

Douglas A. Melton, Ph.D.

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Professional Profile

- Dr. Melton has become a leading researcher and public advocate in the field of human embryonic stem cells.
- Dr. Melton is an Investigator of the Howard Hughes Medical Institute and the Thomas Dudley Cabot Professor in the Natural Sciences at Harvard University. He is also a co-director of Harvard's Stem Cell Institute and Harvard's Center for Genomic Research.
- The goal of his work is to make pancreatic tissue for transplantation into people with diabetes. To this end, his laboratory has significantly advanced the understanding of the genes and cells that normally make the pancreas during animal development and they are using that information to instruct embryonic stem cells to make pancreatic tissue.

Scientific Positions

- **Thomas Dudley Cabot Professor in the Natural Sciences**, Harvard University, Department of Molecular and Cellular Biology, Cambridge, Massachusetts, 1999-Present
- **Howard Hughes Medical Institute Investigator**, 1994-Present
- **Associate Member**, Children's Hospital, Boston, Massachusetts, 1994-Present
- **Biologist (Medicine)**, Massachusetts General Hospital, Boston, Massachusetts, 1993-Present
- **Professor of Molecular and Cellular Biology**, Harvard University, Cambridge, Massachusetts, 1988-Present
- **John L. Loeb Associate Professor of the Natural Sciences**, Harvard University, Cambridge, Massachusetts, 1987-1988
- **Associate Professor**, Department of Biochemistry and Molecular Biology, Harvard University, Cambridge, Massachusetts, 1984-1987
- **Assistant Professor**, Department of Biochemistry and Molecular Biology, Harvard University, Cambridge, Massachusetts, 1981-1984

University Education

- **Ph.D. in Molecular Biology**, Trinity College & MRC Laboratory of Molecular Biology, Cambridge University, Cambridge, England, 1980 (Supervisor: J.B. Gurdon)
- **B.A. in History and Philosophy of Science**, Cambridge University, Cambridge, England, 1975-1977
- **B.S. in Honors Biology**, University of Illinois, Champaign-Urbana, Illinois, 1971-1975

Academic Honors

- Eliot P. Joslin Medal, 2002
- Member, Institute of Medicine of the National Academy of Sciences, 2001
- Honorary Member, Japanese Biochemical Society, 1996

- Member, National Academy of Sciences, 1995
- Member, American Academy of Arts and Sciences, 1995
- Richard Lounsbery Award, National Academy of Science, 1995
- George Ledlie Prize, 1991
- American Society of Biochemistry & Molecular Biology Young Investigator Award, 1991
- Searle Scholar Award, 1983-1986
- Camille and Henry Dreyfus Award, 1981
- Max Perutz Prize, 1981
- Marshall Scholarship, awarded for study at Cambridge University, 1975-1978
- Edmund J. James Scholar, University of Illinois, 1971-1975; Phi Beta Kappa, 1975

Scientific Journals

- Editorial Board of Proceedings of the National Academy of Sciences, 2003-2004
- Editor of electronic journal Regenerative Medicine, 2003-2004
- Advisory Board, Genome Biology, 2003-2004
- USA Editor of Development, 2003
- Editor at Neurobiology, 2003
- Editor at Cytokine & Growth Factor Reviews, 2003
- Review Board Editor at Science, 1997-2001

Publications

1. Laskey, R.A. and Melton, D.A. (1977) Synthesis of SV40 DNA in eggs of *Xenopus laevis* in the absence of viral gene expression. Inserm 69: 253-258.
2. Gottesfeld, J. and Melton, D.A. (1978) The length of nucleosome associated DNA is the same in both transcribed and non-transcribed regions of chromatin. *Nature* 273: 317-319.
3. Cortese, R., Melton, D.A., Tranquilla, T. and Smith, J.D. (1978) Cloning of nematode tRNA genes and their expression in the frog oocyte. *Nucleic Acids Research* 5: 4593-4611.
4. Gurdon, J.B., Melton, D.A. and DeRobertis, E. (1979) Genetics in an oocyte. *Ciba Foundation Series* 66: 63-80.
5. Melton, D.A. and Cortese, R. (1979) Transcription of cloned tRNA genes and the nuclear partitioning of a tRNA precursor. *Cell* 18: 1165-1172.
6. Melton, D.A., DeRobertis, E., and Cortese, R. (1980) RNA processing: order and intracellular location of the events involved in the maturation of a spliced tRNA. *Nature* 284: 143-148.
7. Cortese, R., Harland, R. and Melton, D.A. (1980) *In vivo* transcription of tRNA genes: single stranded vs. double stranded templates. *Proc. Natl. Acad. Sci. USA* 77: 4147-4151.
8. Gurdon, J.B. and Melton, D.A. (1981) Gene transfer in amphibian eggs and oocytes. *Ann. Rev. Genetics* 15: 189-218.
9. Miller, J. and Melton, D.A. (1981) A transcriptionally active pseudogene in *Xenopus laevis* oocyte 5S DNA. *Cell* 24: 829-835.

10. Ciliberto, G., Castagnoli, L., Melton, D.A., and Cortese, R. (1982) Promoter of a eucaryotic tRNA gene is composed of three non-contiguous regions. *Proc. Natl. Acad. Sci. USA* 79: 1195-1199.
11. Ciampi, S., Melton, D.A., and Cortese, R. (1982) Site directed mutagenesis of a tRNA gene: base alterations in the coding region affect transcription. *Proc. Nat. Acad. Sci. USA* 79: 1388-1392.
12. Tranquilla, T., Cortese, R., Melton, D.A., and Smith, J.D. (1982) Sequences of four tRNA genes from *Caenorhabditis elegans* and the expression of *C. elegans* tRNA in *Xenopus* oocytes. *Nucleic Acids Research* 10: 7919-7934.
13. Green, M.R., Maniatis, T. and Melton, D.A. (1983) Human β globin pre-mRNA synthesized *in vitro* is accurately spliced in *Xenopus* oocyte nuclei. *Cell* 32: 681-694.
14. Perry, H. and Melton, D.A. (1983) A rapid increase in acetylcholinesterase mRNA during ascidian embryogenesis as demonstrated by microinjection into *Xenopus laevis* oocytes. *Cell Differentiation* 13: 233-238.
15. Krieg, P. and Melton, D.A. (1984) Formation of the 3' end of histone mRNA by post-transcriptional processing. *Nature* 308: 203-206.
16. Melton, D.A., Krieg, P.A., Rebagliati, M.R., Maniatis, T., Zinn, K., and Green, M.R. (1984) Efficient *in vitro* synthesis of biologically active RNA and RNA hybridization probes from plasmids containing a bacteriophage SP6 promoter. *Nucleic Acids Research* 12: 7035-7056.
17. Krieg, P.A. and Melton, D.A. (1984) Functional messenger RNAs are produced by SP6 *in vitro* transcription of cloned DNAs. *Nucleic Acids Research* 12: 7057-7070.
18. Melton, D.A. (1985) Injected anti-sense RNAs specifically block messenger RNA translation *in vivo*. *Proc. Natl. Acad. Sci. USA* 82: 144-148.
19. Rebagliati, M.R., Weeks, D.L., Harvey, R.P. and Melton, D.A. (1985) Identification and cloning of localized maternal RNAs from *Xenopus* eggs. *Cell* 42: 769-777.
20. Krieg, P. A. and Melton, D. A. (1985) Developmental regulation of a gastrula-specific gene injected into fertilized *Xenopus* eggs. *EMBO J.* 4: 3463-3471.
21. Weeks, D.L., Rebagliati, M.R., Harvey, R.P. and Melton, D.A. (1985) Localized maternal mRNAs in *Xenopus laevis* eggs. *Cold Spring Harbor Symp. Quant. Biol. L.* 21-30.
22. Krieg, P.A., Rebagliati, M.R., Weeks, D.L., and Melton, D.A. (1986) Gene Activation during *Xenopus* embryogenesis. pp. 357-369. In Gametogenesis and the Early Embryo, ed. by J. Gall. Alan Liss, Inc., N.Y.
23. Harvey, R.P., Tabin, C. and Melton, D.A. (1986) Embryonic expression and nuclear localization of *Xenopus* homeobox (Xhox) gene products. *EMBO J.* 5: 1237-1244.
24. Melton, D. A. and Rebagliati, M.R. (1986) Antisense RNA injections in fertilized eggs as a test for the function of localized mRNAs. *JEEM* 97: 211-221.

25. Rebagliati, M.R. and Melton, D.A. (1987) Antisense RNA injections in frog eggs reveal an RNA duplex unwinding activity. *Cell* 48:599-605.
26. Kintner, C.R. and Melton, D.A. (1987) Expression of N-CAM RNA in ectoderm is an early response to neural induction. *Development* 99:311-325.
27. Krieg, P.A. and Melton, D.A. (1987) An enhancer responsible for activating transcription at the mid-blastula transition in *Xenopus* development. *PNAS* 84:2331-2335.
28. Weeks, D.L. and Melton, D.A. (1987) A maternal RNA localized to the animal pole of *Xenopus* eggs encodes a subunit of mitochondrial ATPase. *PNAS* 84:2798-2802.
29. Melton, D.A. (1987) Translation of messenger RNA in injected frog oocytes. *Methods in Enzymology, Guide to Molecular Cloning*, ed by S. Berger and A. Kimmel. Vol. 152:288-296.
30. Krieg, P.A. and Melton, D.A. (1987) In vitro RNA synthesis with SP6 RNA polymerase. *Methods in Enzymology, Recombinant DNA*, ed by R. Wu. Part F. Vol 155:397-415.
31. Ruiz i Altaba, A., Perry-O'Keefe, H., and Melton, D.A. (1987) Xfin: an embryonic gene encoding a multifingered protein in *Xenopus*. *EMBO J.* 6:3065-3070.
32. Melton, D.A. (1987) Translocation of a localized maternal mRNA to the vegetal pole of *Xenopus* oocytes. *Nature* 328:80-82.
33. Weeks, D.L. and Melton, D.A. (1987) A maternal messenger RNA localized to the vegetal hemisphere in *Xenopus* eggs codes for a growth factor related to TGF- β . *Cell* 51:861-86.
34. Harvey, R.P. and Melton, D.A. (1988) Microinjection of synthetic Xhox-1A homeobox mRNA disrupts somite formation in developing *Xenopus* embryos. *Cell* 53:687-697.
35. Mercola, M., Melton, D.A. and Stiles, C.D. (1988) Platelet-derived growth factors A chain is maternally encoded in *Xenopus* embryos. *Science* 241:1223-1225.
36. Yisraeli, J. and Melton, D.A. (1988) The maternal mRNA Vg1 is correctly localized following injection into *Xenopus* oocytes. *Nature* 336:592-595.
37. Krieg, P.A., Varnum, S.M., Wormington, M.W. and Melton, D.A. (1989) The mRNA encoding elongation factor 1- β (EF1 β) is a major transcript at the midblastula transition in *Xenopus*. *Dev. Biol.* 133:93-100.
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42. Ruiz i Altaba, A. and Melton, D.A. (1989) Interaction between peptide growth factors and homeobox genes in the establishment of anterior-posterior polarity in frog embryos. Nature 341:33-38.
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47. Yisraeli, J. Sokol, S. and Melton, D.A. (1989) The process of localizing a maternal messenger RNA in *Xenopus* oocytes. Development 1989 Supplement: 31-36.
48. Yisraeli, J., Sokol, S. and Melton, D.A. (1990) A two-step model for the localization of maternal *Xenopus* oocytes: Involvement of microtubules and microfilaments in the translocation and anchoring of Vg1 mRNA. Development 108:289-298.
49. Woolf, T.M., Jennings, C.G.B., Rebagliati, M. and Melton, D.A.(1990) The stability, toxicity and effectiveness of unmodified and phosphorothioate antisense oligodeoxynucleotides in *Xenopus* oocytes and embryos. Nucleic Acids Research 18(7): 1763-1769.
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51. Thomsen, G., Woolf, T., Whitman, M., Sokol, S., Vaughan, J., Vale, W., and Melton, D.A. (1990) Activins are expressed in early *Xenopus* embryogenesis and can induce axial mesoderm and anterior structures. Cell 63(3): 485-493.
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53. Melton, D.A. (1991) Pattern formation during animal development. Science 252: 234-241.
54. Sokol, S. and Melton, D.A. (1991) Induction of *Xenopus* animal pole cells by activin reveals a preexistent pattern in the responding cells. Nature 351:409-411.
55. Gururajan, R., Perry-O'Keefe, H., Melton, D.A. and Weeks, D.L. (1991) The *Xenopus* localized messenger RNA An3 may encode an ATP-dependent RNA helicase. Nature 349: 717-719.

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61. Hemmati-Brivanlou, A., Wright, D.A., and Melton, D.A. (1992) Embryonic expression and functional analysis of a *Xenopus* activin receptor. *Developmental Dynamics* 194:1-11.
62. Woolf, T., Melton, D., and Jennings, C.G. (1992) Specificity of antisense oligonucleotides in vivo. *PNAS* 89:7305-7309.
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64. Hemmati-Brivanlou, A. and Melton, D.A. (1992) A truncated activin receptor inhibits mesoderm induction and formation of axial structures in *Xenopus* embryos. *Nature* 359: 609-614.
65. Dohrmann, C.E., Hemmati-Brivanlou, A., Thomsen, G.H., Fields, A., Woolf, T.M., and Melton, D.A. (1993) Expression of activin mRNA during early development in *Xenopus laevis*. *Devel. Biol.* 157:474-483.
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69. Klein, P.S., and Melton, D.A. (1994) Hormonal regulation of embryogenesis: The formation of mesoderm in *Xenopus laevis*. *Endocrine Reviews*.v.15:326-341.
70. Hemmati-Brivanlou, A., and Melton, D.A. (1994) Inhibition of activin receptor signaling promotes neuralization in *Xenopus laevis*. *Cell*. 77:273-281.

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73. Klein, P. and Melton, D.A. (1994) Translation initiation factor 4E induces mesoderm in *Xenopus laevis* embryos. *Science*. 265:803-806.
74. Graff, J.M., Thies, R.S., Song, J.J., Celeste, A.J. and Melton, D.A. (1994) Studies with a *Xenopus* BMP receptor suggest that ventral mesoderm-inducing signals override dorsal signals in Vivo. *Cell*. 79:169-179.
75. Kessler, D. S., and Melton, D.A. (1994) Vertebrate embryonic induction: Mesodermal and neural patterning. *Science*. 266:596-604.
76. Kelly, O.G., and Melton, D.A. (1995) Induction and patterning of the vertebrate nervous system. *Trends in Genetics*. v.11:273-278.
77. Kessler, D. S., and Melton, D.A. (1995) Induction of dorsal mesoderm by soluble, mature Vg1 protein. *Development* 121:2155-2164.
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79. Henry, G. L., Brivanlou, I. H., Kessler, D. S., Hemmati-Brivanlou, A. and Melton, D. A. (1996) TGF- β signals and a prepattern in *Xenopus laevis* endodermal development. *Development*. 122:1007-1015.
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89. Hebrok, M., Kim, S. K. and Melton, D. A. (1998) Notochord repression of endodermal Sonic hedgehog permits pancreas development. *Genes & Development*. 12:1705-1713.
90. Henry, G. L. and Melton, D. A. (1998) Mixer, a novel homeobox gene, is required for endoderm development. *Science*. 281:91-96.
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