FOREWORD

Molecular biology is largely involved in the research for new therapeutic strategies. Thus, if the gene/protein underlying a hereditary or acquired disease is identified, it is possible to discover new tracks for the "design" of drugs which reduce the deficits or the excess activity of this gene/protein. For example, in the case of an anomaly in a particular receptor (cell surface protein intended to convey an external message to internal cellular structures) which causes a certain disease, it is possible to design and develop some molecules, future drugs that are able to act specifically on the receptor or replace its poor function in a different way.

Research conducted on therapeutic molecules is based nowadays on computer-assisted molecular modeling techniques, on the synthesis of synthetic analogues of these molecules and on high-level selection tests of these numerous analogues. All of these techniques will enable, in a very short time, a selection of the therapeutic efficacy of a particular target out of the several candidate molecules.

The first part of the book, based on molecular study, namely molecular signals, analyzes different cell testing technologies. When mentioning these techniques, we refer not only to the mere detection of a single cell product, but to the monitoring of a variety of metabolic processes aimed at the multidimensional phenotypic characterization of cell behavior. The second chapter introduces the reader to knockout gene models, a technique that allows us to create and introduce a model of pathological mechanism in a complex organism, thus seeking to obtain an analytical tool of increased relevance in the molecular biology of pharmaceutical drugs. The next section presents the details of a molecular analysis technique, based on the so-called "reporter genes".

The recent deciphering of the human genome has provided new support to the entire research area. Suddenly, a large number of molecular targets have be-

come available for analysis. First, we need to answer the question: what does this target molecule do in terms of cellular and biochemical processes and how is it controlled? The answer to these questions will be found in Chapter 4, which deals with the "orphan" G protein-coupled receptors (GPCR) and implicitly tries to present new challenges and opportunities in finding new ligands with still unknown biological effects.

The second part of this book is entirely devoted to the drug synthesis process. Two areas of concern can benefit enormously from the research on the synthesis process in molecular biology and the use of appropriate techniques for this purpose: the elucidation of the stereo-selective synthesis of natural compounds and their analogues and the synthesis of pharmacological compounds derived from DNA or proteins. The first chapter of this second part provides a comprehensive overview on the use of enzymes in stereo-selective synthesis, involving the use of genetic recombination techniques. The fascinating field of pharmacological products that interact with nucleic acids, their structure and synthesis, their agonists and the mechanisms of action are the subject of Chapter 6.

The third part presents the analytical methods involved in determining drug-target interactions. In this sense, we discuss the use of proteins in affinity chromatography and the enantioseparation of enantiomers (a molecule which is part of a compound consisting of two molecules, one of which is the mirror image of the other one, without being identical to it). The use of nuclear magnetic resonance (NMR) and related techniques in the study of molecular structures is another topic approached in this part of the book.

Elements of kinetics, metabolism and toxicology, involved in pharmacogenomics and toxicogenomics, constitute the final part of this book.

Now we know that a disease is a combined result of hundreds of proteins and, in this context, it is difficult to hope that we might find a single active principle capable of curing the disease. Indeed, out of 100 drugs that go beyond the human testing stage, only three reach the market. The others will prove to be toxic or ineffective. Perhaps all "good" targets on which a drug may have an effect have already been found, which means that, to produce new drugs, one must return to the old ones, which would be reused in a different way. Like nature, scientists will develop the new from the old, with the help of molecular biology.

The Author