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Intranuclear Dynamics -- 3.3.3 Androgen Receptor Nuclear Accumulation and Intranuclear Dynamics -- 3.3.3.1 Androgen Receptor Nuclear Accumulation -- 3.3.3.2 Androgen Receptor Intranuclear Dynamics -- 3.4 Ligand-Dependent Intranuclear Localization -- 3.5 Ligand-Independent Trafficking -- 3.5.1 Thyroid Hormone Receptor Intracellular Trafficking -- 3.5.2 Retinoic Acid Receptor Intracellular Trafficking -- 3.6 Retinoid X Receptor and Vitamin D Receptor Intracellular Trafficking: A Bin of Their Own? -- 3.7 Conclusions. References -- Chapter 4: Chemical Considerations in Discovery of Receptor Modulators -- 4.1 Introduction -- 4.2 Intermolecular Binding Forces Drive Ligand Action -- 4.3 Sterics and Hydrophobicity in Ligand Binding -- 4.4 Stereochemical Considerations -- 4.5 Molecular Dynamics as a Tool for Modulator Design -- 4.6 Case Study: A Holistic Approach to Liver X Receptor Modulator Design -- 4.7 Conclusions -- References -- Chapter 5: Structure-Based Design of Estrogen-Related Receptors Modulators -- 5.1 Introduction -- 5.2 Structure and Function -- 5.3 Medicinal Chemistry of ERR Modulators -- 5.3.1 ERR Inverse Agonists -- 5.3.2 ERRs Agonists -- References -- Chapter 6: PPAR and Ligand Design: Honing the Traditional Empirical Method with a More Holistic Overview -- 6.1 Introduction to the PPAR Protein -- 6.1.1 Overall PPAR LBD Protein Structure -- 6.1.2 Mechanism of PPAR Gene Transcription -- 6.1.3 Differences in LBD Between PPAR Subtypes -- 6.2 Catalogue of Known Ligands -- 6.2.1 PPAR Ligands -- 6.2.1.1 PPAR Full Agonists -- WY14643 or Pirinixic Acid -- GW590735/Compound 25a -- Pemafibrate -- 6.2.1.2 PPAR Antagonist -- GW6471 -- 6.2.2 PPAR Ligands -- 6.2.2.1 PPAR Full Agonists -- GW2433 -- GW2331 -- LC1765 -- Compound 48 -- Isoquinoline Compound 5 -- TIPP-204 -- GW0742 -- GW501516, Compounds 1-16 -- Compound 18 and Compound 13 -- 6.2.2.2 PPAR Partial Agonists -- Compound 2 -- GW9371 -- 6.2.3 Dual or Pan Agonist Ligands -- 6.2.3.1 PPAR/ Dual Agonists -- GW409544 -- Azetidinone Compounds 17 and 35 -- GL479 -- 6.2.3.2 PPAR/ Dual Agonists -- TIPP-401 -- 6.2.3.3 PPAR/ Dual Agonists -- Phenoxyacetic Acid Compounds 10 and 21 -- Sulfonylthiadiazole Compounds 6, 11t and 20a -- 6.2.3.4 Pan Agonists -- Indeglitazar -- TIPP-703 -- AL29-26 -- 6.2.3.5 Endogenous Agonists -- Eicosapentaenoic Acid (20:5 EPA) -- Vaccenic Acid (18:1) -- Iloprost. 17(S)-oxoDHA (22:6) -- 6.3 Ligand Design Factors -- 6.4 Tools and New Information -- 6.4.1 Examples of Computer-Aided Drug Design -- 6.4.2 Pharmacokinetics and Pharmacodynamics -- 6.4.3 Wider Considerations for PPAR -- 6.4.3.1 LBD Mutations -- 6.4.3.2 PPAR Intact Structure and Implications -- 6.4.3.3 Coregulators and FABPs -- 6.5 Conclusion -- References -- Chapter 7: Pregnane X Receptor: Understanding Its Function and Activity at the Molecular Level -- 7.1 Introduction -- 7.2 The Chemical Landscape of PXR Ligands -- 7.3 The Structural Architecture of PXR -- 7.4 Dimerization of PXR -- 7.5 Coregulatory Recruitment to PXR -- 7.6 AF-2 Helix Orientation Dictates PXR's Activation -- 7.7 Ligand Binding Stabilizes the Structure of PXR -- 7.8 Ligand-Binding Site of PXR and Ligand Promiscuity -- 7.9 Species Selectivity in PXR Activation -- 7.10 PXR Inhibitors -- 7.11 PXR Agonists as Therapeutics -- 7.12 Conclusion -- References -- Chapter 8: Strategies for the Design of Vitamin D Receptor Ligands -- 8.1 Introduction -- 8.2 Secosteroid VDR Ligands -- 8.3 Non-secosteroid VDR Ligands -- 8.4 VDR Antagonists -- 8.5 Concluding Remarks and Future Directions -- References -- Chapter 9: What Makes a Good Antagonist: Lessons Learned from the Estrogen and Aryl Hydrocarbon Receptors -- 9.1 Introduction: What Is an Antagonist? -- 9.2 Identification and Development of ER Antagonists -- 9.2.1 A Brief

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14.10 Sjögren's Syndrome (SS).
