red Jungle Fowl, a wild species from which domestic poultry originated several thousand years ago. The DNA has been sequenced and analysed by the International Chicken Genome Sequencing Consortium, encompassing scientists from 49 countries. Most of the DNA sequencing was done by the Genome Sequencing Center at Washington University in St Louis.

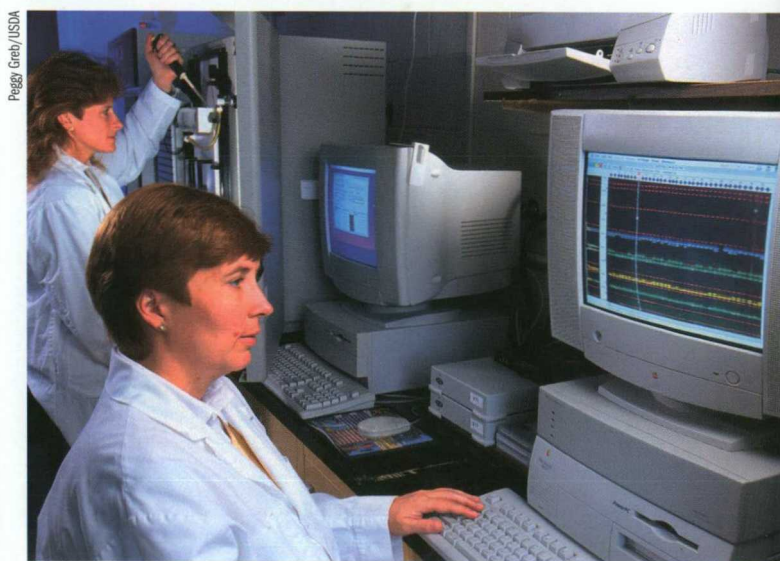
Even once the entire DNA sequence of the genome is known, it is still difficult to identify sequence fragments that correspond to individual genes. Our understanding of the cellular mechanisms responsible for "reading" and "interpreting" DNA sequences is still not sufficient to make accurate predictions of genes from the genome sequence alone. In other words, the molecular machinery of the cell is able to precisely locate DNA fragments

which should be interpreted as genes, yet we are still not able to grasp how this is done and use this knowledge to predict gene locations. Therefore, genomic DNA sequencing projects are usually accompanied by large scale cDNA (complementary DNA) sequencing work. cDNA are sequences that are "deciphered" by the cellular machinery and transcribed into RNA sequences. Some of these RNA sequences will further serve as templates for protein production.

International bioinformatics

cDNA sequencing formed part of the chicken genome project and the results have been used for gene localization. The present author's group from the Polish Academy of Sciences took part in this effort. The task of the Polish group was to participate in implementing a database system for the Jean-Marie Buerstedde laboratory in Munich, which was sequencing chicken transcripts. The Polish team also performed an analysis of the resulting sequences. This collaboration was funded by a European Union grant.

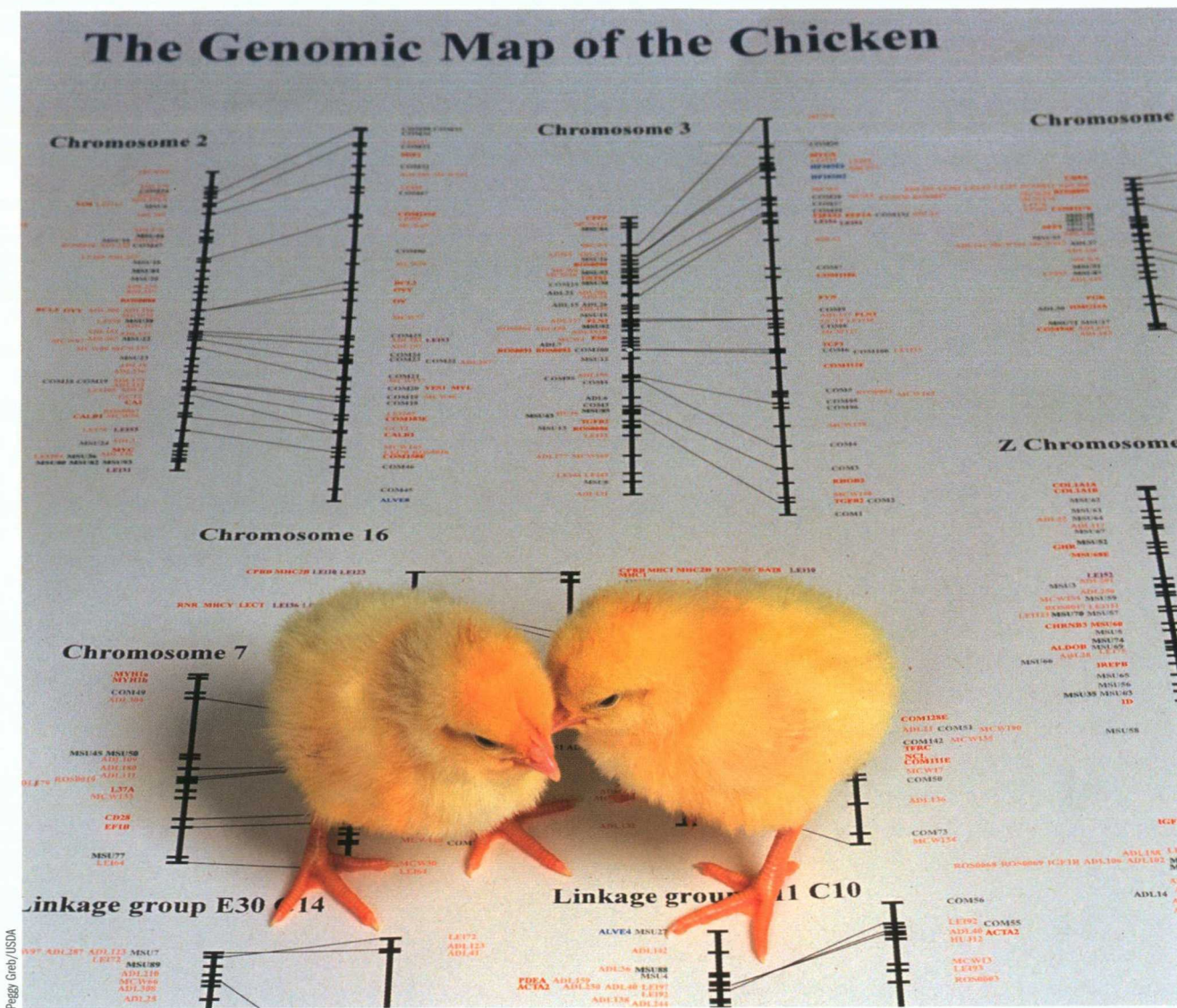
The major challenge of the data analysis was to compare the full chicken DNA sequence with the human genome sequence. Scientists believe that the bits of genome which are most strongly conserved in evolution (i.e. most resistant to change), are most crucial for our survival. Thus, a comparison of chicken and human sequences can be used to identify the human genes that



Peggy Gray/USDA

Chicken DNA sequencing involved scientists from 49 countries

The Genomic Map of the Chicken



Peggy Grab/USDA

are responsible for essential functions. The first surprising result of such comparative genome studies is that the chicken genome sequence is three times shorter than human DNA. The chicken genome is very parsimonious; it does not contain many repeated, non-coding sequences, such as are present in the human genome.

Further analysis has revealed that only 2.5% of the human genome can be matched to chicken DNA. This 2.5% corresponds to about 70 million DNA letters which have been largely preserved over 310 million of evolutionary history, since humans and birds shared a common ancestor. Not even half (44%) of these conserved regions correspond to protein coding genes. Most of the conserved regions seem to have a “meaning” still unknown to science. One of their possible functions could involve the regulation of gene activity. Before the recent success at sequencing the chicken genome, such comparisons were only possible between human and mouse sequences. Because the mouse is much more closely related to humans than the chicken is, such comparisons did not detect many conserved, protein non-coding sequences. The evolutionary distance between chickens and humans appears to be optimal for analyzing these features. Therefore, comparative analysis of human and chicken sequences will direct further experimental research towards essential but ill-understood portions of

our genome. The chicken genome project thus provides valuable insights into human biology and medicine.

One of the challenges ahead for modern science is to find ways of halting the global spread of infectious viral diseases. Bird flu has recently become one of the most feared of them. Knowledge of the chicken genome may offer scientists insight into resistance mechanisms, something that may help researchers to identify poultry strains least likely to be susceptible to pathogens. Breeding these strains could help stop the spread of avian-borne diseases.

The results obtained by the International Chicken Genome consortium are publicly available and can be accessed via Internet servers. These servers offer not only access to the raw data itself, but also to an array of sophisticated data analysis software that may be used to query the data. Such publicly available data and software will help scientists to design new experiments that will facilitate the breeding of new economically valuable and resistant chicken strains and deepen our understanding of human molecular biology. ■

Further reading:

Hillier et al. (2004). Sequence and comparative analysis of the chicken genome provide unique perspectives on vertebrate evolution. *Nature*. 432: 695-716.