Chapter 1

Biotechnology in Japan - An Introduction

1. Historic Aspects

Biotechnology has been defined as "the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services" [OECD, 1].

The Japanese have made early claims in this field. Most readers of this book might have enjoyed the delicacies of the traditional Japanese cuisine, which is strongly built on fermented products. The manufacture of sake is documented since AD 600, and there are still more than 2000 companies which produce this national alcoholic beverage. Fermented soy products such as tofu or natto laid the foundation for many of today's food companies, and food flavors, in particular soy sauce, have been playing an important commercial role.

After the opening of Japan to Western influence and technology, during the Meiji period, traditional production methods were gradually substituted by procedures based on natural science. The first Japanese to become involved in fermentation technology, in a modern sense, may have been Jokichi Takamine, who concentrated on improvements in brewing. After a successful business career in Japan, he established the Takamine Chemical Laboratory in Chicago in 1890 and, during his 40 years in the USA, became an early pioneer in applied biochemistry [2].

With the strong industrialization in the pre-war period, many companies involved in fermentation were established or considerably enlarged. To cite just a few examples: Suntory Co. was established in 1899 (main product: whiskey), Kirin Brewery Co. in 1907 (main product: beer), and Ajinomoto Co. in 1925 (main product: sodium glutamate). The advent of molecular biology, in the post-war period, led to rapid improvements in fermentation technology. An outstanding example is the industrial application of auxotrophic strains or
regulatory mutants to produce lysine in yields several times above the standard level (Kyowa Hakko, 1957)[3]. Especially in the field of amino acids, more breakthroughs were to come from Japan: the enzymatic manufacture of L-lysine from caprolactam (Toray, 1970)[4], and the use of immobilized esterases to produce L-amino acids from racemic precursors (Tanabe Seiyaku, 1974)[5,6].

As a result, Japan seemed in a very good competitive position as to the commercial exploitation of fermentation, when, in 1972, Cohen and Boyer's discovery of in-vitro DNA recombination opened the gate to the "new biotechnologies" which soon included not only microbial fermentation, but also the manufacture of recombinant products (hormones, vaccines, immunomodulators), monoclonal antibodies, the application of animal and plant cell culture, novel production technologies for animals and plants, and the combination of biological and electronic elements. In the USA, companies mostly based on venture capital quickly formed in these new niches and, as a result, Japan perceived herself under a "patent attack" from abroad, as illustrated in Fig. 1.1 [7,8].

![Fig. 1.1. Recent patent applications in Japan (rDNA, cell fusion)](image-url)