



Prof., M.D., Ph.D. Edward M. De Robertis 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 and the European Molecular Biology Organization. He is also a corresponding member of the Latin American Academy of Sciences, the Buenos Aires National Academy of Sciences and the Academy of Sciences of Uruguay. Active in Latin American affairs, he serves on the council of the Latin American Academy of Sciences, and has been on the scientific board of the Pew Charitable Trusts Latin program for over 25 years. De Robertis received *honoris causa* doctorates from the Universit s Sorbonne and his *alma mater* the University of the Republic of Uruguay. From 2002 to 2006 he was President of the International Society of Developmental Biologists. He received the Ross Harrison prize in developmental biology, the Society for Developmental Biology (USA) Lifetime Achievement Award, and the Kowalevsky Medal in Evolution and Development.

Summary of scientific research

Edward De Robertis studies the molecular patterning mechanisms that control the evolution of the animal body plan. He has cloned several genes that code for secreted antagonists of growth factors that are used by embryonic cells to form morphogen gradients. These proteins control tissue differentiations in all bilateral animals. In 1984 Edward De Robertis, together with his close

colleague the late Walter Gehring, isolated the first vertebrate development-controlling gene, now called Hox-C6. Hox genes encode DNA-binding proteins that determine the differentiation of cells along the antero-posterior body axis, both in fruit flies and vertebrates. 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 had 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 the Tolloid protease, releasing BMPs for signaling. This flow of growth factors determines dorsal (back) to ventral (belly) tissue differentiations in most bilateral animals, such as fruit flies, spiders, early chordates and mammals. However, the Chordin/Tolloid/BMP axis was inverted during evolution between invertebrates and vertebrates. The De Robertis laboratory is currently investigating the regulation of the Wnt signaling pathway by pinocytosis, multivesicular endosomes and lysosomes, and its integration with embryonic patterning. 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. These discoveries were foundational for the young scientific discipline of Evolution and Development, commonly known as Evo-Devo. The 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, 2470-74; De Robertis, E.M. and Mertz, J.E. (1977). Coupled transcription-translation of DNA injected into *Xenopus* oocytes, *Cell* 12, 175-82; 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; Cho, K.W.Y., Blumberg, B., Steinbeisser, H. and De Robertis, E.M. (1991), Molecular Nature of Spemann's Organizer: the Role of the *Xenopus* Homeobox Gene *gooseoid*, *Cell* 67, 1111-20; 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; De Robertis, E.M. and Sasai, Y. (1996), A common plan for dorso-ventral patterning in Bilateria, *Nature* 380, 37-40; 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; Leyns, L., Bouwmeester, T., Kim, S.H., Piccolo, S. and De Robertis, E.M. (1997), Frzb-1 is a secreted antagonist of Wnt signaling expressed in the Spemann organizer, *Cell* 88, 747-56; 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; Piccolo, S., Agius, E., Leys, L., Battacharyya, S., Grunz, H., Bouwmeester, T. and De Robertis, E.M. (1999), The head inducer Cerberus is a multifunctional antagonist of Nodal, BMP and Wnt signals, *Nature* 397, 707-10; Bachiller, D., Klingensmith, J., Kemp, C., Belo, J.A., Anderson, R.M., May, S.R., McMahon, J.A., McMahon, A.P., Harland, R., Rossant, J. and De Robertis, E.M. (2000), The organizer secreted factors Chordin and Noggin are required for forebrain development in the mouse, *Nature* 403, 658-61; Abreu, J.G., Ketpura, N.I., Reversade, B. and De Robertis, E.M. (2002), Connective tissue growth factor modulates cell signalling by BMP and TGF- β , *Nature Cell Biology* 4, 599-604; 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; Plouhinec, J.L., Zakin, L., Moriyama, Y. and De Robertis, E.M. (2013), Chordin forms a self-organizing morphogen gradient in the extracellular space between ectoderm and mesoderm in the *Xenopus* embryo, *Proc. Natl. Acad. Sci. USA* 110, 20372-79; Bier, E. and De Robertis, E.M. (2015), BMP gradients: a paradigm for morphogen-mediated developmental patterning, *Science* 348, aaa5838; De Robertis, E.M., Moriyama, Y. and Colozza, G. (2017), Generation of animal form by the Chordin/Tolloid/BMP gradient: 100 years after D'Arcy Thompson, *Dev. Growth Differ.* 59, 580-92; Moriyama, Y. and De Robertis, E.M. (2018), Embryonic regeneration by relocalization of the Spemann organizer during twinning in *Xenopus*, *Proc. Natl. Acad. Sci. USA* 115, E4815-22; De Robertis E.M. and Sánchez Sorondo M. Eds (2018), *Cell Biology and Genetics*, Libreria Editrice Vaticana; Tejeda-Muñoz, N., Albrecht, L.V., Bui, M.H. and De Robertis, E.M. (2019), Wnt canonical pathway activates macropinocytosis and lysosomal degradation of extracellular proteins, *Proc. Natl. Acad. Sci. USA* 116, 10402-11; Colozza, G., Jami-Alahmadi, Y., Dsouza, A., Tejeda-Muñoz, N., Albrecht, L.V., Sosa, E., Wohlschlegel, J.A. and De Robertis E.M. (2020), Wnt-inducible Lrp6-APEX2 interactive proteins identify ESCRT machinery and Trk-fused gene as components of the Wnt signaling pathway, *Sci. Rep.* 10, 21555; Albrecht, L.V., Tejeda-Muñoz, N., Bui, M.H., Cicchetto, A., Azzolin, L., Colozza, G., Schmid, E., Piccolo, S., Christofk, H.R. and De Robertis, E.M. (2020), GSK3 inhibits macropinocytosis and lysosomal activity through the Wnt destruction complex machinery, *Cell Reports* 32, 107973.