



## Prof. Har Gobind Khorana

Professor, Nobel laureate in Physiology or Medicine, 1968



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

*Awards:* Dannie-Heinneman Preiz, Göttingen, Germany (1967); Louisa Gross Horwitz Prize (1968); Lasker Foundation Award for Basic Medical Research (1968); Nobel Prize in Physiology or Medicine (1968); William Gibbs Medal of the Chicago Section of the American Chemical Society (1974); Gairdner Foundation Annual Award, Toronto, Canada (1980); M.I.T. School of Science Distinguished Service Award (2000); Centennial Honorary Degree, Rockefeller University (2001). *Academies:* National Academy of Sciences, Washington, DC (1966); American Academy of Arts and Sciences (1967); Deutsche Akademie der Naturforscher Leopoldina, Halle/Saale, Germany (1968); Foreign Member, USSR Academy of Sciences (1971); Foreign Member, Indian Academy of Sciences (1978); Pontifical Academy of Sciences (1978); Foreign Member, Royal Society, London (1978); Foreign Member, Royal Society of Edinburgh, London (1982).

### **Summary of scientific research**

With his background as an organic chemist and interest in biology, he always attempted to attack current biological problems by chemical approaches. In the fifties, his laboratory was interested in studying energy-rich phosphate esters, e.g. ATP and coenzyme A and related compounds, and general methods for their synthesis were developed. This was followed by investigations of the chemistry of nucleic acids and especially the synthesis of polynucleotides containing specific

sequences. The methods thus developed made possible definitive studies of the genetic code by the synthesis of defined messenger RNAs. Following elucidation of the genetic code, he then became interested in the problem of the total synthesis of genes in the laboratory. These studies carried out in the sixties and early seventies led to simple and general methods that have now led to the synthesis of large numbers of genes in different laboratories. His interests then turned to studies of biological membranes. In his final years he was particularly interested in membrane proteins that transduce light. Thus, Bacteriorhodopsin uses light energy to pump protons and the membrane potential thus generated is used by the organism for the synthesis of ATP. Vision in vertebrates and invertebrates depends on light transduction by photo receptors in the rod cells. These were the topics he was engaged in up to his death.

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### Main publications

Khorana, H.G., Carbodiimides. Part V. A Novel Synthesis of Adenosine Di- and Triphosphate and P1,P2-Diadenosine-5'-pyrophosphate, *J. Am. Chem. Soc.*, 76, p. 3517 (1954); Khorana, H.G., Studies on Polynucleotides. XLIV. The Synthesis of Dodecanucleotides Containing the Repeating Trinucleotide Sequence, Thymidyl-(3'→5')- thymidyl-(3'→5')-deoxycytidine (with Jacob, T.M.), *J. Am. Chem. Soc.*, 87, p. 2971 (1965); Khorana, H.G., *et al.*, Studies on Polynucleotides. XLVII. The in vitro Synthesis of Homopeptides as Directed by a Ribopolynucleotide Containing a Repeating Trinucleotide Sequence. New Codon Sequences for Lysine Glutamic Acid and Arginine, *J. Mol. Biol.*, 13, p. 283 (1965); Khorana, H.G., *et al.*, Studies on Polynucleotides. XLVII. The in vitro Synthesis of a Co-polypeptide Containing Two Amino Acids in Alternating Sequence Dependent upon a DNA-like Polymer Containing Two Nucleotides in Alternating Sequence, *J. Mol. Biol.*, 13, p. 302 (1965); Khorana, H.G., Nucleic Acid Synthesis in the Study of the Genetic Code, *Les Prix Nobel en 1968*, pp. 196-220 (1969); Khorana, H.G., Total Synthesis of a Gene, *Science*, 203, p. 614 (1979); Khorana, H.G., *et al.*, Refolding of an Integral Membrane Protein: Denaturation, Renaturation and Reconstitution of Intact Bacteriorhodopsin and Two Proteolytic Fragments, *J. Biol. Chem.*, 256, pp. 3802-9 (1981); Khorana, H.G., *et al.*, The Bacteriorhodopsin Gene, *Proc. Natl. Acad. Sci.*, 78 11, pp. 6744-8 (1981); Khorana, H.G., *et al.*, Specific Amino Acid Substitutions in Bacterio-opsin: Replacement of a Restriction Fragment in the Structural Gene by Synthetic DNA Fragments Containing Altered Codons, *Proc. Natl. Acad. Sci. USA*, 81, pp. 2285-9 (1984); Reeves, P.J., Thurmond, R.L., and Khorana, H.G., Structure and Function in Rhodopsin: High Level Expression of a Synthetic Bovine Opsin Gene and its Mutants in Stable Mammalian Cell Lines, *Proc. Natl. Acad. Sci. USA* 93:11487-92 (1996); Hwa, J., Garriga, P., Liu, X. and Khorana, H.G., Structure and Function in Rhodopsin. Packing of the Helices in the Transmembrane Domain and Folding to a Tertiary Structure in the Intradiscal Domain are Coupled, *Proc. Natl. Acad. Sci. USA* 94: 10571-6 (1997); Khorana, H.G., Molecular Biology of Light Transduction by the Mammalian Photoreceptor, Rhodopsin, *J. Biomolecular Structure & Dynamics* 11 (R.H. Sarma and M.H. Sarma, eds) Adenine Press, pp. 1-16 (2000); Hwa, J., Klein-Seetharaman, J., and Khorana, H.G., Structure and Function in Rhodopsin: Mass Spectrometric Identification of the Abnormal Intradiscal Disulfide Bond in Misfolded Retinitis Pigmentosa Mutants, *Proc. Natl. Acad. Sci.*

USA 98:4872-6 (2001); Cai, K., Itoh, Y., and Khorana, H.G., Mapping of Contact Sites in Complex Formation Between Transducin and Light-activated Rhodopsin by Covalent Crosslinking: Use of a Photoactivatable Reagent, *Proc. Natl. Acad. Sci. USA* 98:4877-82 (2001).