Chapter 11

Plant-Derived Antibodies: The Medicines of Tomorrow
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Abstract: With the advent of hybridoma and recombinant antibody technologies, antibodies have been expressed in various production systems such as mammalian cells and bacteria. In order to address the increasing demand and safety requirements of the biomedical industry, plant-based bioreactors have been recently developed, leading to the cost-effective production of various pharmaceutically important antibodies in plants. Plants have proven to be highly flexible bioreactors, where high levels of antibodies and antibody fragments could be expressed intracellularly in various organelles, as well as extracellularly in various organs or in culture media. Plant-derived antibodies are potent reagents that could be used in both disease diagnosis and therapy, as well as in plant protection, environmental monitoring and food safety. Antibodies endowed with new and specific properties that could not otherwise be produced in animals or bacteria have been created, potentially providing large and safe supplies of medically useful products that correspond to the health-care needs. Although further optimization of plant-based bioreactors is still required, antibodies obtained so far have been successfully used in disease prevention and diagnosis, as well as in both topical and passive immunotherapy.

1. INTRODUCTION

Recent advances in medical research have resulted in a more detailed understanding of the molecular bases of many human and animal diseases (1). Better disease characterization has led to the development of new protein-based strategies such as immunotherapy, where antibodies (Abs) are used to prevent or treat pathogenic infections. These new strategies have led
to an increased demand for large amounts of Abs for the health care and pharmaceutical markets. Since limited supplies of Abs are currently available, the development of cost-effective systems for large-scale production of complex and functional Abs is critical for the success of these new therapeutic strategies. Although bacterial and mammalian systems have been mainly used so far, increased production on a commercial scale could be difficult and very expensive (1). Thus, transgenic plants expressing Abs may solve some of the limitations that currently hinder wider applications of Abs in medicine.

2. FROM MURINE ABS TO RECOMBINANT AB FRAGMENTS

Abs are Y-shaped proteins produced by the vertebrate immune system. They consist of four polypeptide (two heavy and two light) chains, stabilized through disulfide bonds. The antigen-binding domains form the tips of the Y structure, whereas the effector (or constant) domains form the stem of the molecule (Figure 1). In animals, a first encounter with an antigen results in the production of low affinity Abs. Upon this primary exposure, cells producing higher-affinity Abs are selected, and undergo a process called “affinity maturation”, where the Ab genes from the initial repertoire are randomly mutated, thereby generating Abs with varying affinity for the given antigen. The diversity thereby obtained is astronomical (2). Upon secondary exposure, cells displaying the highest affinity Abs are rapidly induced and generate a heightened response. Abs highly specific for virtually any molecule can, therefore, be obtained following immunization of animals with a given antigen.

The advent of hybridoma technology gave rise to monoclonal Abs, i.e. Abs issued from one single clone of cells, possessing all the same binding characteristics and affinity for a given antigen (3). Shortly after, researchers in molecular biology and Ab engineering worked jointly to take advantage of the domain structure of Abs, allowing the use of the antigen-binding domains and effector domains separately (2). These technologies have led to recombinant Abs (rAbs) such as the single-chain variable fragment (scFv), as well as the antigen-binding fragment (Fab) and variable heavy (VH) Abs (Figure 1). Recently, the development of phage-display technology has helped in obtaining rAbs with higher specificity and affinity through the use of Ab panning, thereby allowing a more efficient selection of Abs with desired properties (4,5).