

Roy John Britten (1919-2012) ^[1]

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Roy John Britten studied DNA sequences in the US in the second half of the twentieth century, and he helped discover repetitive elements in DNA sequences. Additionally, Britten helped propose models and concepts of [gene regulatory networks](#) ^[5]. Britten studied the [organization](#) ^[6] of repetitive elements and, analyzing data from the Human Genome Project, he found that the repetitive elements in DNA segments do not code for proteins, enzymes, or cellular parts. Britten hypothesized that repetitive elements helped cause cells to differentiate into more specific cell kinds among different organisms.

Britten was born on 1 October 1919 in Washington, D.C., to Marion Hale, who worked for the US National Research Council, and Rollo Britten, a statistician at the National Bureau of Standards. His mother exposed Britten to science early, and he shared a chemistry lab in the basement with his brother. Britten attended the University of Virginia in Charlottesville, Virginia, in 1936, earning his degree in physics in 1940. He then earned his Master's degree in physics at [Johns Hopkins University](#) ^[7] in Baltimore, Maryland, in 1941 while working on isotope separation, a process of removing isotopes from a chemical element to isolate other isotopes.

Britten worked on the Manhattan Project until 1946. Upon leaving the Manhattan Project, he began his doctoral work in 1946 at [Princeton University](#) ^[8] in Princeton, New Jersey. Britton earned his PhD in nuclear physics in 1951, working with a particle accelerator called a cyclotron. At Princeton, he met Barbara Hagen, and they married in 1947. They had two sons, Greg and Ken, born in 1956 and 1958 respectively. Britten and his wife divorced in 1976, and in 1986 Britten married Jacqueline Reid, who died in 2001.

After taking a post-doctoral position in biophysics at the Department of Terrestrial Magnetism at the [Carnegie Institution of Washington](#) ^[9] in Washington, D.C., where he stayed from 1951 to 1971, Britten took a course on bacteriophages at the [Cold Spring Harbor Laboratory](#) ^[10] in Cold Spring Harbor, New York, and he shifted his research to DNA hybridization at the Carnegie Institution. At the Carnegie Institution, Britten observed single stranded DNA segments combine to form double stranded DNA through a process called renaturation, or the re-pairing of complementary base pairs. To form the double strand, the DNA base pairs must find their complementary pairs. Britten hypothesized that if the strands had repeat sequences, it would then be easier and quicker for the base pairs to locate their complementary base pairs. However, if there was no repeat sequence, then the rate at which the base pairs form the double strands depended on the size of the whole [genome](#) ^[11].

Britten, along with Michael Waring, another scientist at the Carnegie Institution, denatured [mouse](#) ^[12] DNA in 1964. They published their results in a 1966 paper titled "Nucleotide Sequence Repetition: a Rapidly Reassociating Fraction of Mouse DNA." Britten's team had discovered how to isolate single copies of DNA through hydroxyapatite column

chromatography in 1962. Utilizing chromatography, Britten and Waring isolated DNA of other animals and noted that related species have the same repeat sequences.

Working with his colleague David Kohne at the Carnegie Institution in 1965, Britten compared the eukaryotic DNA from a [mouse](#) [12] with the DNA of a single-celled bacterium. Knowing that mice had greater than one hundred times the amount of DNA per cell as compared to a bacterium *Escherchia coli* [13], they hypothesized that bacterial DNA would reform quicker than eukaryotic DNA. They hypothesized that as there was less DNA, the base pairs should find their complementary pairs quicker. However, they found that the eukaryotic mice DNA reformed double strands quicker than did the bacterial DNA, and this data suggested that the *E. coli* took longer to find its complementary base pairs. This work, published in the 1968 article "Repeated Sequences in DNA,, hinted that there were more complex interactions between base pairs of DNA than previously theorized.

Britten and Kohne tested to see how much of the [mouse](#) [12] [genome](#) [11] coded for proteins, as the majority of the [mouse](#) [12] DNA seemed to be made of repetitive elements, which don't code for proteins. To test to see if mRNA duplicated all of the portions of the DNA, they radioactively labeled mRNA before dissociating the strands of the DNA to see how the mRNA compared with the DNA. The mRNA then combined with the DNA, but only on portions that were not repetitive, and Britten, noting that mRNA is a precursor to cell products, showed that the repetitive elements did not code for any cell product. Britten and Kohne confirmed that repetitive elements were large portions of noncoding regions of the [genome](#) [11] in mice, calf, and salmon in their 1968 paper "Repeated Sequences in DNA, Hundreds of Thousands of Copies of DNA Sequences have been Incorporated into the Genomes of Higher Organisms."

The question remained, however, as to why DNA that does not code for proteins would exist in genomes. Britten and Kohne argued that the repetitive portion of DNA most likely comes from errors during DNA replication. As they found many repetitive units near the centromere, the part of the chromosome that links sister chromatids, they hypothesized that the repetitive portions of DNA functioned in cell division. During cell division, the centromere attaches to spindle fibers that allow the sister chromatids to be pulled apart.

Between 1967 and 1969, Britten worked with [Eric Davidson](#) [14] at the [California Institute of Technology](#) [15] (CalTech) to propose a gene [regulation](#) [16] network model, in which [genes](#) [17] interacted to control cell [differentiation](#) [18] through expression of [genes](#) [17]. They sought to predict the development of different organisms by following the regulatory [genes](#) [17] that controlled specific [genes](#) [17] that were turned on at specific times. At the time, embryologists could not distinguish what processes controlled cell [differentiation](#) [18] and cell [determination](#) [19]. Britten and Davidson connected regulatory RNAs to repetitive sequences in their model, showing that RNA could interact and regulate DNA. However, the method in which the RNAs functioned in gene expression was not clearly outlined. Since the introduction of the Britten-Davidson model, researchers have used it to model the functioning of [genes](#) [17] in many animals. They published their theory in 1969, in an article titled "Gene Regulation for Higher Cells: A Theory."

Through the 1970s, Britten developed methods for identifying genetic similarities between organisms. In 1971, Britten took a visiting associate professorship at the Kerckhoff Marine Lab, a part of CalTech, in Newport Beach, California. Davidson joined Britten at CalTech to work on The Macroproject during the same year. Funded by the National Institute of Child Health and Human Development headquartered at Bethesda, Maryland, Britten and Davidson

developed The Macroproject to examine how [genes](#) [17] affected organisms as they developed. Britten and Davidson used the [sea urchin](#) [20] embryo as their model system. In 1971, Britten and Davidson published "Repetitive and Non Repetitive DNA Sequences and a Speculation on the Origins of Evolutionary Novelty," in which they concluded that legs and fins develop as a direct result of specific [genes](#) [17] turned on during specific times of development.

After this work, Britten and Davidson partnered to study the [regulation](#) [16] of gene in animal development until Britten's death in 2012. To study how repetitive DNA sequences were distributed throughout the [sea urchin](#) [20] [genome](#) [11], Britten and Davidson in the early 1970s sheared DNA at different lengths and then reattached the sheared base pairs (re-natured) to their complementary pairs. They discovered that large portions of the sea urchins' genomes contained repetitive elements that interspersed among smaller coding regions. In 1971, they found that mammalian and [frog](#) [21] DNA also had large portions of repetitive elements. However, the repetitive elements differed in composition between different species, and even between closely related species.

Britten was promoted to senior research associate at CalTech in 1973. While teaching a class in the summer of 1973, Britten used his students to help sequence the DNA of multiple marine organisms. Using the sequenced data, he showed that genomes were organized in many different ways, and that the ranges for repetitive units varied extensively across species. He showed that the fruit fly, for instance, had no repetitive units. In the 1980s, Britten studied messenger RNA in embryos, culminating in the 1980 publication "Messenger RNA Prevalence in Sea Urchin Embryos Measured with Cloned cDNAs." Britten discovered that different [genes](#) [17] were expressed at different intervals in the [sea urchin](#) [20] embryo as it developed, and he showed how to measure the rates of synthesis of nuclear RNA and the corresponding mRNA levels in the cytoplasm of the cells.

Beginning in 1990, Britten focused on genomics and [evolution](#) [22]. With computational analyses, Britten used data generated by the Human Genome Project to determine how repetitive elements affected the human [genome](#) [11]. Britten studied repetitive DNA and how it influenced evolutionary history. At first, Britten only accounted for substitutions, in which a single base pair in a DNA sequence replaces, over the course of [evolution](#) [22], a different base pair in that sequence. Later Britten started observing indels, or whole sections of DNA that were removed or added to DNA sequences over the course of [evolution](#) [22]. He published this research in 2002. He found that 1.4 percent of differences between chimpanzee and human DNA were caused by substitution, while 3.9 percent were caused by indels. This paper challenged the 1975 theory proposed by Alan Wilson and Mary-Claire King, working at the University of California Berkeley in Berkeley, California, that chimps and [humans](#) [23] shared greater than 98 percent of their DNA. In addition to primates, Britten also used sea urchins to look for similar patterns in the genomes caused by the repetitive DNA elements.

Beyond his work in science, Britten sailed, played the flute, and painted. In 1972, he was elected into the US National Academy of Sciences in Washington, D.C. Britten studied [primate](#) [24] genomes at CalTech until his death on 21 January 2012, of pancreatic cancer.

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Subject

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Topic

People [48]

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