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Trajectories of genetics, 150 years after Mendel/Trajectoires de la génétique, 150 ans après Mendel

Foreword

The pioneering work by Gregor Mendel, published 150 years ago, opened an entirely new intellectual approach to study the behavior of traits put together in hybrids that, a few decades later, gave rise to a new scientific discipline called "genetics". Over the years, the discoveries of genetics have laid the most fundamental bases of our understanding of the living world, including us. The recognition of genetic factors as discrete elements rapidly designated *genes*, their susceptibility to abrupt changes or *mutations*, their precise location along chromosomes, their rules of transmission to the progeny and their action in the organism by virtue of the specific products that they determine, illuminated the first half of the 20th century and offered clear-cut heuristic rules to experimenters. If the seemingly endless variety of mutations explained the diversity of natural populations and their evolution, it also rapidly pointed out that the genes themselves were complex elements subsequently to be understood at the molecular level. At the same time, the fact that some traits in various organisms seemed to escape Mendelian rules of inheritance were early signs that the genetic material of a cell had a broader basis than its chromosomes and that the determinism of the phenotype by the genotype was more complex than the one-to-one relationship between a gene and a character. The discovery of organelle genomes and their inheritance, the presence of autonomous or mobile genetic elements, and the formation of complex metastable equilibriums in gene expression, now designated under the term epigenetic, retrospectively explain these apparent anomalies.

The elucidation of the structure of DNA in the middle of the 20th century, the central dogma of molecular biology in which RNA molecules played a role of intermediates for the synthesis of proteins and the elucidation of the genetic code offered the conceptual framework for the subsequent development of molecular genetics. Genes became molecular entities amenable to biochemical analysis and manipulations. DNA and RNA molecules became the tools for their own study, accelerating a virtuous circle of discoveries prone to reveal numerous surprises. The possibility to form DNA–hence the genes–from copies of RNA–the gene products–did upset the classical view of inheritance and evolution, when the fact that genes were in pieces raised questions about their origin and expression. The conceptual landscape was rapidly evolving, as cloning, cutting and pasting pieces of DNA molecules together with cellular transformation became universal methods. Genes became editable sequences using specific molecular tools, primarily enzymes that could themselves be engineered according to needs. Soon afterwards, the possibility to determine long DNA sequences opened unlimited fields of exploration of living organisms in normal or pathological conditions as well as the route to genetically engineer them. While DNA sequencing methods progressed, the sequencing of entire genomes became possible. More than a quantitative change, genomics brought a qualitative change to genetics. Rather than identifying genetic determinants of hereditary traits, genomics offered us, for the first time, the comprehensive description of the genetic make-up of an organism, containing all the determinants at the origin of its phenotype in the form of a sequence. The interpretation of such sequences is of course not simple, but the rapid progress in this field, including the sequencing of RNA molecules, has entirely remodeled our understanding of the nature, function, and evolution of the genetic material.

This Colloquium, based on presentations of their most recent results, conclusions, and prospects by 25 prestigious authors, will illustrate important trajectories of genetics today and will try to anticipate the immediate future. It will start by replacing the evolution of genetics in its historical perspective by reviewing the successive metamorphoses from the original Mendelism to molecular genetics, by illustrating the recent rise of genomics and its profound influence on many biological research fields and, finally, by discussing the late application of genetics to the field of plant development, a paradox given its origin. The colloquium will continue with four specialized scientific sessions. The first one will discuss the mechanisms of meiotic recombination and the diversity of sex determinisms, two bases of Mendelian genetics. It will also show the impact of the reproduction process on the evolution of

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natural populations and on the selection of domesticated plants and animals. The second specialized session will address the genetic diversity of populations, including the human one, showing how ancestral events can be reconstructed from their traces left in genomes and how a same trait may behave as monogenic or multigenic, depending on the sexual partner. The session will then illustrate an example of extreme gene fragmentation, raising the question of the origin of such structures, and terminate by exploring the mechanisms at the basis of natural or artificial evolution. The third session will be entirely dedicated to the applications of genetics for human health. Examples will show the impact of genetics to unravel the bases of complex diseases, and help cure them. The last update on gene therapy will be presented, as well as the most recent developments on cancer genomics and on the exploration of normal or pathological intestinal microbiomes. Finally, a short session will be devoted to genome engineering, with the history and developments of the recent programmable CRISPR-cas9 system, and the complete synthesis of artificial chromosomes in yeast. The colloquium will end with discussions on the expectations raised by the most recent developments of genetics, transgenesis and genome editing and the concerns they may raise. Between hopes and fears, the closing conferences will examine where the danger lies on scientific grounds and how to use genetic discoveries in the context of our individual and collective freedom.

Most of the oral presentations at this colloquium are included in this thematic issue. We thank the authors for their excellent contributions in due time, which has allowed its timely release.

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