n.le douarin editor

cell lineage, stem cells and cell determination

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CELL LINEAGE, STEM CELLS AND CELL DETERMINATION

Proceedings of the International Workshop on Cell Lineage, Stem Cells and Cell Determination held in Seillac, (France), 20-24 May, 1979.
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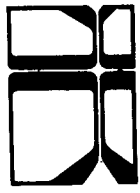

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PREFACE

This book contains the proceedings of an International Workshop, held in May 20-24, 1979 in Seillac - France, the aim of which was to assemble scientists from different fields such as Embryology, Hematology and Neurobiology, who shared a common interest in problems related to cell commitment, stem cell properties and cell line segregation. Such subjects, which have always been at the centre of the preoccupations of Embryologists, are of added topicality in view of recent advances in the field of hematology, since the blood-forming system offers particularly suitable models for the study of stem cells functions as well as cell line commitment and differentiation. The methods used to analyze hemopoietic differentiation and the results obtained in this area appeared of considerable relevance for scientists dealing with the more complex problems raised by cell diversification in the embryo itself.

In addition to articles concerned with hemopoiesis, the segregation of cell lines and the stability of the determined state are discussed with reference to various embryonic systems and to the model provided by the mouse teratocarcinoma. In the development of the nervous system, the subjects selected deal with the modulation of both architectural and biochemical differentiation of nervous tissue by environmental factors.

The Scientific Committee of the Workshop, Nicole Le Douarin, Alberto Monroy, Walter Gehring and Fritz Melchers, wish to thank l'Institut National de la Santé et de la Recherche Médicale, the European Molecular Biology Organization and the International Society of Developmental Biologists for their help and support which made this workshop possible.

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STABILITY OF THE DETERMINED STATE

SEGREGATION OF CELL LINES, AN EARLY DEVELOPMENTAL EVENT

Cell Lineage, Stem Cells and Cell Determination
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INTRODUCTORY REMARKS ON THE SEGREGATION OF CELL LINES IN THE EMBRYO

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In all multicellular organisms, the cleavage of the egg gives rise to cells which differ from one another and which, through successive cell divisions, will eventually give rise to homogeneous cell populations (cell lines) each endowed with its own specific developmental program. This not only implies a process of sorting out of molecules (either pre-existing in the egg before fertilization or being synthetized in the course of development) into the various blastomeres; but also of cells recognizing one another and coordinating their movements, their rate of cleavage, their metabolic activities, and the like.

In this Introduction I shall discuss some examples drawn from our work and from the work of other Laboratories to direct attention to some of the events which I consider as among the most important not only in connection with the segregation of cell lines but indeed with embryonic development as a whole.

Before entering into the subject, I would like briefly to present some speculations on the phylogenetic history of the segregation of cell lines in multicellular organisms.

We have recently suggested (Monroy and Rosati[1]) that one of the major events, if not *the* major event, connected with the appearance of multicellular organisms is the segregation of the somatic from the germ cell line. We have postulated that the dichotomy between the two cell lines involves:

(a) That in the somatic cell line, the genes which in the unicellular organisms code for the surface structures responsible for the recognition of and interaction between cells of the two gametic types, are silenced. The evidence for this is indirect. Although to our knowledge the matter has never been investigated with this question in mind, the formation of mouse chimaeras (Tarkowski[2]; Mintz[3]; see also review by Herbert and Graham[4]) shows that genetically male and female embryonic cells do not discriminate one another as dif-

ferent. Also, hybrid hystotypic aggregates can be formed in culture from such species as far apart as chick and mouse (Moscona[5]; Moscona and Moscona[6]). (However, the possibility should be taken into consideration that *in vitro* conditions may alter the organization of the cell surface in such a way that some of its properties such as the species-specificity are lost while the tissue-specificity is retained). These observations are compatible with the view that the structures discriminating between male and female are not expressed at the surface of these cells.

(b) The retention of a largely derepressed genome by the cells of the germ line. This is inferred from the fact that in the oocyte, the complexity of the transcripts is several-fold greater than in the somatic cells (see e.g. Galau et al.[7]). Although to our knowledge there is no such direct evidence in the case of the male germ cells, it has been shown that at least in *Drosophila*, spermatocytes exhibit lampbrush chromosomes comparable to those of the oocyte (Hess[8]).

In addition, we would like also to argue that the emergence of multicellular organisms has required the establishment of cell junctions; not only as a means of holding the cells together, but as a vehicle of functional coordination between cells (Monroy et al., unpublished).

A classical example of a very precocious segregation of the somatic from the germ line is that of *Ascaris* first described by Boveri[9] (Fig.1). In this nematode while the lineage cells of the germ line retain their full chromosome complement, in the cells of the somatic line pieces of chromosomes are lost; the loss amounts to about 27% of the total DNA of the cell. Interestingly, about one-half of the eliminated DNA consists of repetitive sequences and the other half of unique sequences (Tobler et al.[11])

Chromosome elimination is a frequent occurrence in Hemiptera; one of the most interesting cases is that of *Sciara*, first described by C.W.Metz (see review[12]). In *Sciara coprophila* the zygote carries three X chromosomes, one contributed by the egg and two by the spermatozoon (this results from an equational non disjunction of the maternally derived X chromosome at the second meiotic division in the male following the selective elimination of paternal homologues at the

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