

An exceptional friend

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In the summer of 1972, Ernst Hadorn convened in Zürich an especially interesting group of people. Hadorn was an embryologist. He had first studied the embryos of amphibians. However, in face of the difficulty of analyzing with this material the genetic factors of development, he shifted to *Drosophila*. He then did a very remarkable work on imaginal disks. He showed that imaginal disk cells could be grown in the abdomen of adult flies without losing their specific commitment to a particular differentiation. If, after many passages in adult flies, imaginal disk cells were injected in larvae, they underwent differentiation at the time of metamorphosis. This differentiation corresponded to what was expected from that disk. There were some good reasons to believe that differentiation is under genetic control.

This was the time when molecular genetics had exploded in the study of bacteria and viruses. Higher organisms, however, were not amenable yet to such an analysis. In order to try to fill the gap between the genetic study of bacteria and that of *Drosophila*, Hadorn had invited about fifteen *Drosophila* people and fifteen molecular biologists. Each team told its own story, trying to be simple and to be understood by the other. Between both groups, however, a large gap remained. Nobody then could foresee the way to use, in *Drosophila*, the tools that had proved to be so efficient in bacteria.

Among the *Drosophila* people who attended this meeting, there was quite an unusual young fellow. Medium size, dark hair, dark eyes, he spoke at the speed of a machine gun with a strong Spanish accent, a mixture which, for me, made his speech very difficult to

understand. Antonio García-Bellido was an indefatigable talker at every opportunity. A tireless storyteller able to discourse for hours. To deliver long monologues on every conceivable subject. Science, politics, economy, philosophy, literature, anything that cropped up. But always in a very original and imaginative way. Antonio's imagination, I could recognize later on when we became very good friends, was exceptional. Antonio chose to be a scientist. He could just as well have been a very successful historian, an art critic, or a writer.

However, he is a scientist and it is in science that he exerts his imagination. Having decided to work on insects, he managed to receive, in various places, the best possible education: physiology in Cambridge with W.B. Wigglesworth, embryology in Zürich with Hadorn, genetics in Pasadena with A.H. Sturtevant and E.B. Lewis. He had always been convinced that embryology and genetics, which remained too long separated, had to merge on a common ground and that this common ground could only be the cell. For him, the action of any gene involved in development had therefore to be analyzed at the cellular level. Only at this level did it seem possible to understand how the genome, present in every cell, determines the specific behavior and the differentiation of the cells as well as the way in which these cells get organized in supra-cellular systems.

Actually, in the last twenty five years or so, Antonio García-Bellido has been a constant source of new ideas and new data. The amount of new concepts he has contributed to developmental biology can only be compared to his outstanding experimental

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results. Experiments of cellular dissociation and reassociation allowed him to demonstrate cell autonomy and to show that the effect of a gene is most often limited to the cell and its neighbors. By clonal analysis of mosaics, in particular in the *Drosophila* wing, he discovered the existence of developmental decisions generally taken by small groups of cells. Such decisions lead to the formation of compartments of polyclonal origin, which are maintained in the cell progeny. The successive segregation of cell lineages allows a combinatorial determinism by the use of a limited number of regulatory genes. The homologies found in other organisms (nematodes, vertebrates) show that this is a general strategy for the genetic determinism of development.

Among the key concepts proposed by García-Bellido, the following could be cited in particular: the notion of a hierarchy of regulatory genes, with activator, selector and realizator genes; the existence of transregulator genes and the use of dosage effect for their detection; the use of absence or excess of a gene to deduce its function; the analysis of supracellular processes (position information) in local terms (communication between a cell and its neighbors). All these ideas are now used by many scientists all over the world.

Recently, Antonio García-Bellido was among the first to realize the tremendous change occurring in the biological landscape. This change stems from the discovery of the extraordinary conservation

of gene structures associated with functions since Precambrian times. In particular, Antonio pointed out the role of genes ensembles which he called "syntagmata" which remain together and performed high order operations. The existence of such ensembles, which can be used again and again in different contexts, as well as the modular nature of development suggest that one should be able to dissect biological complexity into invariant operations. As stressed by Antonio, it becomes possible for the first time to envisage a large synthesis linking evolution and embryonic development.

On several occasions, Antonio took me on long trips throughout Spain. The son of a historian, he loves Spain as he loves to show his friends his country, its history and its art. In a small village of Andalousia, he can talk for hours about the fights between Christians and Arabs that took place there some centuries ago. He can describe the history of the place, tell which king spent some time in this castle, report under which conditions the mosque and the church were built. He also knows why this particular garden exhibits this particular configuration with these particular trees and flowers. On all these subjects, he can talk endlessly and obviously with an extreme pleasure.

Antonio García-Bellido is not only a very exceptional scientist. He is also an exceptional human being. For me, he is above all an exceptional friend.