



## Edward M. De Robertis



**Date of Birth** 6 June 1947

**Place** Boston, MA (USA)

**Nomination** 8 September 2009

**Field** Biology

**Title** Professor

### Most important awards, prizes and academies

Edward De Robertis is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the European Molecular Biology Organization, an honorary member of the Société de Biologie, Paris, France, and a corresponding member of the Latin American Academy of Sciences. He is active in Latin American affairs and has served on the scientific board of the Pew Charitable Trusts Latin program for 20 years. He received the Ross G. Harrison prize in developmental biology. From 2002 to 2006 he was President of the International Society of Developmental Biologists.

### Summary of scientific research

The research of Edward De Robertis centers on the molecular mechanisms of embryonic induction in vertebrate embryos. He has cloned several genes that code for secreted antagonists of growth factors that are used by embryonic cells to communicate with each other. These proteins are used to control cell differentiation and have been conserved in all bilateral animals. His work has led to the realization that the molecular machinery for embryonic patterning is common to all animal embryos. In 1984 Edward De Robertis, together with his close colleague Walter Gehring, isolated the first vertebrate development-controlling gene, now called Hox-C6. The conservation of Hox genes between vertebrates and fruit flies, which regulate the antero-posterior body axis, marked the beginning of the young scientific discipline of Evolution and Development, Evo-Devo. In the 1990s De Robertis carried out the systematic dissection of the molecular mechanisms that mediate embryonic induction. In 1924 Hans Spemann and Hilde Mangold identified a region of the amphibian embryo that was able to induce the formation of Siamese twins after transplantation. De Robertis isolated genes expressed in this region. He discovered Chordin, a protein secreted by dorsal cells that binds Bone Morphogenetic Protein (BMP) growth factors, facilitating their transport to the ventral side of the embryo, where Chordin is digested by a protease so that BMPs can signal. This flow of growth factors determines dorsal (back) to ventral (belly) cell and tissue differentiations in many bilateral animals, such as fruit flies, spiders, early chordates and mammals. Recently, his laboratory is studying the close relationship between the Wnt signaling pathway, multivesicular endosomes and protein degradation. In sum, De Robertis has been a pioneer in the remarkable current realization that the molecular mechanisms of antero-posterior and dorsal-ventral patterning are common to all animal embryos. This use of conserved gene networks during development has channeled the outcomes of evolution by Natural Selection arising from *Urbilateria*, the last common ancestor of vertebrates and invertebrates.

### Main publications

De Robertis, E.M. and Gurdon, J.B. (1977). Gene Activation in somatic nuclei after injection into amphibian oocytes. *Proc. Natl. Acad. Sci. USA* 74, 2470-2474; Carrasco, A.E., McGinnis, W., Gehring, W.J. and De Robertis, E.M. (1984), Cloning of a *Xenopus laevis* gene expressed during early embryogenesis that codes for a peptide region homologous to Drosophila homeotic genes: implications for vertebrate development, *Cell* 37, 409-14; Sasai, Y., Lu, B., Steinbeisser, H., Geissert, D., Gont, L.K. and De Robertis, E.M. (1994), *Xenopus* chordin: a novel dorsalizing factor activated by organizer-specific homeobox genes, *Cell* 79, 779-90; Piccolo, S., Sasai, Y., Lu, B. and De Robertis, E.M. (1996), Dorsoventral patterning in *Xenopus*: Inhibition of ventral

signals by direct binding of Chordin to BMP-4, *Cell* 86, 589-98; Bouwmeester, T., Kim, S.H., Sasai, Y., Lu, B. and De Robertis, E.M. (1996), Cerberus, a head-inducing secreted factor expressed in the anterior endoderm of Spemann's Organizer, *Nature* 382, 595-601; Piccolo, S., Agius, E., Lu, B., Goodman, S., Dale, L. and De Robertis, E.M. (1997), Cleavage of Chordin by the Xolloid metalloprotease suggests a role for proteolytic processing in the regulation of Spemann organizer activity, *Cell* 91, 407-16; Reversade, B. and De Robertis, E.M. (2005), Regulation of ADMP and BMP2/4/7 at opposite embryonic poles generates a self-regulating morphogen field, *Cell* 123, 1147-60; Lee, H.X., Ambrosio, A.L., Reversade, B. and De Robertis, E.M. (2006), Embryonic dorsal-ventral signaling: secreted Frizzled-related proteins as inhibitors of Tolloid proteinases, *Cell* 124, 147-59; Fuentealba, L.C., Eivers, E., Ikeda, A., Hurtado, C., Kuroda, H., Pera, E.M., and De Robertis, E.M. (2007), Integrating patterning signals: Wnt/GSK3 regulates the duration of the BMP/Smad1 signal, *Cell* 131, 980-93; De Robertis, E.M. (2008), Evo-Devo: Variations on Ancestral themes, *Cell* 132, 185-95; Taelman, V.F., Dobrowolski, R., Plouhinec, J.L., Fuentealba, L.C., Vorwald, P.P., Gumper, I., Sabatini, D.D. and De Robertis, E.M. (2010). Wnt signaling requires the sequestration of Glycogen Synthase kinase 3 inside multivesicular endosomes. *Cell* 143, 1136-1148; Dobrowolski, R., Vick, P., Ploper, D., Gumper, I., Snitkin, H., Sabatini, D.D. and De Robertis, E.M. (2012). Presenilin deficiency or lysosomal inhibition enhance Wnt signaling through relocalization of GSK3 to the late endosomal compartment. *Cell Reports* 2, 1316-1328.