

This Week's Citation Classic®

Le Douarin N M & Teillet M-A. The migration of neural crest cells to the wall of the digestive tract in avian embryo. *J. Embryol. Exp. Morphol.* 30:31-48, 1973.
[Laboratoire d'Embryologie, Université de Nantes, France]

This paper reported on studies to determine the precise levels of origin on the neural crest of the autonomic ganglia, in particular, those composing the enteric nervous system. Regions of the neural primordium in a chick embryo were replaced by their quail counterparts (and vice versa). The cells from host and donor could be easily distinguished by the differences in the structure of their nuclei, thus making it possible to deduce the ontogenetic history of any of the cells forming the autonomic ganglia. [The SCI® indicates that this paper has been cited in over 200 publications.]

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Anyone trying to understand how embryos develop would want to visualize embryo component cells while they migrate and interact until differentiation and morphogenesis are completed. This was impossible in 1968, when I noticed that cells in the vertebrate embryo of the Japanese quail had extremely prominent nucleoli due to their association with large masses of heterochromatin. This feature, which distinguishes quail nuclei from those of most animal species, in which the heterochromatin is dispersed, can be readily perceived after staining with any dye having an affinity for DNA.

Before this observation my research interest was centered on the role of mesoderm/endoderm interactions in the development of liver in the chick embryo.

However, it so happened that a French geneticist, E. Bösiger, working at that time on hybrid vigor in quails, became so overrun by quail eggs that he offered them to embryology laboratories as a replacement for the classical chick material. I thought it would be worth checking whether mesoderm/endoderm inter-

actions could occur when quail hepatic mesenchyme was associated with chick endoderm in organotypic culture.

When endodermal cells become hepatocytes, they undergo a striking enlargement of the nucleolus. To my surprise, in the chimeric cultures the nucleolus was very large, not only in the hepatocytes, but also in the cells derived from the mesoderm. When I discovered the same feature in all other cell types of the quail, it struck me that quail/chick chimeras could be used to study cell migration *in situ*. As a model I chose the neural crest, an intriguing structure whose cells migrate all over the embryo and differentiate into a large variety of cell types.

The description of the marker and its application to neural crest ontogeny were published in French in 1969.¹ About then, I was joined by several young students, including M-A. Teillet. At first our results were reported in various French journals.² It was only after 1973 that our results were published in English. In my view the 1973 paper has been quoted often because it was the first in which the quail marker and its potential use were exposed to the international community in English, and it settled a long-standing controversy about the embryonic origin of the enteric ganglia. (The French papers were not cited frequently until after 1973, as well.) We had no difficulty publishing this paper: it was reviewed by C.L. Yntema, who immediately recognized the promise of this new tool.

Work on neural crest ontogeny using quail/chick chimeras has since been actively pursued by my group and in other laboratories as well. Revived interest in this subject incited me to write a monograph on the neural crest³ 30 years after S. Hörstadius's⁴ book on the same subject. The quail/chick chimera system has also contributed to the resolution of many other questions in developmental biology.⁵

Thanks to the quail/chick marker and its applications, I became laureate of the Royal Academy of Belgium in 1973 and was awarded the Lacassagne prize of the Collège de France in 1973, the Kyoto Prize in 1986, and the Gold Medal of the Centre National de la Recherche Scientifique in 1986.

1. Le Douarin N M. Particularités du noyau interphasique chez la Caille japonaise (*Coturnix coturnix japonica*). Utilisation de ces particularités comme "marqueur biologique" dans les recherches sur les interactions tissulaires et les migrations cellulaires au cours de l'ontogenèse (Characteristics of the interphase nucleus in the Japanese quail [*Coturnix coturnix japonica*]). Utilization of these characteristics as a biological marker in studies of tissue interactions and cell migration during ontogeny. *Bull. Biol. Fr. Belg.* 103:435-52, 1969. (Cited 260 times.)
2. Le Douarin N & Le Lièvre C. Démonstration de l'origine neurale des cellules à calcitonine du corps ultimobranchial chez l'embryon de poulet (Demonstration of the neural origin of calcitonin cells in the ultimobranchial body of the embryonic chick). *C. R. Hebd. Séances Acad. Sci. Sér. D* 270:2857-60, 1970. (Cited 160 times.)
3. Le Douarin N. *The neural crest*. Cambridge, England: Cambridge University Press, 1982. 259 p. (Cited 185 times.)
4. Hörstadius S. *The neural crest: its properties and derivatives in the light of experimental research*. London: Oxford University Press, 1950. 111 p. (Cited 325 times since 1955.)
5. Le Douarin N M & Mac Laren A. *Chimeras in developmental biology*. London: Academic Press, 1984. 456 p.