

General Principles of Drug Design. Molecular Mechanisms of Disease

1. One rational approach to drug discovery that was discussed in the class relied on identification of molecular target, determining its three-dimensional structure, and then proceeding with the design based on the 3D structure of the target protein. However, for many important diseases, including osteoporosis, the targets are not well understood, and structures of some possibly good targets are not known. Discuss:
 - a) The prevalence and seriousness of osteoporosis; and which subgroups of population are most affected
 - b) What is known about molecular mechanisms behind osteoporosis
 - c) What approaches have been used, or could be used, to design drugs for the treatment of osteoporosis

2. Explain why good understanding of molecular mechanisms of the disease, combined with screening of random combinatorial libraries against well-identified targets may produce lead compounds that have reasonable in vitro activity but are likely to show low potency in vivo.