



## Prof. Nicole Marthe C. Le Douarin Professor



### **Most important awards, prizes and academies**

*Awards:* Academy of Sciences, France; Royal Academy of Belgium; Kyoto Prize in Advanced Technology, Japan; Jeantet Prize in Medicine; Grand Prix de la Fondation pour la Recherche Médicale; Ross Harrison Prize of Columbia University, New York; The Pearl Meister Greengard Prize, The Rockefeller University, New York; The Conklin Award of the American Society for Developmental Biology, San Francisco; Grand Officier dans l'Ordre National du Mérite; Commandeur dans l'Ordre de la Légion d'honneur; Grand Croix dans l'Ordre National du Mérite; Commandeur dans l'Ordre des Palmes académiques. *Academies:* Académie des sciences, France; American Academy of Arts and Sciences; Academia Europaea; Pontifical Academy of Sciences; National Academy of Sciences, USA; Royal Society, UK; Royal Academy of Medicine of Spain; Royal Academy of Belgium; Academy of Athens.

### **Summary of scientific research**

My work deals with the development of the nervous and the hemopoietic and angiogenic systems in the vertebrate embryo. I devised a cell marking technique which enables the migration and fate of cells to be followed within the embryo during the entire developmental period. With my colleagues, we have particularly studied the fate of the neural crest, an embryonic structure composed of pluripotent stem cells. Neural crest cells undergo extensive migrations within the

embryo and differentiate into a large variety of cell types. The neural crest plays a crucial role in the construction of the vertebrate head and of the peripheral nervous system. It also yields pigment and endocrine cells. We established the embryonic origin of the hemopoietic stem cells and how the development of the immune system proceeds in the embryo and early post-natal life. We demonstrated that immune tolerance to self involves, in addition to the elimination of self reactive T cells in the thymus, an active mechanism which consists in the production in the thymic environment of regulatory cells that suppress the activity of the effector T cells that have escaped thymic elimination.

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### Main publications

*Books:* Le Douarin, N.M., *Les cellules souches, porteuses d'immortalité* (Odile Jacob, 2007); Le Douarin, N.M., *The Neural Crest* (Cambridge University Press, 1982; 2000); Le Douarin, N.M., *Des Chimères, des Clones et des Gènes* (Odile Jacob, 2000). *Articles:* A Biological Cell Labeling Technique and its Use in Experimental Embryology, *Dev. Biol.*, 30, 217-22 (1973); Le Douarin, N.M. and Jotereau, F.V., Tracing of Cells of the Avian Thymus through Embryonic Life in the Interspecific Chimeras, *J. Exp. Med.*, 142, 17-40 (1975); The Ontology of the Neural Crest in Avian Embryo Chimeras, *Trends in Neurosciences*, 3, 39-42 (1980); Teillet, M.-A. and Le Douarin, N.M., Consequences of Neural Tube and Notochord Excision on the Development of the Peripheral Nervous System in the Chick Embryo, *Dev. Biol.*, 98, 192-211 (1983); Cell Line Segregation during Peripheral Nervous System Ontogeny, *Science*, 231, 1515-22 (1986); Baroffio, A., Dupin, E. and Le Douarin, N.M., Common Precursors for Neural and Mesectodermal Derivatives in the Cephalic Neural Crest, *Development*, 112, 301-5 (1990); Embryonic Neural Chimeras in the Study of Brain Development, *Trends in Neurosciences*, 16, 2m, 64-72 (1993); Les chimères de caille et de poulet pour étudier l'embryogenèse, *Pour la Science*, 252, 46-54 (1998); Problèmes éthiques liés aux progrès de la biologie du développement, *C. R. Soc. Biol.*, Cent cinquanteième, 192, 869-82 (1998); Fournier-Thibault, C., Pourquoi, O., Rouaud, T. and Le Douarin, N.M., BEN/SC1DM-GRASP Expression during Neuromuscular Development: A Cell Adhesion Molecule Regulated by Innervation, *J. Neurosci.*, 19 (4), 1382-92 (1999); Charrier, J.-B., Teillet, M.-A., Lapointe, F., and Le Douarin, N.M., Defining subregions of Hensen's node essential for caudalward movement, midline development and cell survival, *Development*, 126, 4771-83 (1999); Dupin, E., Glavieux, C., Vaigot, P. and Le Douarin, N.M., Endothelin 3 induces the reversion of melanocytes to glia through a neural crest-derived glial-melanocytic progenitor, *Proc. Natl. Acad. Sci. USA*, 97, 7882-7 (2000); Monsoro-Burq, A.-H. and Le Douarin, N.M., BMP4 plays a key role in left-right patterning in chick embryos by maintaining Sonic Hedgehog asymmetry, *Mol. Cell.*, 7, 789-99 (2001); Charrier, J.-B., Lapointe, F., Le Douarin, N.M. and Teillet, M.-A., Anti-apoptotic role of Sonic Hedgehog protein at the early stages of nervous system organogenesis, *Development*, 128, 4011-20 (2001); Creuzet, S., Couly, G., Bennaceur, S., Vincent, C., and Le Douarin, N.M., Negative effect of Hox gene expression on the development of the neural crest-derived facial skeleton, *Development*, 129, 4301-13 (2002); Burns, A.J., Delalande, J.-M. and Le Douarin, N.M., In ovo transplantation of enteric nervous system

precursors from vagal to sacral neural crest results in extensive hindgut colonization, *Development*, 129, 2785-96 (2002); Charrier, J.-B., Lapointe, F., Le Douarin, N.M. and Teillet, M.-A., Dual origin of the floor plate in the avian embryo, *Development*, 129, 4785-96 (2002); Dupin, E., Real, C., Glavieux-Pardanaud, C., Vaigot, P. and Le Douarin, N.M., Reversal of developmental restrictions in neural crest lineages: transition from Schwann cells to glial-melanocytic precursors in vitro, *Proc. Natl. Acad. Sci. USA*, 100, 5229-33 (2003); Dupin, E. and Le Douarin, N.M., Development of melanocyte precursors from the vertebrate neural crest, *Oncogene*, 22, 3016-23 (2003); Real, C., Dupin, E., Glavieux-Pardanaud, C. and Le Douarin, N.M., Melanocytes can reverse into self-renewing multipotent cells in vitro, *Pigment Cell Res.*, 16, 573 (2003); Thibert, C., Teillet, M.-A., Lapointe, F., Mazelin, L., Le Douarin, N.M. and Mehlen, P., Sonic hedgehog controls survival of the neuroepithelial cells of the developing neural tube by regulating Patched-induced apoptosis, *Science*, 203, 843-6 (2003); Le Douarin, N.M., *et al.*, Neural crest cell plasticity and its limits, *Development*, 131, 4637-50 (2004); Trentin, A., Glavieux-Pardanaud, C., Le Douarin, N.M. and Dupin, E., Self-renewal capacity is a widespread property of various types of neural crest precursor cells, *Proc. Natl. Acad. Sci. USA* 101, 4495-4500 (2004); Charrier, J.-B., Catala, M., Lapointe, F., Le Douarin, N. and Teillet, M.-A., Cellular dynamics and molecular control of the development of organizer-derived cells studied in quail-chick chimeras, *Int. J. Dev. Biol.*, 49, 181-91 (2005); Brito, J.M., Teillet, M.-A. and Le Douarin, N.M., An early role for sonic hedgehog from foregut endoderm in jaw development: insuring neural crest cell survival, *Proc. Natl. Acad. Sci. USA*, 103 (31): 11607-12 (2006); Creuzet, S.E., Martinez, S. and Le Douarin, N.M., The cephalic neural crest exerts a critical effect on forebrain and midbrain development, *Proc. Natl. Acad. Sci. USA*, 103:1433-8 (2006); Real, C., Glavieux-Pardanaud, C., Le Douarin N.M. and Dupin E., Clonally cultured differentiated pigment cells can dedifferentiate and generate multipotent progenitors with self-renewing potential, *Developmental Biology*, vol. 300(2), 656-69 (2006); Calloni, G.W., Glavieux-Pardanaud, C., Le Douarin, N.M. & Dupin, E., Sonic Hedgehog promotes the development of multipotent neural crest progenitors endowed with both mesenchymal and neural potentials, *Proc. Natl. Acad. Sci. USA*, 104 (n. 50), 19879-84 (2007); Le Douarin, N.M., Brito, J.M., and Creuzet, S., The role of the neural crest in face and brain development, *Brain Res. Reviews*, 55(2), 237-47 (2007).