

## A pioneer of experimental mammalian embryology: Jacques Mulnard

HENRI ALEXANDRE\*

*Laboratoire de Cytologie et Embryologie  
moléculaires, Université Libre de Bruxelles,  
Rhode-Saint-Genèse, Belgium*

Since October of 1987, Jacques Mulnard has been Professor Emeritus of the Faculty of Medicine and Pharmacy of the Université Libre de Bruxelles. He arrived as a student in 1939 and achieved a brilliant record in his medical studies. The difficult circumstances of the war were soon to reveal his attachment to his Institution and his exceptional qualities as a pedagogue and humanist. During his third year in medical school, the University closed down. Unlike many students who quite understandably chose to leave, Mulnard decided to continue his training in Brussels and to actively participate, despite the enormous risks, in the organization of clandestine courses. So at the age of 21, there he was, teaching anatomy and embryology to students a year younger than he while successfully passing his third- and fourth-year exams before the State Board of Examiners.

In 1945, as he was finishing his studies in «his» University which had reopened one year earlier, Jacques Mulnard took part in the British medical mission to the Bergen-Belsen concentration camp. Although his sense of decency drew a curtain of silence over this dramatic episode in his career, it is reasonable to believe that this trying mission reinforced his natural determination to defend justice and freedom of expression and to firmly reject all forms of intolerance. He was to place this determination at the service of the Faculty of Medicine and of the whole University when, just after the troubles in 1968, he was called upon to occupy a position of responsibility and decision.

The very peculiar conditions under which he completed his studies had prevented him from spending much time in a research laboratory like all of the other embryologists of the Brussels school. And unlike them, Jacques Mulnard felt a strong attraction towards

medical practice, especially surgery. But his vocation as a teacher and his passion for basic research led him to accept an assistantship under Professor Albert Dalcq in 1946.

His first works concerned various aspects of spermatogenesis, oogenesis, and the development of insect embryos. He notably demonstrated the very unusual character of the regulation of spermatogenesis in the bean beetle (Coleoptera), which produces di- and even polyploid spermatids in addition to haploid ones. His cytochemical studies enabled him to establish the reality of the morphogenetic RNA gradient concept in insects and to demonstrate the mesoblastic origin of intestinal endoderm. He also observed the presence of DNA-rich structures in the giant nucleoli of diptera larvae, thus generalizing Jean Brachet's 1940 observation on amphibian oocytes. As early as 1949, he proposed an interpretation which, in its essentials, is confirmed today: nucleoli arise from definite zones of the chromosomes during reconstitution of the nuclei at the end of the telophase.

From 1948 to 1957, Professor Mulnard made a series of trips which enabled him to learn and work in many laboratories: the Marine Biology Stations at Roscoff and Arcachon (France), at Woods Hole (USA), the Zoological Institute of the University of Cambridge, the Strangeways Institute at Cambridge (UK), the Laboratorium voor Experimentele Histologie in Leiden (the Netherlands), the National Cancer Institute in Bethesda (USA), and the Department of Embryology of the Carnegie Institution of Washington in Baltimore (USA). This is the period in which he carried out his remarkable studies on *in vivo* metachromasy in the eggs of various marine Invertebrates (*Barnea candida*, *Gryphaea angulata*, *Chaetopterus pergamentaceus*, *Psammechinus miliaris*, and *Arbacia punctulata*),

\*Address for reprints: Laboratoire de Cytologie et Embryologie moléculaires, Université Libre de Bruxelles, 67, rue des Chevaux, B-1640 Rhode-Saint-Genèse Belgium. FAX: 32-2-650.9999.



Professor Jacques Mulnard (b. 1922)

studies which he later extended to cultured chicken cells. As he recalls in his article devoted to the Brussels school of Embryology in this issue, he was also an active participant in the histochemical studies of mammalian development which Albert Dalcq had undertaken in 1950.

Upon returning from the USA in 1957, he was given an impressive number of courses to teach: human anatomy, human embryology, radiobiological anatomy, topographic anatomy, and special anatomy for dental students. This did not prevent him from continuing his research. Indeed, he went on to create a unit for culturing organ anlagen *in vitro*, a unit which he continues to direct today. There, he conducted studies on the differentiation of mesonephritic anlagen, human endometrium, hypophyseal explants, caudal vertebra anlagen, and limb buds. But the subject to which he devoted the most time was the early development of mammalian ova. Having devised a technique allowing continuous *in vitro* development of the mouse ovum from the 2-cell stage to the blastocyst stage, he made the first microcinematographic recording establishing the exact sequence of morphogenetic events as well as blastomere allocation. He then demonstrated two phenomena which would become the focus of

many studies worldwide: the regulatory phenomenon occurring after destruction of a blastomere at stage II in the mouse, and membrane polarization during compaction at stage VIII.

As always in the past, this pioneer of experimental mammalian embryology continues to welcome many young students to his laboratory. They come from the Medical and Science Faculties in Brussels, of course, but also from the Faculties of Veterinary Medicine of the Universities of Liège and Louvain. This has made it possible to develop research programmes on the *in vitro* fertilization and development of cow ova, on the reorganization of endoplasmic reticulum that accompanies oocyte maturation and activation, on the role of the cytoskeleton in the regulation of these events, and on the morphogenesis of the middle ear in Mammals.

Professor J. Mulnard's competence and dynamic enthusiasm are the qualities that justify his many past and present functions and responsibilities within the University (where he recently served as ombudsman), the Royal Academy of Medicine and in various foundations and scientific societies. He is notably the President of the Belgian Society for Cell Biology (BSCB), having been its treasurer from the time of its creation. On the initiative of Professor M.

Chèvremont of the Université de Liège, the Society was founded on February 12th, 1972. Jean Brachet was its first President. This year, the BSCB is thus celebrating its 20th anniversary, an event that coincides, I am pleased to note, with the 70th birthday of the Society's President, Professor Jacques Mulnard.

## Selected References

- ALEXANDRE, H. and MULNARD, J. (1988). Time-lapse cinematography study of the germinal vesicle behaviour in mouse primary oocytes treated with activators of protein kinases A and C. *Gamete Res.* 21: 359-365.
- ALEXANDRE, H., VAN CAUWENBERGE, A. and MULNARD, J. (1989). Involvement of microtubules and microfilaments in the control of the nuclear movement during maturation of the mouse oocyte. *Dev. Biol.* 136: 311-320.
- ALEXANDRE, H., VAN CAUWENBERGE, A., TSUKITANI, Y. and MULNARD, J. (1991). Pleiotropic effect of okadaic acid on maturing mouse oocytes. *Development* 112: 77-85.
- KELLY, S., MULNARD, J. and GRAHAM, C. (1978). Cell division and cell allocation in early mouse development. *J. Embryol. Exp. Morphol.* 48: 37-51.
- MASSIP, A. and MULNARD, J. (1980). Time-lapse cinematographic analysis of hatching of normal and frozen-thawed cow blastocysts. *J. Reprod. Fertil.* 58: 475-478.
- MASSIP, A., MULNARD, J., HUYGENS, R., HANZEN, C., VAN DER ZWALMEN, P. and ECTORS, F. (1981). Ultrastructure of the cow blastocyst. *J. Submicrosc. Cytol.* 13: 31-40.
- MASSIP, A., MULNARD, J., VAN DER ZWALMEN, P. and ZWIJSEN, W. (1983). Atypical hatching of a cow blastocyst leading to separation of complete twin half-blastocysts. *Vet. Rec.* 112: 301.
- MILLAIRE, J. and MULNARD, J. (1968). Le rôle de l'épiblaste dans la chondrogénèse du bourgeon de membre chez la souris. *J. Embryol. Exp. Morphol.* 20: 215-236.
- MILLAIRE, J. and MULNARD, J. (1984). Histogenesis in 11-day mouse embryo limb buds explanted in organ culture. *J. Exp. Zool.* 232: 359-377.
- MULNARD, J. (1947). Contribution à l'étude de l'origine de l'endoblaste chez les insectes. *Acta Anat.* 4: 208-212.
- MULNARD, J. (1950). Origine et signification des principaux constituants de l'oocyte chez *Acanthoscelides obtectus* Say (Bruchide-Coléoptère). *Bull. Cl. Sci. Acad. Roy. Belg.* 36: 767-778.
- MULNARD, J. (1951). La spermatogénèse double d'*Acanthoscelides obtectus* Say. *Ann. Soc. Roy. Zool. Belg.* 82: 399-445.
- MULNARD, J. (1954). Etude morphologique et histochimique de l'oogénèse chez *Acanthoscelides obtectus* Say (Bruchide-Coléoptère). *Arch. Biol.* 65: 261-314.
- MULNARD, J. (1955). La phosphatase alcaline dans les premiers stades du développement du rat et de la souris – Essai de localisation intra-cellulaire de l'enzyme. *Bull. Cl. Sci. Acad. Roy. Belg.* 41: 224-237.
- MULNARD, J. (1955). Contribution à la connaissance des enzymes dans l'ontogénèse. Les phosphomonoestérases acide et alcaline dans le développement du rat et de la souris. *Arch. Biol.* 66: 525-685.
- MULNARD, J. (1956). Présence d'inclusions Feulgen-positives dans les nucléoles larvaires de quelques Diptères. *Arch. Biol.* 67: 485-498.
- MULNARD, J. (1958). La métachromasie *in vivo* et son analyse cytochimique dans l'oof de l'annélide *Chaetopterus pergamentaceus*. *Arch. Biol.* 64: 645-685.
- MULNARD, J. (1964). Développement *in vitro* d'ébauches précartilagineuses de vertèbres caudales de souris. *Arch. Biol.* 75: 107-118.
- MULNARD, J. (1964). Obtention *in vitro* du développement continu de l'oof de souris du stade II au stade du blastocyste. *C.R. Acad. Sci. Paris* 258: 6228-6229.
- MULNARD, J. (1965). Studies on regulation of Mouse ova *in vitro*. *Ciba Foundation Symp. on Preimplantation Stages of Pregnancy* (Eds. G. Wolstenholme and M. O'Connor). Churchill Publ., London, pp. 123-138.
- MULNARD, J. (1967). Analyse microcinématographique du développement de l'oof de souris du stade II au blastocyste. *Arch. Biol.* 78: 107-138.
- MULNARD, J. (1967). Les propriétés phagocytaires du trophoblaste au cours des premières phases de l'ovoiimplantation chez la souris. *Arch. Biol.* 78: 575-594.
- MULNARD, J. (1973). Formation de blastocystes chimériques par fusion d'embryons de rat et de souris au stade VIII. *C.R. Acad. Sci. Paris* 276: 379-381.
- MULNARD, J., ALEXANDRE, H. and VAN CAUWENBERGE, A. (1991). Rôle du cytosquelette dans la translocation du matériel nucléaire au cours de la maturation de l'oocyte de souris. *Bull. Mém. Acad. Roy. Méd. Belg.* 146: 89-91.
- MULNARD, J., AUCLAIR, W. and MARSLAND, D. (1959). Metachromasia observed in the living egg of *Arbacia punctulata* and its cytochemical analysis. *J. Embryol. Exp. Morphol.* 7: 223-240.
- MULNARD, J., CRETEUR, V. and VERBRUGGEN, J.L. (1977). Contribution à l'étude des mécanismes de différenciation du mésenchyme des Mammifères. I. Comportement chez la souris de la portion caudale du mésenchyme mésenchymé placé dans diverses situations expérimentales. *Arch. Biol.* 88: 15-23.
- MULNARD, J. and FLAXMAN, A. (1961). A cytological and cytochemical approach to the problem of the nature and origin of the meta-granules in chick cells cultivated *in vitro*. *Arch. Biol.* 72: 573-609.
- MULNARD, J. and GIANGUZZA, M. (1972). Quelques aspects ultrastructuraux de l'activité lysosomiale dans les premiers stades du développement de la souris. *Arch. Biol.* 83: 499-512.
- MULNARD, J. and HUYGENS, R. (1978). Ultrastructural localization of non-specific alkaline phosphatase during cleavage and blastocyst formation in the mouse. *J. Embryol. Exp. Morphol.* 44: 121-131.
- MULNARD, J. and LEROY, F. (1962). Studies of human endometrium in tissue culture. I. Development of eosinophilic intranuclear inclusions in the epithelial cells. *Life Sci.* 9: 419-425.
- MULNARD, J. and LEROY, F. (1962). Studies of human endometrium in tissue culture. II. Successful cultivation of isolated glands and stroma. *Life Sci.* 9: 427-435.
- MULNARD, J. and MILLAIRE, J. (1964). Analyse expérimentale de la chondrogénèse dans le bourgeon de membre de la souris. *C.R. Acad. Sci. Paris* 258: 6525-6526.
- MULNARD, J. and PUISSANT, F. (1984). Development of mouse embryos after ultracentrifugation at the pronuclei stage. *Arch. Biol.* 95: 461-473.
- MULNARD, J. and PUISSANT, F. (1986). Effects of ultracentrifugation on primary and secondary mouse oocytes: an ultrastructural study. *Arch. Biol.* 97: 301-315.
- PASTEELS, J.J. and MULNARD, J. (1957). La métachromasie *in vivo* au bleu de toluidine et son analyse cytochimique dans les oeufs de *Barnes candida*, *Gryphaea angulata* (Lamellibranches) et *Psammechinus miliaris*. *Arch. Biol.* 68: 115-163.
- PASTEELS, J.L. and MULNARD, J. (1961). Caractères morphologiques d'explants hypophysaires cultivés *in vitro*. *C.R. Acad. Sci. Paris* 253: 1985-1987.