Part

2

Theoretical Considerations

The use of appropriate measures of nicotine dependence remains a key area for future research on the effects of genes and gene-environment interaction on tobacco use. This part examines the theoretical basis for constructs that may link heritable genetic traits with observable measures of nicotine dependence, including phenotypes representing a causal path between specific genetic actions and measures of nicotine dependence, as well as endophenotypes measuring indirect influences such as those found prior to nicotine exposure.

The first chapter of this part examines theoretical issues in establishing nicotine-dependence phenotypes in humans, including new and existing measures of nicotine dependence, as well as traits that may link specific genetic actions and measures of nicotine dependence. A subsequent chapter explores key issues in using mouse models of nicotine dependence. These issues include the use of nicotinic acetylcholine receptors to examine tissue-specific responses to nicotine within specific genetic strains, relating routes of administration in mice to the physiology of human smoking, and correlating mouse models of nicotine-response behavior with nicotine dependence in humans.