

agnostic approach that was based on ethnobotanical knowledge often fueled by serendipity. With the advent of modern molecular biology methods and based on knowledge of the human genome, drug discovery has now largely changed into a hypothesis-driven target-based approach, a development which was paralleled by significant environmental changes in the pharmaceutical industry. Laboratories became increasingly computerized and automated, and geographically dispersed research sites are now more and more clustered into large centers to capture technological and biological synergies. Today, academia, the regulatory agencies, and the pharmaceutical industry all contribute to drug discovery, and, in order to translate the basic science into new medical treatments for unmet medical needs, pharmaceutical companies have to have a critical mass of excellent scientists working in many therapeutic fields, disciplines, and technologies. The imperative for the pharmaceutical industry to discover breakthrough medicines is matched by the increasing numbers of first-in-class drugs approved in recent years and reflects the impact of modern drug discovery approaches, technologies, and genomics.

Keywords

Pharmaceutical research · Pharmaceutical industry · R&D productivity · Target-based drug discovery · Phenotypic screening · Lead discovery · Target discovery

1 The Beginnings of Modern Drug Discovery

Modern drug discovery is one of the most complex scientific areas and involves many different scientific disciplines. It has its origins at the end of the nineteenth century in the experimental biological and medical research of Claude Bernard, Louis Pasteur, Robert Koch, Paul Ehrlich, and Joseph Lister, as well as in the great advances in organic chemistry at the same time, and has ever since dramatically changed the practice of medicine, our culture, and sociology. About 1,500 unique drugs are currently known which act through more than 350 different mechanisms (Overington et al. 2006). With these, many diseases are now curable or can at least be controlled at the symptomatic level including bacterial, parasitic and viral infections, rheumatoid arthritis, asthma, osteoporosis, thrombosis and other cardiovascular disorders, diabetes, psychiatric diseases, and various cancers. Moreover, drugs have enabled many surgical procedures of modern medicine and even made cell and solid organ transplantation possible.

The first 100 years of modern drug discovery were largely target and mechanism agnostic and primarily driven by chemocentric approaches, i.e., approaches based on a specific compound or compound class which served as starting point for further optimization. These chemotypes were either discovered through ethnobotanical knowledge or derived from natural ligands and substances. Serendipity, however, was also an important success factor in many instances. In the following we list a few examples to illustrate how drugs were discovered during this time period.