

## On the present situation of Developmental Biology in France

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Developmental Biology, an outgrowth of traditional embryology now tightly linked with modern molecular genetics, has seen considerable growth during the second half of this century. The historical aspects of its evolution in France since the 1890s will be related in detail by Dr. J.L. Fischer. Here I shall try to give an account of the present – somewhat complex – situation that has arisen relatively recently following a period of geographical concentration.

During the early 1950s, developmental biology in France was closely linked to the experimental study of sex differentiation and teratogenesis in vertebrates. Two distinguished University professors were prominent in these specialized fields: Louis Gallien in Paris for frogs and newts, and Etienne Wolff in Strasbourg for birds. After having been elected to the Chair of Experimental Embryology, E. Wolff subsequently moved to the Collège de France in Paris with a group of collaborators, including P. Sengel and T. Lender.

Most of the scientists working under Wolff's direction were soon established in a suburban laboratory of the Collège de France in Nogent sur Marne, which became the Institute of Experimental Embryology and Teratology, under the auspices of the National Council for Scientific Research (CNRS). This is now the Institute of Cellular and Molecular Embryology of both the CNRS and the Collège de France. In the late 1950s, the creation of an embryology laboratory headed by L. Gallien at the University of Paris, with a concomitant recruitment of enthusiastic young researchers, led to a rapid diversification of research topics in both laboratories. Trained embryologists then migrated from Paris to provincial Universities. For example, J. Cl. Beetschen, a former student of Gallien,

moved in 1960 to Toulouse University where he initiated work on the developmental biology of amphibians in the General Biology laboratory. P. Sengel, vice-director of E. Wolff's laboratory, obtained a professorship in Grenoble in 1964, and transformed most of the Zoology Laboratory into a center for developmental biology. He was later joined by P. Chibon, also from Gallien's laboratory. Similarly, J. Signoret created an embryology laboratory in Caen, and A. Capuron moved from Paris to Lille, introducing amphibian embryology into a department mostly devoted to the biology of annelids under the direction of M. Durchon. An experimental embryology group and a physiological laboratory were created in Nantes in the early 1970s by Nicole and Georges Le Douarin, respectively, both of whom had come from E. Wolff's laboratory.

At the same time, specialists in the regeneration of annelids were active in Marseille (Marcel Abeloos) and Bordeaux (Marcel Avel). In the latter University, experimental embryology in amphibians and insects was also developed in the 1950s along with the endocrinology of reproduction in insects (Jean-Jacques Bounhiol). It is of interest that arthropod endocrinology became a most active field of research in France at this time. The reproductive endocrinology of annelids was investigated in Lille by Maurice Durchon. Although these fields have special relationships with developmental biology, they will not be considered in this volume.

In recent years, research on cell differentiation has been expanding at a rapid pace, and now represents the activity of hundreds of investigators, although it tends to be pursued outside the holistic framework of traditional developmental biology. Some examples of

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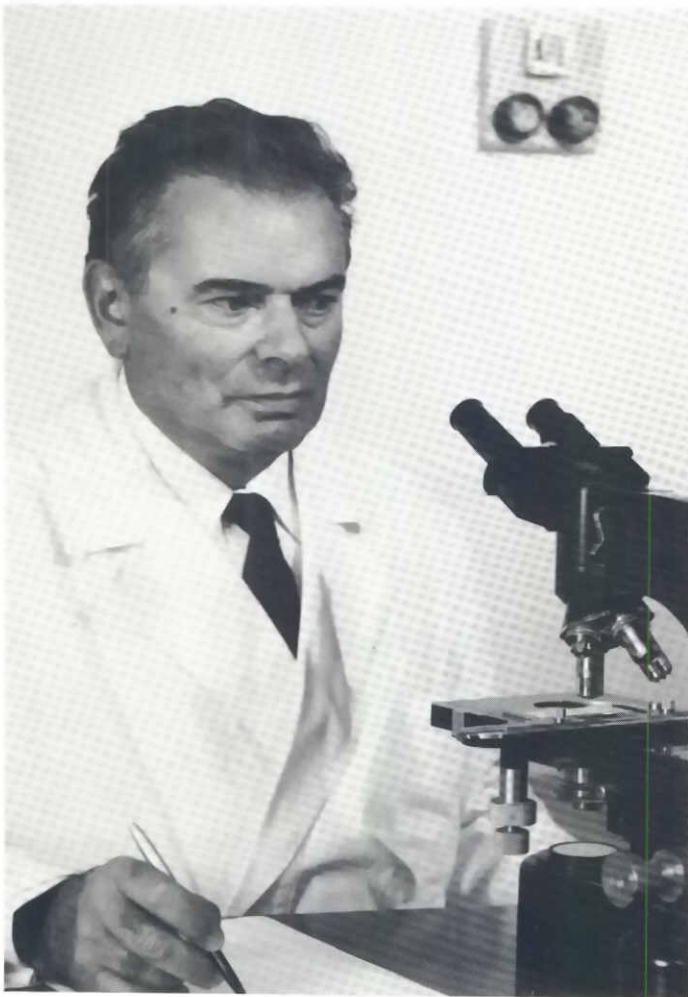


Fig. 1. Professor Etienne Wolff (b. 1904) in 1967.

these approaches will be included in this volume.

Returning to the changes that have taken place in developmental biology in France during the last thirty years, the foundation of new laboratories in a number of French Universities was a direct consequence of the renewal of the biological curriculum during the 1960s, a period during which many new Universities were built, and when many younger embryologists obtained Professorships. The present situation has stemmed from these developments. Paradoxically, experimental embryology ceased to be taught as a separate discipline in the Collège de France when Professor E. Wolff retired, in 1975. But a professorship of Cellular and Molecular Embryology was again created in 1989, and Nicole Le Douarin, a former student of E. Wolff and the present head of the Institut d'Embryologie, gave her inaugural lecture last October. During the intervening period, other eminent scientists teaching in the Collège de France and working in the Institut Pasteur gave lectures on related topics, including developmental cell genetics (François Jacob), molecular biology of cell differentiation (François Gros) or neurobiology (Jean Pierre Changeux).

It is noteworthy that the Institut Pasteur in Paris became a new

center for developmental biology of the mouse when F. Jacob decided in the 1970s to move from investigation of prokaryotic gene regulation to research on genetical problems of mammalian early development. Three separate laboratories are now working on this topic in the Institut Pasteur.

The link between the Institut Pasteur and the Collège de France has also benefited high-level science teaching. Elsewhere, the various Paris Universities harbor several laboratories or Institutes, either partly or wholly devoted to developmental biology. Among the most recent University appointments, a former collaborator of F. Jacob, Hubert Condamine, who works on homeogenes, has recently been elected as a professor of developmental genetics at Paris VII University. Paris VII already included a strong University-CNRS organization, the Jacques Monod Institute, for biochemistry, and cell and molecular biology. Several groups are active in the developmental biology of *Xenopus*, *Drosophila* and mouse in this Institute, which is directed by a biochemist, François Chapeville.

Close to Paris VII, Pierre and Marie Curie (Paris VI) University, where Gallien's "Laboratoire d'Embryologie" was split into smaller units after his death in 1977, remains one of the main centers for developmental biology in France. Several of its groups are associated with the CNRS. Both of these Universities include laboratories for developmental biology and developmental genetics. Many laboratories of animal and experimental biology and physiology are also interested in developmental biology. The embryology and immunology of amphibians and fish are the main topics investigated at this central Paris campus. C. Aimar, J.C. Boucaut, H. Boulekbache, J. Charlemagne, A. Collenot, C. Houillon, J.C. Lacroix and R. Ozon will be cited here, most of whom were collaborators of Gallien. In the largely medical René-Descartes University (Paris V), a laboratory of developmental biology also works on animal models (C.L. Gallien).

Mention should be made here of a basic aspect of the scientific community in France. The two big national research organizations, the above-mentioned "CNRS" and "INSERM" (Institut for Health and Medical Research), have long been involved in the expansion of biological disciplines. The CNRS created a few large specialized centers ("Unités de Recherche Propres"), but also established numerous associations with University laboratories ("Unités de Recherche Associées"). These contractual associations are revised every 4 years, and new ones are only set up in the event of non-renewal of contracts. Full-time research scientists and technical assistants appointed by the CNRS work together with faculty members in the same URPs or URAs.

At the present time, around 10 CNRS units are entirely devoted to reproductive physiology and developmental biology. A larger number are involved in these areas if one counts members of a group working on cellular or molecular biology (e.g. Centre de Génétique moléculaire in Gif sur Yvette and Laboratoire de Génétique moléculaire des Eucaryotes in Strasbourg).

A similar policy is applied by INSERM in various hospital and University laboratories. At least 12 INSERM units are involved in human and mammalian reproduction and developmental biology, including research on *in vitro* fertilization, chromosomal anomalies, fetal endocrinology, neurobiology, muscle and skeletal differentiation, etc.

A few special situations deserve mention as they are likely to lead to further expansion over the next few years. Among the elitist French "Grandes Ecoles", the "Ecoles Normales Supérieures" are





**Fig. 2.** Professor Louis Gallien (1908-1976) in his laboratory in 1951.





**Fig. 3. Distribution of the main developmental biology laboratories in France.** Cities with centres that have contributed articles published in the present volume are in bold. Articles from Clermont, Nancy, Toulouse, Strasbourg, Grenoble and Banyuls already appeared in this journal in 1989.

now setting up biological research laboratories for their students, since the majority will no longer become teachers in high schools but will be applicants for faculty or full-time research positions. In the ENS in Paris, a developmental physiopathology laboratory is now headed by Jean-Paul Thiery, whose collaboration with Gerald Edelman on cell adhesion molecules started in 1975 in the United States. J.P. Thiery previously worked in the Embryological Institute in Nogent before moving to the ENS. Similarly, a laboratory of developmental neurobiology will open in 1990, headed by Alain Prochiantz of the Collège de France. In Lyon, the newly built ENS already includes a group working on the role of oncogenes in hemopoiesis (Jacques Samarut), and one of the earlier specialists of starfish oocyte maturation, Pierre Guerrier, previously working in the marine Zoological station at Roscoff (Brittany). All these new laboratories are associated with the CNRS.

Four years ago, the General Biology laboratory in Toulouse (Paul-Sabatier University) was transformed into a Center for Developmental Biology. Associated with the CNRS since 1972, under the responsibility of Jean-Claude Beetschen, the Center is now headed by a specialist in developmental neurogenesis, Anne-Marie Duprat. Another research theme, the determination of dorsal-ventral polarity in amphibians, pioneered by AnceI and Vintemberger in Strasbourg 40 years ago, is still under active investigation in this Center.

This brings us on to a brief survey of the general distribution of developmental biologists in provincial Universities and Research Centers. In summary, modern developmental biology first arose in a small number of Universities, and has only expanded elsewhere over the last 30 years. Laboratories devoted to developmental

biology were created in several Universities as a result of curriculum reform. Nevertheless, the more commonly encountered situation has been to include this discipline as a subdivision of cell and/or molecular biology. In the past few years, research funding from the Universities themselves has been dramatically reduced, and most of the financial support now comes from the national research organizations (CNRS and, to a much lesser extent in basic science, INSERM). Contractual funds for applied research can also be obtained in certain specific areas.

The geographical distribution of developmental biology laboratories is shown in Fig. 3. Not all these towns are represented in the following papers, where only a limited number of themes and investigators will appear. The scope of this volume has been restricted to give an idea of the diversity of problems which have been and are still being investigated in France. A number of them will not be illustrated here for two main reasons: either they are already of international status and largely known, or, conversely, they have just started exploring new areas and are still in the early stages of scientific production (e.g. developmental biochemistry in Rennes and Orsay). An intermediate situation is that of laboratories that changed or abandoned their previous orientations and are reorganizing.

At variance with the research carried out during the first half of the century, most biological models now employ vertebrate species. Amphibians are again widely used in France (in 20 laboratories), with a special emphasis on *Pleurodeles waltli*, and avian embryology has benefited from the discovery of the quail nuclear marker by N. Le Douarin nearly 20 years ago. Unfortunately, mouse embryology remains largely a speciality of the Institut Pasteur. Invertebrate models are still used in a few marine stations: oocyte maturation in several species (Roscoff and Banyuls sur Mer), cell physiology of fertilization in sea-urchin and ascidian eggs (C. Sardet, Villefranche sur Mer), or the early development of cephalopods (H. Marthy, Banyuls sur Mer). Historically, these three stations are offshoots of Paris VI University, but, here too, CNRS funding is essential for research. Foreign scientists have been and are welcome in these stations: mention should be made of J. Van der Biggelaar, working in Roscoff on early molluscan development. Several other small marine laboratories are attached to other universities (Luc sur Mer to Caen, Arcachon to Bordeaux, Sète to Montpellier), or, in Brittany, to the Collège de France (Concarneau) and the Museum National d'Histoire Naturelle (Dinard). Research in developmental biology is occasionally carried out in those stations.

No special contribution devoted to the development of *Drosophila* will appear in this volume. Only a few French scientists are involved in this area at present. Among them, groups headed by Professors Echalié and Best-Belpomme and by Dr. Lepesant in Paris, Professor Rosset in Marseille, and Dr. Simpson in Strasbourg are carrying out a cellular and molecular analysis of several mutant phenotypes. The dramatic breakthroughs in procaryotic and yeast genetics around the late 1960s oriented most molecular geneticists in France towards these simpler models, rather than towards complex whole organism systems which could not immediately support a reductionist approach. For the same reasons, other molecular microbiologists turned successfully to cell differentiation systems (e.g. myogenesis or erythropoiesis). Thus, very few French developmental geneticists have been trained in the analysis of *Drosophila*. There is therefore a considerable lag in international competitiveness in this area.



This situation might be a further mishap of "the singular fate of genetics in the history of French biology" (Burian *et al.*, 1988). These authors point out that, in spite of L. Cuénot and a few others, Mendelian genetics was not integrated into research and University curriculae until 1945, but paradoxically, molecular genetics grew out of the Pasteurian tradition of microbiology and physiology. It could be argued, in this respect, that the same tradition may have led molecular geneticists in France to consider *Drosophila* as an obsolete Mendelian tool, despite the pioneering work on pigment formation in *Drosophila* carried out by Ephrussi and Beadle in Paris (1935) "to lay a bridge between causal embryology and genetics" (Burian *et al.*, 1988). More recently, but in Switzerland, a similar process successfully led W. Gehring to pioneer the molecular developmental genetics of *Drosophila*.

To come back to the general situation of developmental biology in France, predictions on the future development of this polymorphic discipline would be hazardous. Cell lineage studies represent a strong component of development biology in France and certainly will stand at a high level. Cellular interactions and cell adhesion in developmental processes still deserve further analyses, in order to solve the old problems of "induction": in interacting systems, the specific properties of target cells (= competence) will have to be investigated carefully, since the inductive signals frequently appeared to be rather unspecific. The studies on molecular and genetical aspects of development thus will have to expand at a high rate, the delays accumulated in some areas being important. Oncogene products and growth factors might be the next fields in which we should expect exciting developments.

Finally, mention should be made of the existing networks of communication between the various workers in the field. The French Society for Developmental Biology (SFBD) was only founded in 1976, its first president being Professor Hubert Lutz (Clermont), a former collaborator of E. Wolff in Strasbourg, now retired. The SFBD was unfortunately considered to be a mere outgrowth from the much older and more traditional Zoological Society. For this reason, it remained too confined within University laboratories, and is still far from recruiting its potential membership (there are now around 200 members). Its financial support is obtained exclusively from members' fees (with an exception for symposia). This unsatisfactory situation does not enable organization of frequent meetings, although it does fund participation in international conferences and symposia for young scientists. The French Cell Biology Society is a much stronger and more active body, but it covers a variety of domains, and its journal *Biology of the Cell* is still strongly linked to its founders. There is no valid comparison between the organization of the SFBD and that of the British Society for Developmental Biology, which publishes books every year.

In summary, the topics included in this volume should provide a fairly good – though certainly incomplete – idea of the various fields that are currently under investigation in French laboratories. The gaps can be filled in to some extent from this introduction and the historical chapter in this volume.

## References

BURIAN, R.M., GAYON, J. and ZALLEN, D. (1988). The singular fate of genetics in the history of French biology. *J. Hist. Biol.* 21: 357-402.

## APPENDIX 1

### MAIN CNRS and CNRS-ASSOCIATED LABORATORIES WITH RESEARCH ACTIVITIES IN DEVELOPMENTAL BIOLOGY

LABORATORIES	DIRECTOR(s)	ADDRESS	ACTIVITIES
UMR9 - Institut d'Embryologie cellulaire et moléculaire du Collège de France et du CNRS	Prof. Nicole LE DOUARIN	49 bis avenue de la Belle Gabrielle 94736 NOGENT SUR MARNE CEDEX	<i>This issue</i>
URA 1148 - Différenciation cellulaire	Profs. François GROS, François JACOB and Dr. Antoinette RYTER	Institut Pasteur Bâtiment de Biologie moléculaire 25 rue du Docteur Roux 75724 PARIS CEDEX 15	<i>Myogenesis</i> <i>Mouse developmental</i> <i>genetics</i>
URA 1284 - Neurobiologie moléculaire	Prof. Jean-Pierre CHANGEUX	Institut Pasteur 25 Rue du Docteur Roux 75724 PARIS CEDEX 15	
URA 1337 - Physiologie du Développement embryonnaire et foetal	Dr. Jean-Paul THIERY	Ecole Normale Supérieure 46 rue d'Ulm 75230 PARIS CEDEX 05	<i>Extracellular matrix</i> <i>and cell adhesion</i> <i>molecules</i>
UMR 3 - Institut Jacques Monod	Prof. François CHAPEVILLE	Université de Paris 7 - Tour 43 2 place Jussieu 75251 PARIS CEDEX 05	<i>This issue</i>
<i>Several groups from the CNRS and INSERM are working on development and differentiation in this Institute.</i>			
URA 1135 - Différenciation moléculaire et cellulaire au cours du développement.	Profs. Jean-Claude BOUCAUT and Martin BEST-BELPOMME	Université de Paris 6 - Bât. A 7 quai Saint-Bernard 75230 PARIS CEDEX 05	<i>This issue</i>
URA 361 - Expression génétique et variabilité dans des systèmes multigénétiques.	Prof. Gérard BUTTIN	Institut Pasteur 28 rue du Docteur Roux 75724 PARIS CEDEX 15	<i>(Mouse development:</i> <i>Drs C. BABINET</i> <i>and J.L. GUENET)</i>

LABORATORIES	DIRECTOR(s)	ADDRESS	ACTIVITIES
<b>URA 675 - Biologie du Développement et de la Différenciation</b>	Dr. Anne-Marie DUPRAT	Centre de Biologie du Développement Université Paul-Sabatier (Toulouse 3) 118 route de Narbonne 31062 TOULOUSE CEDEX	<i>This issue</i>
<b>UPR 2420 - Centre de Génétique moléculaire</b>	Prof. Piotr SLONIMSKI	C.N.R.S. Bât. 26 Avenue de la Terrasse 91198 GIF SUR YVETTE CEDEX	<i>(Biochemistry and genetics of development: Prof. H. DENIS)</i>
<b>UPR 6520 - Laboratoire de Génétique moléculaire des Eucaryotes</b>	Prof. Pierre CHAMBON	Université de Strasbourg 1 Bât. 3 11 rue Human 67085 STRASBOURG CEDEX	<i>(Drosophila development group: Dr. P. SIMPSON) (Homeogenes in mouse limb development: Dr. P. DOLLE)</i>
<b>UPR 6511 - Centre de Neurochimie CNRS-INSERM</b>	Prof. Guy VINCENDON	Université de Strasbourg 1 5 Rue Blaise Pascal 67085 STRASBOURG CEDEX	<i>This issue</i>
<b>UMR 49 - Laboratoire de Biologie moléculaire et cellulaire</b>	Prof. Jacques DAILLIE	Ecole Normale Supérieure de Lyon 46 Allée d'Italie 69364 LYON CEDEX 07	<i>This issue</i>
<b>UMR 106 - Génétique moléculaire et cellulaire</b>	Prof. Jacqueline GODET	Université de Lyon 1 43 boulevard du 11 novembre 1918 69622 VILLEURBANNE CEDEX	<i>Hemoglobin genetics</i>
<b>UPR 3 - Laboratoire de Génétique et Biologie cellulaires</b>	Prof. Roland ROSSET	Université d'Aix-Marseille 2 Case 907 13288 MARSEILLE CEDEX 9	<i>Drosophila development.</i>
<b>URA 179 - Biologie de la Différenciation cellulaire</b>	Prof. Yves THOUVENY	Université d'Aix-Marseille 2 70 route Léon Lachamp 13288 MARSEILLE CEDEX 09	<i>Regeneration</i>
<b>URA 1189 - Spermatogenèse, ovogenèse et méiose chez l'homme et chez l'animal</b>	Prof. André STAHL	Université d'Aix-Marseille 2 27 boulevard Jean Moulin 13385 MARSEILLE CEDEX 05	
<b>UPR 3101 - Centre de Biologie cellulaire</b>	Prof. Daniel SANDOZ	CNRS, 67 rue Maurice Gunsbourg 94200 IVRY SUR SEINE	<i>This issue</i>
<b>URA 256 - Biologie cellulaire et Reproduction</b>	Prof. Jean JOLY	Université de Rennes 1 - B.P. 25A Avenue du Général Leclerc 35042 RENNES CEDEX	<i>(Developmental genetics of Xenopus: Prof. M. PHILIPPE)</i>
<b>URA 671 - Biologie cellulaire marine</b>	Dr. Christian SARDET	Station Zoologique (Université Paris 6) 06230 VILLEFRANCHE SUR MER	<i>This issue</i>
<b>URA 687 - Biologie du Développement et Sexualité</b>	Prof. Lucien GOMOT	Université de Besançon Place Leclerc 25030 BESANCON CEDEX	<i>Snail development</i>

## APPENDIX 2

## INSERM UNITS INVOLVED IN DEVELOPMENT AND CELL DIFFERENTIATION (MOSTLY ON HUMAN AND MAMMALIAN MODELS)

LABORATORIES	DIRECTOR(s)	ADDRESS	ACTIVITIES
<b>U30 - Biologie et pathologie de la croissance et du développement</b>	Dr. Raphael RAPPAPORT	Hôpital Necker - Enfants Malades 149 rue de Sèvres 75743 PARIS CEDEX 15	
<b>U 73 - Génétique et Pathologie foetale</b>	Dr. André BOUE	Centre International de l'Enfance Château de Longchamp 75016 PARIS.	<i>Chromosomal abnormalities</i>
<b>U 257 - Génétique physiologique</b>	Dr. Jacques JAMI	Institut Jacques Monod Université de Paris 7 2 place Jussieu 75251 PARIS CEDEX 05	<i>Transgenic mice</i>

LABORATORIES	DIRECTOR(s)	ADDRESS	ACTIVITIES
<b>U 282 - Hormones et Différenciation cellulaire</b>	Dr. Jacques NUNEZ	Hôpital Henri Mondor 51 av. Mar. De Lattre de Tassigny 94010 CRETEIL	<i>Neural differentiation</i>
<b>U 250 - Cinétique cellulaire</b>	Dr. Emilia FRINDEL	Institut Gustave Roussy 39-53 rue Camille Desmoulins 94805 VILLEJUIF CEDEX	<i>Studies on hemopoietic stem cell differentiation</i>
<b>U 114 - Neuropharmacologie</b>	Prof. Jacques GLOWINSKI	Collège de France 11 place Marcelin Berthelot 75231 PARIS CEDEX 05	<i>(Neural cell differentiation: Dr. A. PROCHIANTZ)</i>
<b>U 29 - Neurobiologie et physiopathologie du Développement</b>	Dr. Yehezkel BEN-ARI	Hôpital Port-Royal 123 bd. de Port-Royal 75764 PARIS CEDEX 14	<i>(Neuronal-glial interactions: Dr. G. BARBIN)</i>
<b>U 106 - Histologie normale et pathologique du système nerveux</b>	Dr. Constantino SOTELO	Hôpital de la Salpêtrière Bâtiment de Pédiatrie 47 bd. de l'Hôpital 75651 PARIS CEDEX 13	<i>Cerebellum development</i>
<b>U 153 - Développement, pathologie, régénération du système neuro-musculaire</b>	Prof. Michel FARDEAU	Bâtiment INSERM 17 rue du Fer à Moulin 75005 PARIS	
<b>U 61 - Biologie cellulaire et physiopathologie digestive</b>	Dr. Katy HAFFEN	3 avenue Molière 67200 STRASBOURG - HAUTEPIERRE	<i>This issue</i>
<b>U 307 - Croissance et différenciation cellulaire: rôle des hormones et des facteurs de croissance</b>	Dr. José-Maria SAEZ	Hôpital Debrousse Bâtiment INSERM 29 rue Soeur Bouvier 69322 LYON CEDEX 05	
<b>U 209 - Dermatologie et immunologie</b>	Prof. Jean THIVOLET	Hôpital Edouard Herriot 5 place d'Arsonval 69437 LYON CEDEX 03	
<b>U 249 - Biochimie des régulations des systèmes contractiles and UPR 8402 (CNRS) Centre de Recherches de Biochimie macromoléculaire</b>	Prof. Jacques DEMAILLE	U 249: Institut de Biologie Faculté de Médecine Boulevard Henri IV - 34033 MONTPELLIER CEDEX UPR 8402: B.P. 5051	<i>(Cell cycle: Prof. M. DOREE) (Neurogenesis: Dr. A. PRIVAT)</i>