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Studi

Gene Expression and Epigenetics: the Link Between Biology, Physiology and Behavior

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Abstract Human speech is considered a specifically human trait. Languages are part of human culture, and are transmitted from parents to offspring. However, language has a strong genetic component too, which has only now begun to be understood more precisely. This paper summarizes some of the recent groundbreaking results on the organization and regulation of our genes and genome and presents some of the challenges that research will need to tackle in the near future. The author argues that scientific progress in this complex field requires an interdisciplinary approach in which the specific competences of philosophers, psychologists, sociologists, biologists, etc. are combined to reach the final objective.
KEYWORDS: Language; Behavior; Biology; Physiology; Genetics; Genome.

Riassunto *Espressione genica ed epigenetica: il nesso tra biologia, fisiologia e comportamento* – La capacità di parlare è considerata un tratto specificamente umano. I linguaggi sono parte della cultura umana e vngono trasmessi dai genitori alla prole. Ad ogni modo, il linguaggio possiede anche una forte componente genetica che soltanto di recente ha cominciato a essere compresa in maniera più precisa. Il presente contributo riassume alcuni dei risultati più innovativi circa l'organizzazione e la regolazione dei nostri geni e del nostro genoma, indicando alcune delle sfide con cui la ricerca dovrà misurarsi nel prossimo futuro. L'autore afferma che il progresso scientifico in questo complicato campo d'indagine necessita di un approccio interdisciplinare, nel quale le competenze specifiche di filosofi, psicologi, sociologi, biologi, etc. devono sostenersi a vicenda, per poter essere all'altezza di queste sfide.
PAROLE CHIAVE: Linguaggio; Comportamento; Biologia; Genetica; Genoma.

HUMAN SPEECH IS CONSIDERED a specifically human trait. Languages are part of human culture, and therefore, they are transmitted, as are other cultural traits (such as religion, or ethical rules), from parents to offspring. However, language has a strong genetic component, since language impairment is found to occur within families, with a concordance rate of about 70% in monozygotic twins and about 45% in dizigotic twins, leading to a hereditability factor of about 0.45.

The first human language gene identified, *FOXP2*, which codes for a transcription factor that plays a crucial role during neural development, was identified in a family affected by a grammatical defect. Interestingly, the amino

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acid sequence of the FOXP2 protein is highly conserved with only three differences between the human and mouse.

Two of these differences, arose in the human lineage after its divergence from other apes suggesting a positive selection for the human lineage. How many human specific genes involved in language like *FOXP2* exist in the human genome?

The Encyclopedia of DNA Elements (ENCODE) project data, providea systematic localisation of specific DNA regions active in transcription, the production of transcription factors, as well as chromatin structure and histone modification.[1] These data have enabled us to assign biochemical functions to 80% of the genome, in particular those outside of the well-studied protein-coding regions. Many of the candidate regulatory elements that have been discovered are physically associated with one another and with expressed genes, providing new insights into the mechanisms of gene regulation.

These newly identified elements also show a statistical correspondence to sequence variants linked to human disease, and can thereby guide interpretation of these variations. Overall, the project provides new insights into the organization and regulation of our genes and genome, and is an expanding resource of functional annotations for biomedical research. Gene expression programs also underlie adaptation to the environment or to extracellular cues and stress signals.

Cell identity can, therefore, be expressed in term of "molecular fingerprinting", the unique combination of active regulatory genes (encoding transcription factors or microRNAs) and active differentiation genes (controlling cell-specific physiological, behavioral and morphological properties). Hence, gene regulatory networks (GRN), composed of on-off switches and rheostats operating at the gene level, serve to specify the particular sets of genes that must be expressed in specific spatial and temporal patterns.

A recent paper published in *Nature*[2] provides for the first time a neuroanatomically precise, genome-wide map of transcripts and correlates functional and genetic brain architecture. The authors demonstrate that transcriptional regulation varies enormously by anatomical location, with different regions and their constituent cell types displaying robust molecular signatures that are highly conserved between individuals.

Analysis of differential gene expression and gene co-expression relationships demonstrates that brain-wide variation strongly reflects the distributions of major cell classes such as neurons, oligodendrocytes, astrocytes and microglia. Notably, the authors also demonstrate that the spatial topography of the neocortex is strongly reflected in its molecular topography-the closer two cortical regions, the more similar their transcriptomes.

Over the next few years, this paper will change our approach to understanding the biological basis of human behavior and to medical applications for complex diseases such as behavioral disorders (including major mood disorders and addictive behaviors) and other neurological or developmental diseases affecting cognition which represent a major public health problem and socioeconomical burden. These diseases affect a large proportion of the population, including over 10% for major depressive episodes and drug abuse, 1% for schizophrenia and 2% for mental retardation with or without autism.

However, to generate knowledge and scientific progress in this fascinating field, it will be necessary to establish an interdisciplinary effort. In fact, new and relevant questions will arise from these studies:

► What are the molecular mechanisms that participate in the maintenance and integrity of molecular and cellular identities?

► What are the systems (genetic and epigenetic) that dictate the establishment of different cellular states and ensure the transmission of identity to subsequent generations?

► What are the consequences of these systems for evolution in terms of cumulative changes in identity over time and throughout populations?

► What is the impact of the environment (at the chemical and cellular level) on defining identities and how are identities perceived externally?

► What are the pathological consequences of deregulation of these mechanisms and how might they be controlled to combat disease?

In the past, such questions were approached and handled differently by philosophers, psychologists, sociologists, biologists etc. but now we have the possibility of combining competences to reach the final objective.

The dawn of the 21st century offers an unprecedented intellectual landscape in which to re-examine the determinants of identity. New discoveries will come from bringing together minds from different disciplines and perspectives, thus catalyzing the cross-fertilization of ideas. It is therefore the time to create an interdisciplinary intellectual environment to generate advances in knowledge and scientific progress in this fascinating field.

The Symposium *The mind in the brain. Historical and epistemological reflections on the anniversary of 150 years from the localization of articulated language by Pierre Paul Broca* represents for me a milestone in this direction.

Notes

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