REPORTES

PRODUCTION OF RECOMBINANT ANTIBODIES IN NON-MAMMALIAN HOSTS

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Introduction

Antibodies are mammalian serum glycoproteins produced by B lymphocytes of the adaptive immune system. Their principal *in vivo* function is to mediate adherence of infectious agents to phagocytes, exploiting their own two unique properties, viz., specificity and memory. Antibodies are classified into three different categories, i.e., polyclonal, monoclonal or recombinant, on the basis of the method of their production and composition. Polyclonal antibodies are produced in rabbits and other animals. On the other hand, monoclonal antibodies (mAbs) are secreted by immortalized hybrid cell lines (hybridomas). Both of these approaches use animals at some stage of the procedure and do not allow manipulation of the structure or function of antibodies. However, application of the recent advances in molecular biology has made it possible to not only eliminate our dependence on vertebrates for antibody production but also design the structure and function of antibodies (1). Here, I consider the suitability of non-mammalian host systems for the production of recombinant/ engineered antibodies/ antibody fragments/ binding molecules.

Materials and Methods

The plasmids, yeast expression vectors, AcMNPV (baculovirus) transfer vectors, insect cell lines (*Sf*-9 and *Sf*-21) and other (host) strains used in the studies discussed here are commercially available. Experimental procedures have been described earlier (1-4).

Results and Discussion

Polyclonal antibodies have found many clinical and non-clinical applications. Polyclonal antibodies are relatively easy and inexpensive to produce and suit most biological and immunochemical applications. However, since they are a mixture of antibodies invariably recognizing more than one epitope, their application in clinical medicine have been limited to diagnosis. Monoclonal antibodies are the second generation antibodies that have found specialized applications in medicine because of their origin from a single clone. However, since large portions of their signature sequences, viz., immunogenic regions are of murine origin, they, similar to polyclonal antibodies, are of limited value in immunotherapy. The recent availability of powerful genetic engineering techniques that permit isolation and manipulation of antibody genes has led to the development of the third generation of antibodies, recombinant antibodies. Production of recombinant antibodies/fragments with tailored structures and functions started with humanization of murine mAbs, followed by their synthesis in *Escherichia coli*, yeast, bacteriophage, fungi, insect cell lines and plants (cf 1, 2).

The focus of our laboratory has been optimal production of soluble antibodies/binding molecules of environmental health importance in non-mammalian hosts and to engineer them to withstand effects of special matrices such as soil and solvents. We have cloned from murine hybridomas/ immunized spleens genes encoding light- and Fd chains and Fab to two different herbicides and expressed them in *E. coli* and insect cell lines (3). We have also produced the light- and Fd chains of a human antibody in insect cell lines, as evidenced by immunoblots probed with goat anti-human Fab antibodies (T. Nagamine and P. Choudary, unpublished). These, together with experiments from other laboratories, pave the way not only for producing antibodies with novel properties but also for bypassing the use of vertebrates for antibody production (4). Multiple applications are envisaged for the alternative hosts expressing antibodies/ binding molecules, e.g., chimeric phage and yeast as affinity-reactors for batch purification of contaminated water/ soil samples and transgenic plants as on-site bioreactors for continuous sequestering and detoxification of pesticides and other hazardous chemicals.

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