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ERI MANELLI *

Continuity of the living, from ontogenesis to phylogenesis

Historical introduction

The title of this seminar may be considered as a different way to define all the research and results, which constitute the biological field usually indicated as "Evolutionary developmental biology" (EDB) or "evo-devo", as taught in several universities abroad.

This biological field would like to shape and give trust to the concept that developmental biology (embryology, or the study of ontogenesis) and evolutionary biology (especially in the sense of study of phylogenesis) constitute a *continuum*.

We will focus today on the continuity of the living belonging to the animal kingdom but I believe that many aspects of animal development and evolution are shared by plants.

Evolutionary developmental biology must be considered mainly as a new area of research, although its origin can be traced back to the XIX century. R. Owen (1841), referring to the way in which the form of an animal body part can be modified into another, believed that the possible reasons for these modifications were either external and impressive or internal and genetic, thus highlighting the environmental and the genetic effects, respectively.

While speaking of Owen, we cannot forget other great biologist of the same century like Darwin, Haeckel, Von Baer, Mendel, Dohrn and many others.

Darwin had the dazzling idea of natural selection (1859) through which he created the basis for an understanding of the evolutionary process, although he failed to link it to the embryonic development. Haeckel and Von Baer compared ontogenesis and phylogenesis but from two different point of views: in fact, while Haeckel decribed ontogenesis as a summary of phylogenesis (this axiom,

* Uno dei XL.

pompously defined law and suddenly become famous, was proposed indeed by Fritz Müller, possibly before Haeckel!),Von Baer denied recapitulation, since development is individualization and proceeds from the general to the special, that is, it is an actual differentiation of something unique from an initial common stage.

Von Baer's statements raised a great deal of interest at that time, they were quoted and supported by various scientists and above all by Darwin. Nevertheless, perhaps because of Haeckel's academic importance and the fame of his school, Von Baer's ideas vanished very soon.

In our days, biologists have rediscovered and re-evaluated this doctrine and in this context Gould (1977) affirmed: "It is difficult for scientists to ignore the anachronistic influence of Von Baer's success since his laws, in renewed evolutionary features, are now more widely accepted than any previous formulation and his descriptions mark the beginning of molecular embryology", and defined Von Baer's contributions "probably … the most important in the field of embryology".

Dohrn contributed greatly to advance our knowledge of embryonic stages, larvae, and possible primitive ancestral forms, all key elements of phylogenesis. With this aim, he founded first a small zoological marine station in Messina and subsequently a more important one in Naples. Many researchers mainly from Europe and the USA, worked at zoological station in Naples from 1870-1950. Among them there were embryologists and zoologists of various animal groups.

More than 17 Nobel laureates worked at the Naples Zoological station, most of them devoting themselves to the study of the embryonic development, rather than to evolution.

Even after the rediscovery, early in the XX century, of Mendel's laws by botanists such as Tshermak, De Vries, Correns, the relationship between ontogenesis and phylogenesis was not be pursued any further. In fact, starting in 1910-20, the study of embryonic development, was approached with experimental methods, first morphological, then chemical and biochemical, and more recently with molecular technology but without considering the phylogenetic aspect. In some ways the two processes were considered, to a few exceptions, more distantly related than they were in the XIX century.

Let's now pass on to a short chronology of research and discoveries leading to the "construction" of EDB.

From my point of view, the scientific event that is at the root of EDB is the conference that took place in St. Louis, in June 1946, during which the "Evolution Society" was founded. Fifty years later, in 1996, E. Mayr stated that the objective of this Society was to "promote the study of organic evolution and the integration of various fields of biology".

As far as researchers are concerned, we can start with C.H. Waddington (1940-50), with his concept of development canalization, integrated with genetic assimilation, and go on to L. Wolpert (1989), to whom we owe the notion of positional information.

After the 1960s and 70s, embryologists and geneticists privileged a few "model" animal species, in particular two invertebrates, *Drosophila* and *Caenorhabditis elegans*. *Drosophila*, in particular, once used as an experimental model for mutation and population genetics, became the first important model in developmental genetics.

Among the first researchers in developmental genetics of *Drosophila*, worth special mention is A. García-Bellido (1973), to whom we owe the discovery of compartments, regions of the embryo in which are confined all cellular clones deriving from the proliferation of an initial pool of founding cells (In *Drosophila*, these compartments are equivalent to either the anterior or the posterior part of a segment).

What followed was the molecular identification and characterization and the study of the expression of different classes of developmental genes (gap genes, pair-rule genes, segment polarity genes, homeotic genes), still in *Drosophila*. For these discoveries, E. Lewis, Ch. Nüsslein-Volhard and E. Wieschaus received the Nobel prize in 1996.

In the '80s, W. Gehring contributed greatly to the study of the function of the homeotic genes, with the discovery of the homeobox . Later (1998), he will introduce the notion of the master control gene, applicable, for example, to *Drosophila* and mouse. These genes seem to be at the top of a "cascade" of processes ending with the realization of a very complex structure like the eye (professor Barsacchi will discuss this subject in her talk) while the *tinman* gene and its homologous, hold a similar position in relation to the realization of the heart in the most different animals.

In the light of these elements the question arises whether or not a common structure exists for all animals, depending on the expression of a limited number of development genes.

Slack, Holland and Graham were the first to point towards this direction and to publish, in 1993, in the magazine *Nature*, a "commentary paper" where they introduced the concept of the zootype, the basic scheme of the anterior-posterior axis organization for all animals, or at least for those having bilateral symmetry (which are by a long way the most numerous). Soon later, when there will be evidence that homologous genes of very different animals, like a mammal and an insect, are responsible for the production of equivalent organs (like the eyes, of the mouse and the fruit fly), despite their obvious differences will take shape the notion of *Urbilateria*: emerged, as that of the hypothetical ancestor, common to all animals with bilateral symmetry, and three-layered, from whom they should have inherited all those genes responsible for the basic plan of body architecture.

In this way, it seems even possible to find a solution to some old big problems of comparative anatomy, like the apparent contrast between the vertebrates, with their main nervous axis on the dorsal side, and the insects, provided with a ventral ganglionic chain. In the two groups, the dorsal-ventral polarity seems to be controlled by the same genes, as first remarked by K. Nübler-Jung and D. Arendt (1987-96).

These researchers, like C. Nüsslein-Volhard and W. Gehring, come from the school of K. Sander, a leader of the experimental embryology of insects in the 1970s and '80s. This school developed in the University of Freiburg i.Br., where previously seated world-renowned biologists like A. Weismann (1873-1912), H. Spemann (1919-37) and O. Mangold (1937-55). It is Sander who developed the concept of phylotypic stage, i.e. a characteristic ontogenetic stage, through which pass, during their development, all animals of a given *phylum*. An example could be the *pharyngula* of vertebrates or the germ band stage of arthropods.

The notion of phylotypic stage represents the bottleneck through which must pass the ontogenetic pathways of animals belonging to the same *phylum*, regardless of what happens before or after that stage, i.e. regardless of the way in which proceed the first phases of the development or the latest, which largely depend on the type of egg from which development starts.

Many other researchers contributed in a decisive way to the progress of the developmental genetics of *Drosophila*: for example, P. Lawrence and M. Akam (1980-1998). M. Akam also started a comparative approach involving other arthropods. On the same line – fundamental for the starting of the modern "evo-devo" biology – are the important works of S. Carrol (1995-2000), N. Patel (1992) and D. Tautz (1992).

In vertebrates, chicken, mouse and amphibians (*Xenopus*) remained for some time the most used experimental models. This until the 1980s, when research on zebra fish (*Danio rerio*) begins. The advantage of this little fish is its transparent embryo. Initially used in the field of developmental genetics by researchers in Oregon, towards the mid 1980s it underwent a total screening, in a search for mutants of genes with possible effects on development (Nakaido *et al*., 1997).

In the meantime, another invertebrate takes over the nematode *Caenorhabditis elegans*. The reasons for this choice are different: the reduced number of cells (about 1000) forming the adult, the constancy of the cell number in the species, the constancy of the cellular genealogy from which they originate. S. Brenner, J. Sulston and R. Horwitz received the Nobel prize in 2002 for their studies on the developmental genetics of this little worm.

Other experimental researches on vertebrates are strictly linked to the contributions, also theoretical, of B.K. Hall, N. Shubin, C. Tabin, G. Wagner and D. Wake (1990-2000). The work of these authors gives rise to animated debates on basic issues like homology, heterochrony and heterotopy (W. Arthur also speaks of heterotypy and heteromery) as well as on equally important problems like the origin of body appendices, the evolution of the hand and the origin of the brain.

More classical experimental models, like the sea urchin, are still fashionable in other researchers' laboratories, like those of R. Raff and G. Wray (1990-2002), or E. Davidson (1990-1997), who develops a new interpretation of marine invertebrate larvae and their metamorphosis. Davidson's interpretation of developmental mechanisms is based, like most of those proposed during the last few years, on an accurate study of the role of the different classes of so-called "developmental genes" in the process of evolution.

Nevertheless, some researchers don't agree completely with this gene-centred approach, first of all F. Nijhout (1990-2001), who carried out many studies on the metamorphosis of insects and on the origin and evolution of the "drawings" on the butterfly wings.

The role of genes in development is downplayed by researchers operating in fields other than genetics or molecular biology. A supporter of a view that we could define as "structuralist" is B. Goodwin (2000), who tends to de-emphasize the importance of genes as essential factors in morphogenesis, placing first the effects of "generic properties" of the living matter, which could be related to very general physical principles.

Finally, there are mathematicians who are interested in biology, like the French topologist R. Thom, who died in 2002. In 1972, he published the book "Structural stability and morphogenesis", based on the catastrophe theory.

The success of the "evo-devo" biology is also marked by the publication of specialized magazines, like "Evolution and Development" started in 1999 or the new section in the "Journal of experimental Zoology" which, in the same year, appears with the subtitle "Molecular and developmental Evolution". Moreover, the glorious journal founded by W. Roux in 1896 "Archiv für Entwickelungs-mechanik", later known with the English title "Roux's Archives of developmental Biology" has been recently renamed "Development, Genes and Evolution".

I would like to mention some books published during the last few years, in particular "The origin of animal body plans" (1977) by W. Arthur, "Evolutionary developmental biology" by B.K. Hall (1998), "The evolution of developmental pathways" by A. Wilkins (2002) and "The development of animal form" by A. Minelli (2003).

I believe that some statements by B.K. Hall could conclude my talk: EDB, or "evo-devo", must be considered not only as the merging of the traditions in onto-genesis and phylogenesis research, but rather as something more. Indeed, it leads to the unification of the genetic, ontogenetic, organismic and natural selection approaches with the actual phylogenetic change. It therefore concerns the ways by which developmental process evolves and the ways by which evolution produces new structures, functions and behaviours. Therefore, EDB also involves the ways by which development, evolution and ecology merge, thus allowing and stabilizing evolutionary change.

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* Citations are limited for only a few authors whose works regard specifically EDB and are mentioned in this historical introduction.