Perhaps the greatest advantages of using mammalian cell cultures are the ease with which the cells can be transfected and the wide array of mAbs that can be produced. Following decades of use for recombinant protein expression, mammalian cell lines have been scrupulously characterized and have been acknowledged by researchers and regulatory agencies alike as viable production platforms for mAb production (Butler and Meneses-Acosta, 2012). Furthermore, the near-human post-translational modification pathways in mammalian cells make them suitable for producing therapeutic mAbs for human use.

Despite their relative ease of use and extensive characterization, the use of mammalian cells for producing mAbs is not without its shortcomings. Because mammalian cell cultures are costly to maintain, their operating costs are transferred to the patient. Large-scale production can be achieved in bioreactors of up to 25,000 L. However, these are costly to operate and maintain due to their high degree of sophistication, and they are poorly suited to meet unexpected high demands for particular mAbs. Also, products produced from mammalian cells must be extensively tested for a larger group of pathogens that are potentially harmful to humans, thereby imposing increased expenditures for rigorous quality control testing and process validation requirements prior to each batch release.

17.3 PLANTS AS BIOREACTORS FOR mAb PRODUCTION

The first demonstration of the successful expression of an IgG in plants was in 1989 (Hiatt et al., 1989); since then, improvements in the production of mAbs by plants have contributed to realistic proposals for the use of plant systems as an alternative platform for the production of therapeutic proteins. This is exemplified by research on plant-based biopharmaceuticals that has been conducted under sponsorship of the US Defense Advanced Research Projects Agency's (DARPAs) "Blue Angel" project, with funding totaling more than $100 million as of 2013 (Bosch et al., 2013; Sheldon, 2012). Furthermore, although not an antibody, the FDA's approval of Elelyso, which is a recombinant form of taliglucerase alpha produced by Protalix and Pfizer using carrot cell culture, in 2012 for the treatment of Gaucher's disease substantiated the ability of a plant-based platform to produce clinically effective biopharmaceuticals (Maxmen, 2012; Sack et al., 2015a). In addition, the recent USFDA approval of ZMapp, an mAb cocktail produced in *Nicotiana benthamiana* for treatment of Ebola virus disease (Qiu et al., 2014), for use on a provisional emergency basis without clinical trials further confirms the viability of using plant-based systems for producing functional mAbs (McCarthy, 2014).

17.3.1 Agrobacterium and Binary Vectors

Recombinant therapeutic proteins can be produced in plants using either a stable transgenic or transient expression system. Both strategies use *Agrobacterium tumefaciens*, a soil bacterium capable of transferring genetic material to the nuclear genome of the plant hosts it infects (Gelvin, 2003; Smith and Townsend, 1907). *A. tumefaciens* transfers select genetic material, termed transfer-DNA (T-DNA), into plant cells by functions encoded on its tumor-inducing plasmid (pTi): a 200-kbp