Reflections about DNA studies, reductionism and the role of Anthropology

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The announcement of the complete DNA sequencing of Chimpanzee genome (Editorial 2005) has raised three orders of questions, which are already been discussed in this forum: a) what makes us humans? Can the distance between humans and the great apes be so reduced to cancel the peculiar status of *Homo sapiens*? b) Is this new event another demonstration of scientific reductionism? c) Is the disciplinary status of anthropology in danger because of the genocentric attitude of sequence programmes?

The analysis of the relevant scientific, cultural, and philosophical aspects raised by these new developments produce a solid negative answer to all three questions.

How much ?

The deciphering of DNA sequence of our closest evolutionary cousin shows that only a tiny difference exists between the two species at this level of analysis. Depending on how the comparison is made, approximately 95% to almost 99% of the chimpanzee genome seems to line up precisely with corresponding regions of the human genome and within these aligned segments, the DNA sequences differ by around 1.2%.

Humans and chimps have evolved separately since splitting from a common ancestor about 4-6 million years ago, and it is not surprising that their DNA remains highly similar. The remarkable similarity of the chimpanzee genome to that of humans was already predicted from overall protein sequence comparison made in the '70s (M. C. King and A. C. Wilson 1975, M. C. King and A. C. Wilson 1975). Direct sequence comparison showed that 98% of these sequences are the same, and at that time already it seemed clear that questions about the genetic basis for human uniqueness would eventually require detailed comparisons with the genomes of great apes.

The sequence comparison tells us that our genome and that of the chimpanzee differ by only a few per cent. But even if the proportion is small, this still amounts to tens of millions of differences because each genome contains some 3 billion nucleotides. Most of these changes will have no significant biological effect, but it is these differences that should attract the attention.

Even the smallest difference in nucleotide sequence can produce relevant and even dramatic results at the phenotypic level. A good example is the first 'molecular disease' which has been discovered, sickle-cell anaemia (L. Pauling, H. A. Itano, S. J. Singer et al. 1949). This severe pathological condition is due to a single-nucleotide substitution (A→T) in the second position of the sixth codon of the β-globin gene. This tiny change in the structure of the haemoglobin protein, because of its spatial position, leads to a change in the shape of the red blood cell to a sickle shape, and this produce their disruption in the passage through capillaries, the anaemia and in most case death in

young age. In this case, one single nucleotide substitution means literally the difference between life and death.

Furthermore, although single-nucleotide substitutions are usually considered when quantifying sequence similarity, insertions/deletions (indels) and duplications of DNA segments account for a significantly larger proportion of the difference between the human and chimpanzee genomes (3% and 2.7%, respectively).

In the third place, the sequence divergence varies among genomic regions, presumably because of variations in mutation rate, selective constraints and the rate of recombination between chromosome pairs during cell division.

Finally, a genome is not a compilation of "elementary units", but a highly structured and coherent system. As a consequence, the position of each element in this system (the 'genomic landscape') can change the way in which each single element is, metaphorically, 'read'.

The interpretation of DNA sequences requires functional information from the organism that cannot be deduced from sequence alone. Functional genomics investigations must determine "when and where" a gene is expressed within an organism, during development and life history, and what the level of expression is at various times and in different "epigenetic landscapes". It is likely that a few mutations that can produce large effects because of their position in the "genetic and epigenetic landscapes" could be responsible for most of the phenotypic differences that separate humans from chimpanzees and other great apes.

It is also quite probable that the major source of individuality is the regulatory system. A tiny change in this genetic component can produce dramatic changes in gene expression differences between the species. In fact, the human-specific duplicated regions exhibit significant differences in gene expression. The differences in gene expression patterns are bigger than what could have been predicted from sequence analyses alone, and are most often upregulated. Regulatory mutations may account for biological differences between the species. The study of about 5000 genes revealed that the expression of 200 genes was significantly different between human and chimpanzees. Patterns of gene activity and protein interactions will certainly be much more explicatory than the mere gene sequence.

We can therefore share Ernst Mayr conclusion, when confronted with the data on molecular similarity between *Homo sapiens* and apes: "Man's shift into the niche of the bipedal, tool-making, speech-using hominid necessitated a drastic reconstruction of his morphology, but his morphology did not, in turn, require a revamping of his biochemical system. Different characters and character complexes thus diverged at different rates" (E. Mayr 1963). A large revamping of the genetic system was not necessary in the passage from apes to man, because evolution is a conservative tinkering and can make use of the same elements in a very different way (F. Jacob 1977). An evolutionary novelty can be the result of a selective carry up as a result of only a few changes, if those changes are strongly advantageous. From an evolutionary standpoint, the difference between men and monkeys can go down to a few genes being switched on in a different place or for a longer period of time.

The unveiling of the chimpanzee genome is a unique opportunity to systematically explore how and why *Homo sapiens* diverged from it closest living relatives and a first relevant step toward finding an answer to the key question: What makes us human?

There are no answers yet about how humans picked up key traits such as walking upright, large cranial capacity, complex language ability, and abstract thought

elaboration. The acquisition of symbolic language is probably the consequence of a quantum jump, which cannot arise by accumulation, something similar to the origin of genetic code. The two most relevant shifts in evolution, that is the origin of life and the origin of language and cultural transmission, seem to be linked with the emergency of a new coding system, able to perpetuate, transmit and read the memory of past events, allowing the action of natural selection and of cultural evolution. These evolutionary novelties introduce in the natural world a major discontinuity between objects endowed with a memory system, a storage of coded information and a mechanism to read it and objects that do not show such properties.

With help from the chimp DNA, molecular geneticists are uncovering several regions of human DNA that apparently contain specific genetic changes that spread rapidly among humans within the past 250,000 years and could have been acted on by natural selection more strongly than others. One area contains the gene FOXP2, which seems involved in acquiring speech and language skills (W. Enard and S. Pääbo 2004).

The route to an understanding the biological differences that enabled us but not chimpanzees to cook exquisite meals, produce symbolic maps from explorations, create symphonies, build complicated artefacts, write novels, and paint (and appreciate) abstract art is surely a long one, but the knowledge produced by comparative genome analyses can contribute a lot to it.

It is quite obvious to note that sequence data must be integrated with information about the related phenotypes, as well as critical environmental influences under which the genotype generates the phenotype, a process is influenced by the physical, biological, and cultural environment. Genes are nothing more that controlling signal or messages, and a genome sequence is just the 'instruction book' of a given organism. But genomes must be described, enumerated and read. In fact, an extreme analytical method is a necessary form of knowledge in this field. This, however, has nothing to do with 'genetic reductionism'.

Reductionism

A 'reduction' is the explanation of events in a given context by law governing another empirical context. In biology many efforts have been deployed to explain physiological and pathological phenomena by the laws of chemistry and physics. The thesis that reductions between two empirical realms are the only way to produce sufficient scientific explanations is called *reductionism*. To state that all biological phenomena are to be explained from a physico-chemical basis is called *physical or mechanical reductionism*.

'Genetic reductionism' wishes to explain every organismic feature with the mere presence and action of genes. A trait is defined as *genetic* if and only if it can be completely reduced to the *genes* and the genetic reductionism implies that *any* trait is genetic. In our context, to ask what genetic changes make us so different from the chimpanzee is apparently a reductionistic approach.

First at all, it should be clearly noted that genetic determinism is different from mechanical determinism, as gene is a biological concept, not a physico-chemical one, even if it is carried on by a chemical structure.

Two different versions of genetic reductionism can be found, which can be called respectively 'soft' and 'hard'. 'Soft genetic reductionism' states that genes and environmental factors interact to produce all biological features. This is

epistemologically useless, as virtually all organismic features would turn out to be genetic because of the simple fact that many genes that act during the earliest stages of embryonic development are necessary for the development of an embryo and cell physiology requires the continuity of gene activity.

The hard version of genetic reductionism affirms that genes are *sufficient* causes for all organismic features. Within this interpretation, an uninterrupted and completely deterministic causal chain links together genes and phenotypic expression. As the presence of a given gene is *necessary* for the manifestation of a given character, then this gene is defined as the *sufficient cause* of the character. In its extreme form this statement is nonsense. There is no life or even less reproduction without O_2, but nobody would say that O_2 is the *cause* of life or reproduction, even if the particular form of life on earth is the evolutionary result of the presence of O_2 in the atmosphere.

The key of the solution of this epistemological paradox is to introduce a clear distinction between sufficient and necessary causation and to clarify that 'genetic determinism' is quite different from mechanical determinism. The presence of a specific gene is *necessary* for the production of a specific trait, but is not a sufficient cause for it. In biology, as it was already clearly shown by Claude Bernard in XIXth century, exists a *dual* determinism: a physical-chemical determinism *produces* every biological phenomenon, *and* a genetic causation *determines* or *governs* its form and function (C. Bernard 1878). As put by Jacques Monod and Francis Crick: life events are nothing but physical processes but their coherent behaviour and specific form is produced and governed by information, by a project moulded through millions of years of evolution by natural selection. Living organisms are « objects with a project » (J. Monod 1970) The knowledge of this project and the understanding of its implementation in every individual instance is the key for biological understanding.

Disciplinary issues

The development of genome programmes has produced between anthropologists the impression that topics as human adaptation, evolution, ethology and cultural evolution are useless when compared with genetics. However, the "danger posed by the reshaping action of bioreductivism on scientific thinking" (R. Lancaster and G. U. Mason 2004) is grossly exaggerated. This reaction is quite similar to the worries of natural historians and evolutionists after the molecular revolution in the '60s, when science seemed to embark on the 'molecular bandwagon' and the idea that « the only worthwhile biology is molecular biology" (T. Dobzhansky 1964) was in fact widely diffudes. The history has at the contrary clearly showed that even for molecular biology "nothing makes sense in biology except in the light of evolution" (T. Dobzhansky 1964). Jacques Monod, wrongly considered as a 'mechanical reductionism' affirm that allosteric interactions and all relevant biological features are 'gratuitous' in respect of their biochemical determinants and are the 'exclusive results' of evolution by natural selection. And Francis Crick in writing his autobiography states that "the most important theme of the book is natural selection" (F. Crick 1988).

The genome comparative analyses show that Humans are unique, as is every other species. The characterization of this uniqueness only makes sense in light of a comparative approach, which documents the anatomy, physiology, and socio-cultural behaviour of other species. In this context anthropology and primatology should interact with ethology, evolutionary biology and molecular biology in order to

understand the uniqueness of the species and the evolutionary pathways that have produced it.

From this point of view anthropology is not a marginal research field, but an essential component of a complex and necessarily multidisciplinary endeavour which can elaborate a general view of biological and cultural evolution. This is even more evident if one considers that in recent decades dedicated field research has brought us the discovery that chimpanzee communities resemble human cultures in possessing patterns of local traditions that uniquely identify them (M. D. Hauser 2002, M. D. Hauser 2005, E. H. McConkey and A. Varki 2005). Different populations use different tools to gain access to their local food resources. Some use sticks to extract termites, others use rocks to crack open hard nuts, and yet others use tree bark as sandals to climb over the thorny needles of trees that hold an appetizing fruit.

Even more interestingly, when certain populations of chimpanzee are infected with certain pathogens, such as the nematodes, they consume plants that act as either chemical or physical defences. For other ailments, including constipation, lethargy, and lack of hunger, they eat the bitter pith of a plant, the same plant used across Africa as a local cure for humans infected with bilharzias and plasmodia. Self-medication, which involves swallowing whole, rough-surfaced leaves and chewing bitter piths increasing links chimpanzee and human behaviour (M. V. Olson and A. Varki 2003).

Even in chimpanzees the variation among populations is not due to genes, but rather to the capacity for social learning that the evolution at the genetic level has built. This is probably the result of the population-level patterning of traditions, of the genetic and social mechanisms which facilitate the transmission of traditions, and suggest a specific behavioural content of traditions.

These developments are making urgent to attempts to grasp what it means to be a chimpanzee, and thus, by comparison, what it means to be the human ape. Comparison among chimpanzees, humans and other species in each of these dimensions helps to delineate what chimpanzees share with humans and just where the differences begin. The very material of interest, genetic and cultural diversity between humans and our primate relatives, is thinning but is not vanishing and the analyses of the complex cultural and social inheritance system must complement the genetic picture.

Understanding the rules that link genetic information, population communication and social behaviour is an essential prerequisite for discerning how a communication system as complex as human language might have evolved. As the biocultural approach to the human evolution is necessarily anthropological, the contribution from physical and cultural anthropologists in the understanding of the meaning of the smallest but highly significant differences between species will remain therefore essential.

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