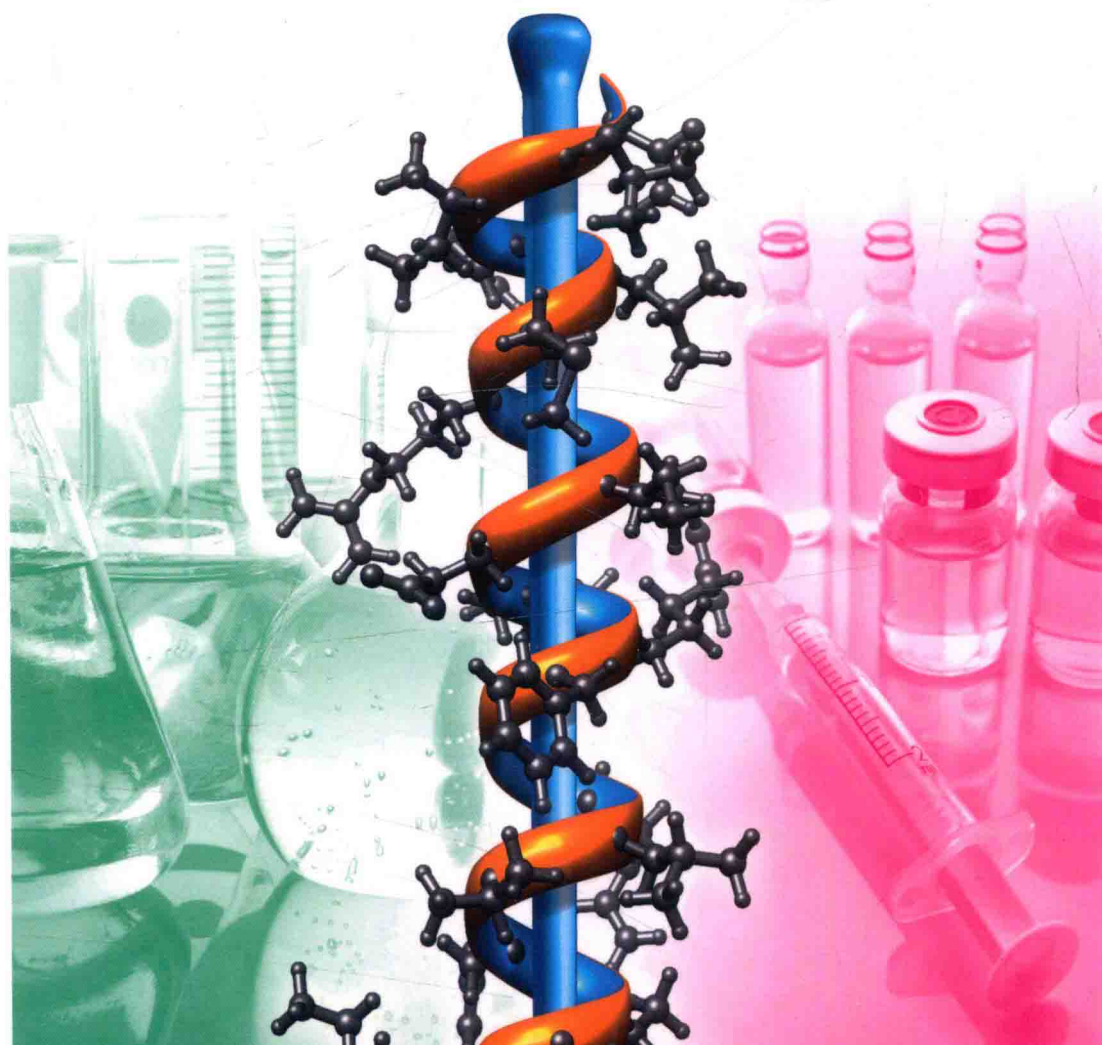


Edited by Miguel Castanho
and Nuno C. Santos

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Peptide Drug Discovery and Development

Translational Research in Academia and Industry



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Preface

The Timeliness of Peptide Drugs

Peptides make good drugs in challenging situations. They may be more expensive and time-consuming to produce than traditional small molecules, have low oral bioavailability, fast clearance in the body, and even, in some cases, be immunogenic. Yet, their ability to be very active, very specific, present very low toxicity, and often to be developed from natural endogenous scaffolds with known biological activity, makes them a desirable solution for unmet complex medical problems. This is not wishful thinking for the future, only. There are examples of very successful peptide drugs in clinical use. The key to this success is very much related to the mutual co-development of peptide biochemistry/biophysics, peptide synthetic chemistry, peptide pharmacology, and peptide biotechnology. This is the basic principle that underlies this book. Peptides have been the passion of many scientists and the investment of many entrepreneurs. Together they made a fantastic world with a very positive contribution to medicine. This book lets the reader know about this world, where peptides bounce between the bench and the bedside.

The numbers that reveal the achievements of peptide drugs are impressive. In 2008 six peptide drugs had attained global sales of US \$750 million. Reichert and colleagues say this figure is a consequence of the widespread acceptance of protein therapeutics by both physicians and patients, together with improvements in tackling problems such as a short half-life and challenges with the delivery of these molecules [1]. In the same study, these authors state that the number of peptide drugs entering clinical trials per year was 1.7 in the 1970s, 4.6 in the 1980s, 9.7 in the 1990s and 16.9 in the 2000s up to 2009. Until now, at least 55 therapeutic peptides have been approved for human clinical use by at least one regulatory agency, although 6 of them were withdrawn from their markets afterwards. The approval success rates for peptides that entered clinical trials from 1984 to 2000 were 21–24%. More than 15 peptide candidates were in phase III trials or under regulatory review in 2009; thus, it is expected the field of peptide drugs will continue its positive trend of progress during the years to come. Given the effort of both academic and industrial R&D to overcome the pitfalls of peptide drug candidates [2, 3] and the “scalability challenges” of peptide production [4], it is

predictable that peptide drug discovery and development will continue to prosper. We are not alone in our enthusiasm and optimism [5, 6].

From 2000 to 2007, peptides entering trials were most frequently treatments for metabolic disorders (26%). During the 1990s this fraction was less than 10% [1]. This variation shows how fast peptide drugs are evolving and their range of application being broadened. Areas which are today among the less frequent, such as infection and central nervous system, are being intensively researched and have a large potential to grow [4, 7–9]. They may be the future trend in peptide drug pipelines.

Despite all the peptide R&D figures above, the most important numbers are yet to be clearly ascertained: the number of lives saved by peptide drugs and the improvement in the patients' quality of life. These are the figures truly worth working for and we hope this book will transmit knowledge, power and enthusiasm to the readers so that this endeavour is reinforced.

Finally, we wish to thank all contributors to the book. We are proud of their collaboration and engagement to turn this book into something different: a book about academic research translated into pharma industrial development, written by people directly involved and/or privileged inside witnesses. The mission of authors and editors has been to involve the reader in this world. Be welcome!

Miguel Castanho

Nuno C. Santos

Lisbon, March 14, 2011

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