Pharmaceutical biotechnology - concepts and applications: Walsh Gary Wiley, Chichester, West Sussex, UK

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Pharmaceutical biotechnology is a relatively new and growing field in which the principles of biotechnology are applied to the development of drugs. A majority of therapeutic drugs in the current market are bioformulations, such as antibodies, nucleic acid products and vaccines. Such bioformulations are developed through several stages that include: understanding the principles underlying health and disease; the fundamental molecular mechanisms governing the function of related biomolecules; synthesis and purification of the molecules; determining the product shelf life, stability, toxicity and immunogenicity; drug delivery systems; patenting; and clinical trials. Although it is rare to find all these topics in a single book, a new textbook by Gary Walsh indeed brings them all together. This well-written, easy-to-read textbook assembles information from multiple resources, and provides additional references for further reading. The book is published as a companion to *Biopharmaceuticals: Biochemistry and Biotechnology*, by the same author, which was published by John Wiley in 2003.

The book starts with a brief history of the discovery and application of therapeutic drugs, such as sulfa drugs, which were one of the very first to be marketed, and then proceeds to various

bioformulations and their widespread use. The pharmaceutical companies that have marketed bioformulations use biotechnology principles such as recombinant DNA technology to design more effective protein-based drugs, such as erythropoietin and fast-acting insulin. The book explains how the advances in other areas such as genomics, proteomics and high-throughput screening have paved the way for exploring new avenues of drug discovery. The author also offers a prospective analysis of the use of gene therapy and whole cell-based therapeutics such as stem cells.

The future of pharmaceuticals belongs to protein based therapeutics. Designing stable and effective therapeutic proteins requires knowledge of protein structure and the interactions that stabilise the structure necessary for function. The book discusses the various levels of protein structure and the types of interactions between amino acid residues that improve protein folding and stability. Structure prediction methods can be used for those proteins for which no structure is available. Therapeutic proteins frequently contain post translational modifications - for example, glycosylation of erythropoietin. The author discusses different types of such modifications, their effect on protein function (with examples from protein formulations that are currently in use) and methods for their production in the laboratory.

The book goes on to address technical aspects of protein drug discovery in sufficient detail to cover the qualitative principles involved. For large-scale protein synthesis, recombinant DNA technology is used. This includes extracting the DNA or RNA of interest from biological samples such as cells or tissues, integrating the DNA encoding the protein of interest into an appropriate cloning vector, finding suitable host cells to express the protein (eg *Escherichia coli* , yeast, insect cells, plants, or animals), designing protocols to obtain highly pure proteins (eg chromatographic purification via size-exclusion, ion-exchange, hydrophobic interaction or affinity) and protein engineering to generate mutants and/or facilitate post-translational modifications. The protocols employed must not cause side reactions such as deamidation, which can change the properties of a protein drug. The drug is finally freeze-dried and packaged for delivery.

The stability/shelf life of a drug also must be assessed, and the book explains the various experimental techniques involved. These include determining the concentration of functional protein and its potency over time, the effect(s) of any contaminants, potential toxic aggregates, product degradation rate and covalent modifications that may occur over time. These quality assurance measures define the conditions under which the drug can be transported, stored and administered to the patient.

The next step is to decide how to deliver the drug to the desired location in the human body. The various delivery routes available include oral, pulmonary, nasal, transmucosal and transdermal. Each route has its own advantages and disadvantages, such as the rate of drug release and its clearance, which may have an impact on the dosage level. The book describes the various options that need to be considered when determining which delivery method should be adopted.

It is important to patent any biomolecule which might have pharmaceutical value. A patent prevents others from exploiting the innovation for up to 20 years. Naturally occurring products cannot be patented unless they involve substantial post-extraction development. The book explains the steps involved, with examples from currently available drugs on the market, including those details that need to be considered at each step.

The book next describes the process involved in taking a potentially marketable drug into clinical trials, where pharmacokinetic and pharmacodynamic experiments reveal the drug's fate and its mode of action in the body, and where the drug's potential toxicity and immunogenicity are assessed. Prior to the trial, approvals need to be obtained from the appropriate regulatory authorities (eg the US Food and Drug Administration), and, of course, the manufacturing facility must comply with industry safety and quality standards. After the drug enters the market, post-marketing surveillance must be carried out to track any side effects or adverse reactions.

The book also contains separate chapters dedicated to biochemical pathways that are commonly targeted by drugs that are on the market, with case studies and their medical uses: cytokines, interferons (eg Rebif, interferon beta-1a), interleukins (eg Ontak, denileukin difitox), tumour necrosis factors (eg Beromun, tasonermin), growth factors (eg Neupogen, filgrastim), hormones (eg Humalog, insulin lispro), enzymes (eg Benefix, nonacog alfa), antibodies (eg Avastin, bevacizumab) and vaccines (eg Engerix B, hepatitis B virus coat). There is also a separate chapter dedicated to nucleic acid- and cell-based therapeutic strategies such as gene therapy and stem cells.

For an investigator like me, who is involved in fundamental research, reading this book was an educational journey that familiarised me with several applicationend topics. The book's strong point is certainly the depth and breadth of the topics covered, and hence I recommend the book both to basic scientists and to more seasoned researchers in the field of pharmaceutical biotechnology.

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