

Preface

The large size and variety of the human protein interactome and the obvious relevance of the protein–protein interactions in every physiological function, render protein–protein interactions at the same time an extremely challenging and attractive target for developing of new therapeutic substances. A further interesting aspect of targeting protein–protein interactions (PPI) for drug discovery is that, at least in some cases, molecules directed against PPI may provide a way to overcome the resistance mechanisms encountered for active site binding enzyme inhibitors. The considerations above can be extended to bacterial and viral interactome, further expanding the vastness and complexity of the subject of PPI inhibition and modulation.

For these reasons, there is no surprise that targeting PPI has become a subject of intense research activity in both industry and academia over the past decade. Reviewing the literature and the available databases shows that over 150 small molecule compounds have been found to inhibit about 20 PPI targets and that some of these molecules have already reached, or are about to reach, the drug market. As usual, these figures can have a double reading: the optimistic interpretation is that these successes demonstrate the validity of the approach, while the critics might say that the huge effort dedicated to find PPI inhibitors has resulted in scarce results. The fact is that exploring PPI is a stimulating new subject of study that is relevant for the basic knowledge on the chemistry of living organisms with the important outcome to offer the possibility of opening a new era of drug discovery.

This book is a collection of essays from Italian research groups from Industry and University involved in drug discovery and, although the book presents different subjects in each chapter, the unifying idea comes from our belief that only an integrated approach of the different techniques nowadays available, may overcome the challenges presented by this new frontier in drug discovery. For this reason,

the book opens with reviews about the current status of the research on PPI in drug discovery and goes on by presenting the state of the art in basic techniques like computational tools, NMR, X-ray crystallography and FRET that, integrated, may give the opportunity of success in this field.

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Stefano Mangani

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In Search of New Inhibitors

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