



Prof. Marshall Warren Nirenberg

Chief of the Laboratory of Biochemical Genetics, Rockville Pike, MD, USA



Most important awards, prizes and academies

Awards: Modern Medicine Award (1964); Award from the Department of Health, Education, Welfare, 1963; National Medal for Science (1965); Louisa Gross Horwitz Prize (1968); Nobel Prize in Physiology or Medicine for deciphering the genetic code, shared with Gobind Khorana and Robert Holley (1968). *Academies:* American Society of Biological Chemistry; American Chemical Society; American Neurochemistry Society; Biophysical Society; American Association for the Advancement of Science; European Academy of Sciences and Arts; Society for Developmental Biology; Washington Academy of Sciences; National Academy of Sciences, USA; National Academy of Medicine, USA; American Academy of Arts and Sciences; American Neurological Association; Leopoldina Deutsche Akademie der Naturforscher; European Academy of Sciences and Arts; American Philosophical Society; Pontifical Academy of Sciences.

Summary of scientific research

Since 1966 Professor Nirenberg was Chief of the Laboratory of Biochemical Genetics at the National Heart, Lung, and Blood Institute of the National Institutes of Health in Bethesda, MD. Dr. Nirenberg and his coworkers deciphered the genetic code. First, they determined the base

compositions of RNA codons by directing cell free protein synthesis with randomly-ordered synthetic polyribonucleotides; then, they determined the nucleotide sequences of RNA codons by directing the binding of aminoacyl-tRNA to ribosomes with trinucleotides of known sequence. They also showed that single-stranded RNA, but not double- or triple-stranded RNA, is a template for protein synthesis. Dr. Nirenberg then entered the field of neurobiology and established many clonal lines of mouse neuroblastoma cells. He found that some cell lines synthesized catecholamines, whereas others synthesize acetylcholine. Elevation of cellular cyclic AMP for a number of days shifted the cells from a relatively undifferentiated state to a differentiated state where many neural properties were expressed. Five cell lines were found that form abundant synapses with cultured striated muscle cells. A neuroblastoma-glioma somatic hybrid cell line was generated that expresses abundant opiate receptors, which was used as a model system to explore the mechanism of opiate dependence. Dual regulation of adenylate cyclase by morphine was shown to account for morphine dependence, tolerance, and withdrawal. The neuroblastoma and somatic hybrid cell lines that were established have been used as model systems to study many properties of neurons. Dr. Nirenberg and his colleagues discovered and characterized *Drosophila* and mouse homeobox genes. He has focused on one of the *Drosophila* homeobox genes, vnd-NK-2, which initiates the neural pathway of development in the ventral portion of the neuroectoderm and gives rise to part of the ventral nerve cord. His final studies focused on determining how a pattern of neuroblasts that expressed the vnd-NK-2 gene was formed in the central nervous system.

Main publications

Nirenberg, M.W. (with Matthaei, J.H.), 'Characteristics and stabilization of DNase sensitive protein synthesis in *E. coli* extracts', *Proc. Natl. Acad. Sci. USA*, 47, pp. 1580-8 (1961); Nirenberg, M.W. (with Matthaei, J.H.), 'The dependence of cell-free protein synthesis in *E. coli* upon naturally occurring or synthetic polyribonucleotides', *Proc. Natl. Acad. Sci. USA*, 47, pp. 1588-1602 (1961); Nirenberg, M.W. *et al.*, 'An intermediate in the biosynthesis of polyphenylalanine directed by synthetic template RNA', *Proc. Natl. Acad. Sci. USA*, 48, pp. 104-9 (1962); Nirenberg, M.W. (with Jones, O.W., Leder, P., Clark, B.F.C., Sly, W.S. and Pestka, S.), 'On the coding of genetic information', *Cold Spring Harbor Symp. on Quant. Biol.*, 28, pp. 549-57 (1963); Nirenberg, M.W. (with Leder, P.), 'RNA codewords and protein synthesis. I. The effect of trinucleotides upon the binding of sRNA to ribosomes', *Science*, 145, pp. 1399-1407 (1964); Nirenberg, M.W. (with Bernfield, M.R.), 'RNA codewords and protein synthesis. IV. The nucleotide sequences of multiple codewords for phenylalanine, serine, leucine and proline', *Science*, 147, pp. 479-84 (1965); Nirenberg, M.W. *et al.*, 'RNA codewords and protein synthesis. VII. On the general nature of the RNA code', *Proc. Natl. Acad. Sci.*, 53, pp. 1161-8 (1965); Nirenberg, M.W. (with Marshall, R.E. and Caskey, C.T.), 'RNA codewords and protein synthesis. XII. Fine structure of RNA codewords recognized by bacterial, amphibian, and mammalian transfer RNA', *Science*, 155, pp. 820-6 (1967); Nirenberg, M.W., *The Genetic Code, Les Prix Nobel en 1968*, Nobel Foundation, Stockholm, P.A. Norstedt and Söner, pp. 221-41 (1969); Nirenberg, M.W. (with Nelson, P. and

Ruffner, W.), 'Neuronal tumor cells with excitable membranes grown in vitro', *Proc. Natl. Acad. Sci. USA*, 64, pp. 1004-10 (1969); Nirenberg, M.W. (with Amano, T. and Richelson, E.), 'Neurotransmitter synthesis by neuroblastoma clones', *Proc. Natl. Acad. Sci. USA*, 69, pp. 258-63 (1972); Nirenberg, M.W. (with Minna, J. and Glazer, D.), 'Genetic dissection of neural properties using somatic cell hybrids', *Nature New Biology*, 235, pp. 225-31 (1972); Nirenberg, M.W. *et al.*, 'Dual regulation of adenylate cyclase accounts for narcotic dependence and tolerance', *Proc. Natl. Acad. Sci. USA*, 72, pp. 3092-6 (1975); Nirenberg, M.W. *et al.*, 'Synapse formation between clonal neuroblastoma x glioma hybrid cells and striated muscle cells', *Proc. Natl. Acad. Sci. USA*, 73, pp. 123-7 (1976); Nirenberg, M.W. (with Puro, D.G.), 'On the specificity of synapse formation', *Proc. Natl. Acad. Sci. USA*, 73, pp. 3544-8 (1976); Nirenberg, M.W. *et al.*, 'Synapse turnover: A mechanism for acquiring synaptic specificity', *Proc. Natl. Acad. Sci. USA*, 75, pp. 2281-5 (1978); Nirenberg, M.W. (with Trisler, G.D. and Schneider, M.D.), 'A topographic gradient of molecules in retina can be used to identify neuron position', *Proc. Natl. Acad. Sci. USA*, 78, pp. 2145-9 (1981); Nirenberg, M.W. (with Wilson, S., Higbashi, H., Rotter, A., Krueger, K., Busis, N., Ray, R., Kenimer, J.G. and Adler, M.), 'Modulation of Synapse Formation by Cyclic Adenosine Monophosphate', *Science*, 222, pp. 794-9 (1983); Nirenberg, M.W. (with Kim, Y.), 'Drosophila NK-homeobox Genes', *Proc. Natl. Acad. Sci. USA*, 86, pp. 7716-20 (1989); Nirenberg, M.W. (with Mellerick, D.M.), 'Dorsal-Ventral Patterning Genes Restrict NK-2 Homeobox Gene Expression to the Ventral Half of the Central Nervous System of Drosophila Embryos', *Developmental Biology*, 171, pp. 306-16 (1995); Nirenberg, M.W. (with Gruschus, J.M., Tsao, D.H.H., Wang, L.-H. and Ferretti, J.A.), 'The Three-dimensional Structure of the vnd/NK-2 Homeodomain-DNA Complex by NMR Spectroscopy', *J. Mol. Biol.*, 289, pp. 529-45 (1999).