KNOW THY INVENTORS

Dr. Har Gobind Khorana

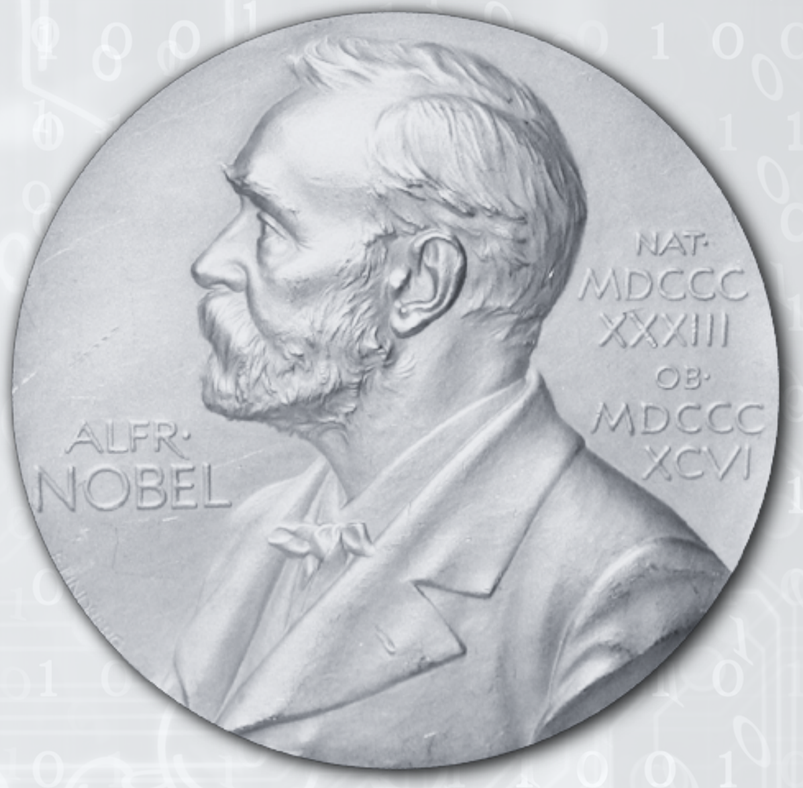
The Artificial Gene Pioneer

METACOG

METACOG

1968

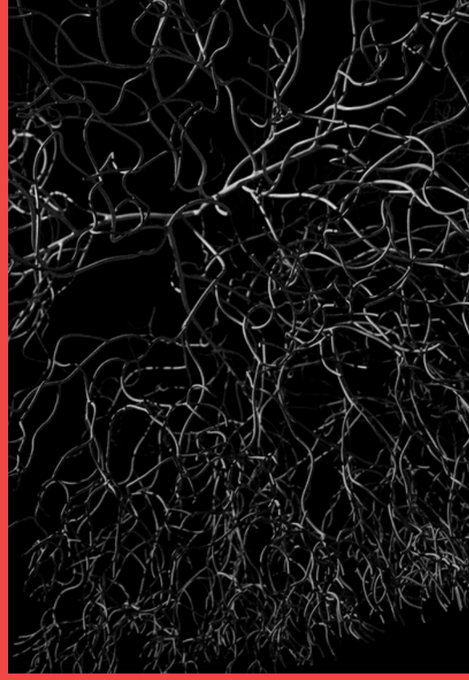
Received Nobel Prize in Physiology or Medicine



for proving that the genetic code consists of 64 different three-letter words

Cell Composition

Har Gobind Khorana confirmed Marshall Warren Nirenberg’s findings that a cell's function depends on how the four nucleotides are arranged on the staircase of a DNA molecule



Total Synthesis of a Gene

The method developed for the total synthesis of a given DNA containing biologically specific sequences consists of the following. The DNA in the double-stranded form is carefully divided into short single-stranded segments with suitable overlaps in the complementary strands. All the segments are chemically synthesized starting with protected nucleosides and mononucleotides. The 5′-OH ends of the appropriate oligonucleotides are then phosphorylated with the use of [γ-32P]ATP and polynucleotide kinase. A few to several neighboring oligonucleotides are then allowed to form bihelical complexes in aqueous solution, and the latter are joined end to end by polynucleotide ligase to form covalently linked duplexes. Subsequent head-to-tail joining of the short duplexes leads to the total DNA. The methods are described for the construction of a biologically functional suppressor transfer RNA gene. The total work involved (i) the synthesis of a 126-nucleotide-long bihelical DNA corresponding to a known precursor to the tyrosine suppressor transfer RNA, (ii) the sequencing of the promoter region and the distal region adjoining the C-C-A end, which contained a signal for the processing of the RNA transcript, (iii) total synthesis of the 207 base-pair-long DNA, which included the control elements, as well as the Eco R1 restriction endonuclease specific sequences at the two ends, and (iv) full characterization by transcription in vitro and amber suppressor activity in vivo of the synthetic gene.

1972

Synthesized the world's first artificial gene