Abstract

Monoclonal antibodies and other biologics, including next generation antibody therapeutics, are the fastest growing segment of the pharmaceutical industry, projected to reach almost 300B in annual sales by 2020. Biologic therapies have had significant impact on the treatment of many cancers, autoimmune diseases, and neurological diseases with newer therapies targeting a wider range of serious health conditions. Most of these drugs are produced in mammalian cell culture systems, requiring extensive downstream purification through multi-step processes. For traditional monoclonal antibodies (mAbs), the most expensive of those steps is affinity capture by Protein A. Protein A is a bacterial protein that binds to the Fc of most mAb or Fc fusion biologic drugs. However, it is expensive, poorly reusable, requires harsh acid elution to recover the captured molecules, and does not work for biologics lacking an Fc domain. We propose a novel form of weak affinity chromatography based on the use of mimetope peptides specific for a given biologic drug. In previous work, we have developed these mimetope peptides as capture reagents for immunoassays and have demonstrated that we can robustly generate mimetope peptides specific to almost any mAb through screening phage displayed peptide libraries. Mimetope Peptide Weak Affinity Chromatography (MPWAC) has several advantages over Protein A. Producing peptide-coupled beads for chromatography is simple as peptides are generally synthesized on-bead during solid phase synthesis. Industrial scale peptide synthesis is already routine in the industry and benefits from significant economies of scale that will make it considerably cheaper than production of Protein A media. Immobilized peptides are robust and reusable, and compatible with mixed mode chromatography approaches. Importantly, the affinity of a mimetope peptide for its target drug product can be tuned for true isocratic chromatography that avoids damaging elution conditions. The annual market for Protein A chromatography is rapidly growing and will exceed half a billion dollars in the next few years. With the proposed MPWAC technology, a broader array of biologic therapies will be manufacturable at reasonable costs to benefit patients in the US and worldwide.