

unsolved problems, structure-based drug design now is an integral part of many drug discovery programs. Major breakthroughs are represented by the publication of high-resolution 3D X-ray crystallographic structures of neurotransmitter receptors and transporters, e.g., determination of full-length GABA_A receptor and full-length dopamine transporter structures, both obtained after many years of extensive research. In Chapter 4, a number of examples of this impressive drug design approach are described.

As structural genomics, bioinformatics, and computational power continue to almost explode with new advances, further successes in structure-based drug design are likely to follow. Each year, new targets are being identified, and structures of those targets are being determined at an amazing rate, and our capability to capture a qualitative picture of the interaction between macromolecules and ligands is accelerating.

1.5 INDIVIDUALIZED MEDICINE AND CONCLUDING REMARKS

The mapping of the human genome leads us to the identification of new targets for therapeutic interventions, and even allows us to dream of the possibility of correcting genetic defects, enhancing our prospects for a longer and more healthy life, and for devising drugs for specific individuals. Presuming that individual variations in therapeutic response may have a genetic origin, and thus dividing populations into subgroups with similar genetic characteristics, might allow us to prescribe drugs and even dosages within these groups. This form of individual gene typing is already possible but still very resource demanding as per day's techniques. It is likely that perplexing species differences in response to, for example, chemotherapy, that complicates drug development, may also be understood, when the individual genome mapping becomes more elaborate and cheap.

The new biological capabilities raise many new prospects and problems for drug companies and, in general, for the society, not only scientifically but also morally. Scientific knowledge by itself is morally neutral, but how it is used, is not.

In conclusion, there has never been a more exciting time to take up the study of medicinal chemistry. The technological developments and the amount of information will grow with increasing speed, and scientists may eventually risk to be drowned in this multitude of possibilities. However, the intelligent, intuitive, and skilled medicinal chemist will be able to maneuver in this ocean of multiplicity and to continue the series of brilliant achievements by the pioneers in drug discovery during the past century.

FURTHER READING

- Anderson, A.C. 2003. The process of structure-based drug design. *Chem. Biol.* 10:787–797.
- Harvey, A.L., Edrada-Ebel, R.A., and Quinn, R.J. 2015. The re-emergence of natural products for drug discovery in the genomics era. *Nat. Rev. Drug Discov.* 14:111–129.
- Hughes, J.P., Rees, S., Kalindjian, S.B., and Philpott, K.L. 2011. Principles of early drug discovery. *Br. J. Pharmacol.* 162:1239–1249.
- Lindsay, M.A. 2003. Target discovery. *Nat. Rev. Drug Discov.* 2:831–838.
- Lipinski, C.A., Lombardo, F., Dominy, B.W., and Feeney, P.J. 2001. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Adv. Drug Deliv. Rev.* 46:3–26.
- Meanwell, N.A. 2011. Synopsis of some recent tactical application of bioisosteres in drug design. *J. Med. Chem.* 54:2529–2591.
- Morgan, S., Grootendorst, P., Lexchin, J., Cunningham, C., and Greyson, D. 2011. The cost of drug development: A systematic review. *Health Policy* 100:4–17.
- Patani, G.A. and LaVoie, E.J. 1996. Bioisosterism: A rational approach in drug design. *Chem. Rev.* 96:3147–3176.