

Antonio García-Bellido at Hadorn's laboratory in Zurich

ROLF NÖTHIGER*

Zoological Institute, University of Zurich, Switzerland

Antonio crossed my way, literally, in the early 1960's when we bumped into each other in the corridor of the "Zoologisch-vergleichend anatomisches Institut der Universität Zürich", he as a postdoc and I as a graduate student in Ernst Hadorn's laboratory. From this early encounter developed a friendship that still lasts.

Antonio selected Zürich because he wanted to work with Hadorn who was then the leading developmental geneticist in Europe. A few years earlier, Hadorn had published his famous book *Developmental Genetics and Lethal Factors*, still worth reading and not only for historical reasons. In this monograph (Hadorn, 1961) he summarized what was mainly his laboratory's work and what led to the profound insight that genes are called into action at different times of development and that different genes are active in different tissues. This was a clear and important step forward, away from the "simple" laws of how genes are transmitted from one generation to the next, towards the much more complex problem of how genes function in development. This work won Hadorn worldwide recognition which culminated in his election as President of the XI. International Congress of Genetics in 1963 in the Hague.

Another, perhaps even more attractive topic for Antonio were Hadorn's analyses of the imaginal discs, in particular the phenomenon of cell determination. Hadorn had entered this new field while still working with lethals. "The choice of the object was perfect", as Dietrich Bodenstein formulated it in his preface to the book *The Biology of Imaginal Discs* which his students, friends and collaborators dedicated to Hadorn on the occasion of his 70th birthday in 1972. Hadorn and his group had constructed fate maps of discs by cutting

these into defined fragments. The developmental fate of these fragments was assayed by transplanting them into larval hosts with which they then underwent metamorphosis and formed cuticular structures. The experiments revealed the mosaic character of the discs: specific imaginal structures could be assigned to specific regions within a disc. Hadorn wanted to go deeper and pushed this analysis to the limits of resolution by testing single cells or small groups of cells for their developmental potential, or state of determination. Two papers had just appeared that studied the fate of dissociated and reaggregated cells of wing imaginal discs (Hadorn *et al*, 1959; Ursprung and Hadorn, 1962). At about the same time, the phenomenon of transdetermination in cultured fragments of imaginal discs was about to be discovered (Hadorn, 1963).

Hadorn's laboratory was boiling with excitement and was a Mecca for young and ambitious scientists. And Antonio was both, young and ambitious. He plunged into this atmosphere with his initiative and ardor and became soon an active participant or even a promoter. He and his wife Maria-Paz formed a team, working long hours and with great and infectious enthusiasm.

The list of publications from those years reflects Antonio's past and future interests. Coming from the laboratory of Sir Vincent Wigglesworth, he was still interested in physiological problems, such as growth and differentiation of larval testes cultured without metamorphosis in adult flies (García-Bellido, 1964a,b;1965a,b). He showed that spermatogenesis proceeds normally despite a somatic testis sheath that remains larval. His favorite tissue, however, were the paragonia, the accessory glands of the male genital tract. I remember him saying: "when I am older, I will study the paragonia because they

*Address for reprints: Zoological Institute, University of Zurich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland. FAX: (0)1 / 635 68 17. e-mail: rolnot@zool.unizh.ch

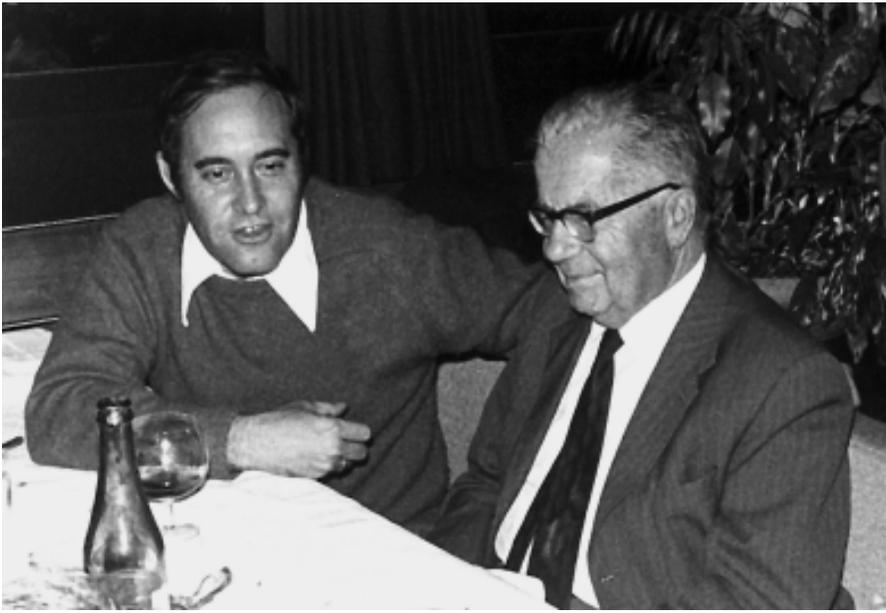


Fig. 1. Antonio Garcia-Bellido and Ernst Hadorn in a relaxed discussion during a dinner party in December 1975 in Zurich. Hadorn died only 4 months later on April 4, 1976.

are a fascinating tissue full of wonderful phenomena!" He was right: the sex peptide, isolated from the paragonia, became a paradigm of a small peptide hormone that acts as a sex pheromone to control the female's behavior in the interest of the male (reviewed by Kubli, 1996). Antonio's publication (García-Bellido, 1964b) can be considered as a seminal paper in this area of research.

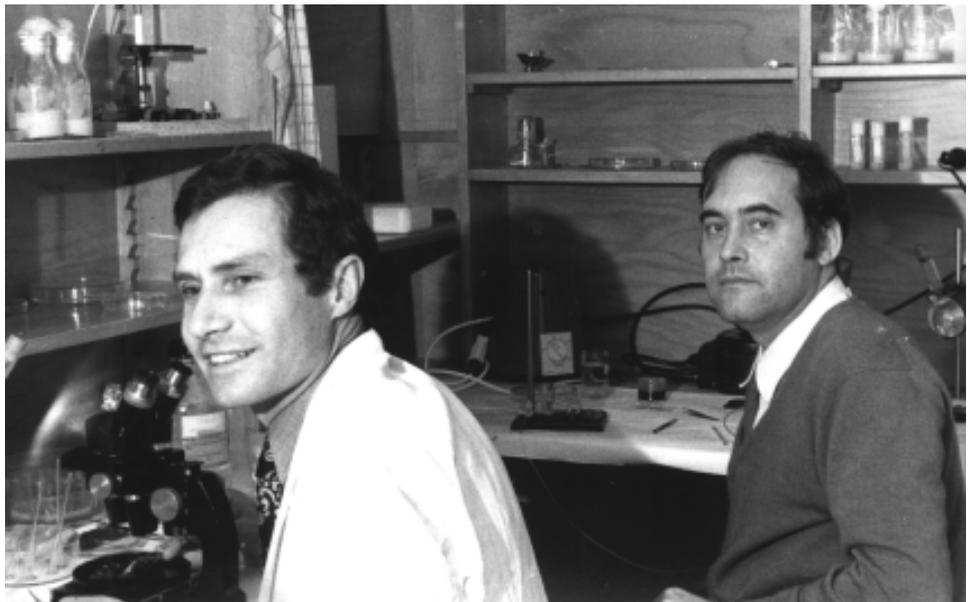
The real topic, however, to which Antonio adhered throughout the rest of his career, was the problem of cell heredity and cell determination in imaginal discs. Hadorn and his collaborators had observed that aggregates of cells isolated from different genetically marked wing discs formed integrated patterns, e.g., a typical anterior wing margin composed of yellow and ebony bristles. They interpreted their results as a consequence of "epigenetic pattern formation in field districts", -today a rather cryptic phrasing, implying extensive developmental flexibility of the isolated cells. It is typical of Antonio's analytical mind and his capacity to "smell" where the real problem is: Hadorn, Anders and Ursprung had mixed whole discs and would thus fail to catch possible regional differences in cell affinities. Therefore, Antonio combined cells from different regions of a disc (García-Bellido, 1966a,1967). Already in 1966 (García-Bellido, 1966b), he noticed that in combinations of isolated cells from proximal and distal regions, or from anterior and posterior regions, of the wing disc, the two components did not form integrated patterns and differentiated strictly according to their regional origin. He concluded that "the isolated cells pos-

sess a definite determination for regional qualities", and that "the determined cell possesses some kind of positional information which characterizes it as a cell in a certain place in a given pattern", -in a compartment?-, we are tempted to ask. Yes, here is the compartment hypothesis anticipated in the terms of those times! When Hadorn learned about these results that contradicted his earlier interpretation, he replied: "That's great, I am not married with my hypotheses!" The concepts still remained somewhat mystical, described in terms such as "fields" and "field properties", "internal field organization" or "field districts". It required the sophisticated use of genetics and the ingenious application of the technique of genetic mosaics with homeotic mutations to drive the analysis to an experimental approach that became eventually so successful. The contributions of Antonio and his laboratory in this endeavour are substantial and undisputed.

Memories of Antonio in Zürich would not be complete without some personal episodes. In those days, Antonio spoke German fluently and also published in German (García-Bellido, 1964a,b,1965a,b). I remember an occasion where I needed a witness in a kind of legal affair without my opponent knowing that the third person who happened to be around understood Swiss German. The trick worked, and my opponent had to admit defeat when Antonio at the end added in German "*Ich habe alles verstanden, Sie haben verloren*". ('I understood everything, you lost')

When Maria-Paz became pregnant, we asked Antonio whether he expected a boy or a girl. Without hesitation, he replied "The first one must be a man!", and with no doubt in mind, he deposited only a boy's name in the hospital where Maria-Paz was to give birth to their

Fig. 2. Antonio (right) and Rolf Nöthiger at the bench in Zurich in 1975.



first child. It appeared impossible to his mind that the outcome could be different. Fortunately for the child, he was right: his first son Antonio was born in Zürich in 1963.

Ever since then, Antonio returned to Zürich again and again, for shorter or longer periods (García-Bellido and Nöthiger, 1976). Antonio's flamboyant discussions are not always relaxing, but always stimulating. I cannot imagine that he will ever get tired developing hypotheses, speculations and ideas. In November 1975, he wrote in my guest book: "We leave again the main discussion for the next time!"

Antonio, thank you for all you gave to me and to Developmental Genetics!

References

- GARCIA-BELLIDO, A. (1964a). Analyse der physiologischen Bedingungen des Vermehrungswachstums männlicher Keimzellen von *Drosophila melanogaster*. *Wilh. Roux's Arch.* 155: 611-631.
- GARCIA-BELLIDO, A. (1964b). Das Sekret der Paragonien als Stimulus der Fekundität bei Weibchen von *Drosophila melanogaster*. *Z. Naturforsch.* 19b: 491-495.
- GARCIA-BELLIDO, A. (1965a). Beziehungen zwischen Vermehrungswachstum und Differenzierung von männlichen Keimzellen von *Drosophila melanogaster*. *Wilh. Roux's Arch.* 155: 594-610.
- GARCIA-BELLIDO, A. (1965b). Larvalentwicklung transplanteder Organe von *Drosophila melanogaster* im Adultmilieu. *J. Insect Physiol.* 11: 1071-1078.
- GARCIA-BELLIDO, A. (1966a). Changes in selective affinity following transdetermination in imaginal disc cells of *D. melanogaster*. *Exp. Cell Res.* 44: 382-392.
- GARCIA-BELLIDO, A. (1966b). Pattern reconstruction by dissociated imaginal disc cells of *D. melanogaster*. *Dev. Biol.* 14: 278-306.
- GARCIA-BELLIDO, A. (1967). Histotypic reaggregation of dissociated imaginal disc cells of *D. melanogaster* cultured *in vivo*. *Wilh. Roux's Arch.* 158: 212-217.
- GARCIA-BELLIDO, A. and NÖTHIGER, R. (1976). Maintenance of determination by cells of imaginal discs of *Drosophila* after dissociation and culture *in vivo*. *Wilh. Roux's Arch.* 180: 189-206.
- HADORN, E. (1961). *Developmental Genetics and Lethal Factors*. Wiley, New York.
- HADORN, E. (1963). Differenzierungsleistungen wiederholt fragmentierter Teilstücke männlicher Genitalscheiben von *Drosophila melanogaster* nach Kultur *in vivo*. *Dev. Biol.* 7: 627-629.
- HADORN, E., ANDERS, G. and URSPRUNG, H. (1959). Kombinate aus teilweise dissoziierten Imaginalscheiben verschiedener Mutanten und Arten von *Drosophila*. *J. Exp. Zool.* 142: 159-175.
- KUBLI, E. (1996). The *Drosophila* sex-peptide: a peptide pheromone involved in reproduction. In *Advances in Developmental Biochemistry*, Vol. 4 (Ed. P. Wassarman). JAI Press, New York, pp. 99-128.
- URSPRUNG, H. and HADORN, E. (1962). Weitere Untersuchungen über Musterbildung in Kombinate aus teilweise dissoziierten Flügel-Imahinalscheiben von *Drosophila melanogaster*. *Dev. Biol.* 4: 40-66.