DLC-427 Intellectual Property and Genetic Resources in the Life Science

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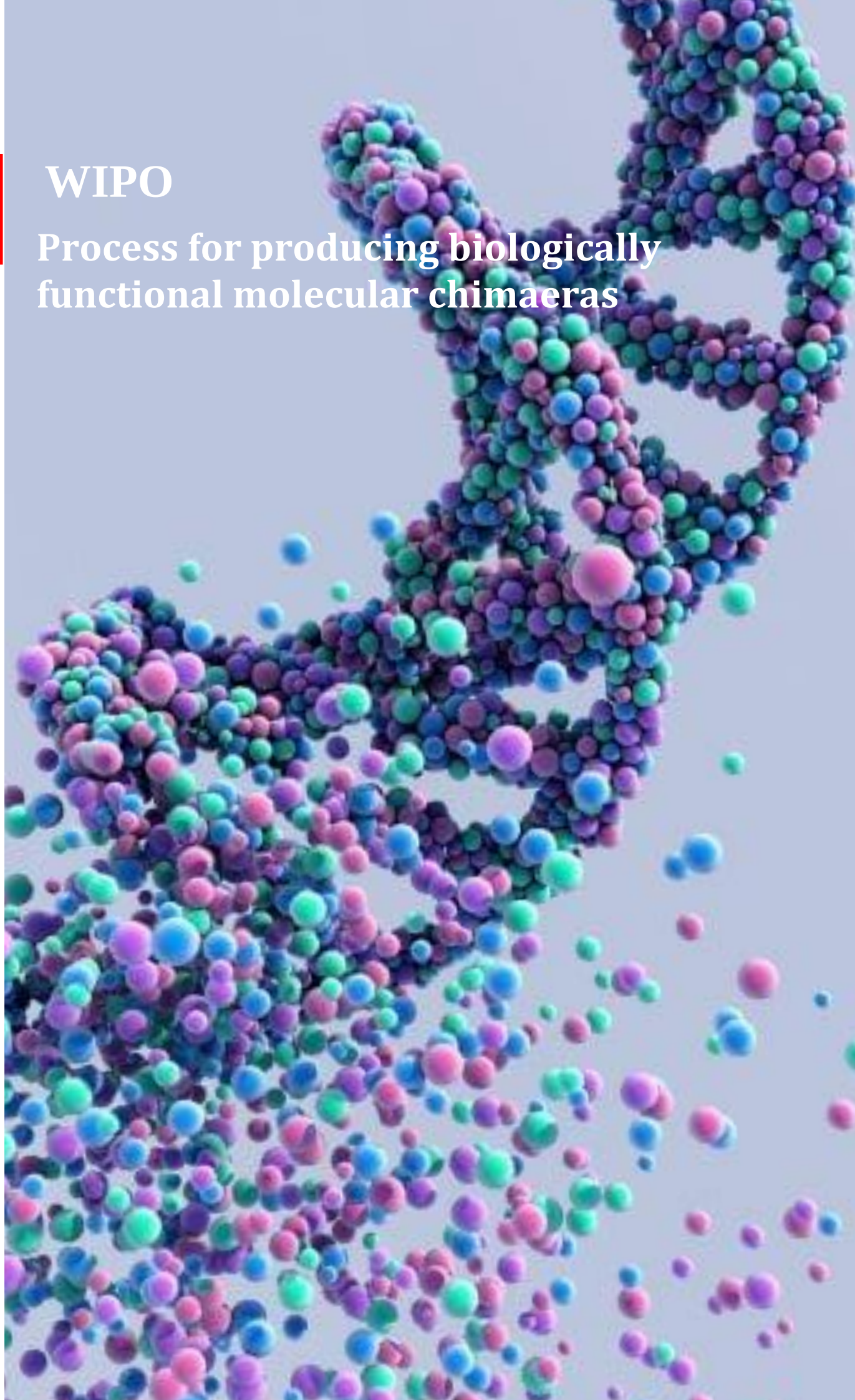
Process for producing biologically functional molecular chimaeras



Case Study A – Process for producing biologically functional molecular chimeras / STANFORD UNIVERSITY – *Path-breaking Patent on Recombinant DNA technology*

Title of the invention	Process for producing biologically functional molecular chimeras
Assignee	LELAND STANFORD JUNIOR UNIVERSITY
The patent	US4237224A – pdf file of the patent

Image ©-cleared of Case Study A

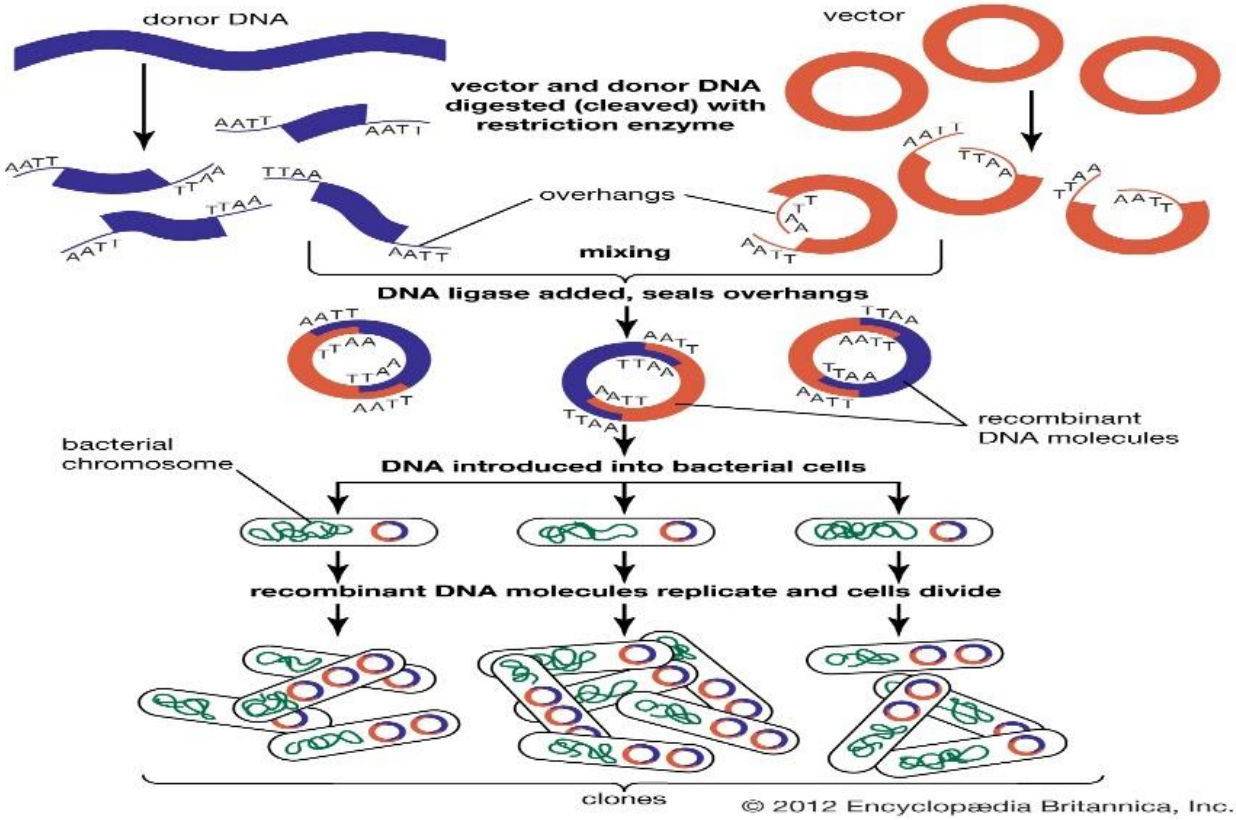


Figure 1 – Steps of DNA cloning

Abstract

In this case study, we will look at one of the most important patents granted in the history of the biotechnology industry. The Cohen-Boyer technology for recombinant DNA is often cited as the most successful patent in the commercialization of molecular biology. The patent application, enentitled "Process for producing biologically functional molecular chimeras", was filed by the Board of Trustees of the Leland Stanford Junior University, with Stanley N. Cohen and Herbert W. Boyer as the inventors. The patent application of Cohen and Boyer was filed on January 04, 1979 and claimed priority from US52069174A (filed on November 04, 1974). The patent relates to a process for preparing for making molecular chimeras. The patent was granted on December 02, 1980, i.e., after six years from the priority date (November 04, 1974).

The Cohen-Boyer licensing program, by any variety of metrics, was widely successful. Recombinant DNA (rDNA) products provided a new technology platform for a range of industries, resulting in over US$35 billion in sales for an estimated 2,442 new products. Over the duration of the life of the patents (they expired in December 1997), the technology was licensed to 468 companies and other licensees. Over the 25 years of the licensing program, Stanford and the University of California system accrued US$ 255 million in licensing revenues (to the end of 2001), much of which was subsequently invested in further research and research

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infrastructure. In many ways, 'Stanford's management of the Cohen-Boyer patents has become the gold standard for university technology licensing. In total, 2,442 known products were developed from the recombinant DNA technology, among them drugs to mitigate the effects of heart disease, lung disease, anemia, HIV-AIDS, cancer, diabetes, and numerous other diseases and disorders[1].

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Case Study A

DNA molecules are formed into the double helix structure, as elucidated by Watson and Crick in 1953. DNA is made up of molecules called nucleotides. Each nucleotide contains a phosphate group, a sugar group, and a nitrogen base. The four types of bases are adenine (A), thymine (T), guanine (G), and cytosine (C). DNA cloning or 'Recombinant DNA' (rDNA) technology refers to the process of joining DNA molecules from two different sources and inserting them into a host organism to generate products for human use. In the process of rDNA technology, DNA (donor DNA) is extracted from the organism under study and is treated with restriction enzymes that chemically cut the DNA at specific target sequences along its length (like scissors) into smaller DNA fragments. The vector or plasmid (another DNA molecule) is cut with the same restriction enzyme used to cut the donor DNA. The cut donor DNA is inserted into the cut vector and is subsequently joined with the help of DNA ligase to obtain recombinant DNA molecules, also called a recombinant plasmid. The recombinant plasmid is next introduced into a host organism or bacteria (e.g. *E. coli*) to produce new bacteria. The new bacteria are called transformants or recombinants. Each time the bacterial cell divides, it will pass the new inserted DNA to the next generation. In a matter of hours, thousands of bacteria containing hybrid DNA are obtained. The new colony, called a genetic clone, can produce a specific protein determined by the inserted DNA. This whole process of DNA cloning is shown in **Figure 1**.

The patent of Cohen and Boyer (US Patent No.: 4,237,224) relates to a method for genetically transforming microorganisms, particularly bacteria, to provide diverse genotypical capability and producing recombinant products. The process employs plasmids or vectors which are spliced using restriction enzymes to produce linear DNA molecule. The linear DNA molecule is ligated to a foreign DNA fragment having one or more intact genes to produce a recombinant plasmid. The recombinant plasmid molecule is referred as a "hybrid" plasmid or plasmid "chimera." The recombinant plasmid is inserted into a microbial cell by transformation methods to produce transformants. Isolation of the transformants (the recombinant microorganism) provides cells for replication and expression of the DNA molecules present in the recombinant plasmid. The method provides a convenient and efficient way to introduce genetic capability into microorganisms for the production of nucleic acids and protein. The proteins include hormones, drugs, antibodies, or commercially useful enzymes.

The priority application of Cohen and Boyer patent was originally filed on November 04, 1974 and covered both the process of making and the composition for biologically functional products. During prosecution at the USPTO, the examiner indicated that he was willing to allow the process claims, which described the method for producing transformants and recombinant products. However, he did not allow the claims directed to the biological material *per se*, i.e., "products." Subsequently, these applications were divided into the process patent and two divisional applications: one claimed recombinant products produced in prokaryotic cells, and the other claimed the recombinant products in eukaryotic cells. The patent application (process patent application) of Cohen and Boyer (US4237224A) was examined for six years, and it was finally granted on December 2, 2020. The recombinant DNA (rDNA) was a revolutionary platform technology and led to a new paradigm shift in modern biotechnology. It brought a quantum leap and opened the floodgates of innovation in recombinant DNA technologies as developed further by several new biotech companies, including Genentech, which employed gene cloning methods to produce recombinant products.

[1] Feldman, Maryann P., Alessandra Colaianni, and Connie Kang Liu. "Lessons from the commercialization of the Cohen-Boyer patents: the Stanford University licensing program." *Intellectual property management in health and agricultural innovation: A handbook of best practices* 2 (2007).

Commercial Value

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