Preface

Alcohol consumption is often characterized as an environmental stress to the organism. In response to the stress of alcohol exposure, complex cellular and organismal adaptations occur to manage this insult. In most individuals, modest alcohol consumption over the course of a lifetime does not result in substantive health risks, and in the pathophysiology of some diseases, such as type 2 diabetes, modest alcohol consumption may actually be protective. Yet, chronic and heavy alcohol consumption poses significant health risks. Scientists who study the effects of acute and chronic alcohol consumption know little about what marks the transition from a benign or even protective effect of alcohol to its pathophysiological effect in the development of tissue injury and disease.

Understanding the transition to injury is an important clinical and public health issue, as excessive alcohol consumption can impact nearly every tissue in the body, contributing to more than 60 different medical conditions. The effects of excessive alcohol occur both in the developing organism as well as in the adult. Although the liver, as the site of ethanol metabolism, is particularly sensitive to chronic alcohol exposure, alcohol consumption also leads to damage of other tissues, including brain, heart, and cardiovascular system, as well as disruptions in regulation of endocrine and immune systems. The contribution of alcohol to the development of chronic diseases, such as osteoporosis, heart disease, and diabetes, is particularly relevant today, given the increased incidence of these diseases in our aging population.

Recent advances in understanding the pleiotropic effects of ethanol have been possible because of the development of relevant and rigorously controlled animal and cell culture models of acute and chronic ethanol exposure. Although each of the various models for ethanol exposure may not model perfectly the exposure of humans to alcohol, many model systems have now been developed that can mimic particular conditions of ethanol exposure in target tissues and organs. One of the primary goals of this volume is to provide detailed procedures for several of the more common models of acute and chronic ethanol exposure, enabling studies on the effects of ethanol in both the developing organism and in the adult. Use of these clearly defined models of ethanol exposure, presented in the first section of this volume, will allow for comparison of results among different laboratories, as well as among multiple tissue and organ targets of acute and chronic ethanol exposure.

One of the themes arising in recent studies that investigate the mechanisms of ethanol action on target tissues is the commonality in the impact of ethanol on regulation of cellular metabolism. Thus, in addition to the effects of acute and chronic

alcohol on the complex physiology of the intact organism, alcohol exposure also has a profound impact on the biology of individual cells. As with studies in whole animals, investigations to study the impact of ethanol on cellular biology must be rigorously controlled and designed. Recent advances in the development of specific methodologies to mimic the impact of ethanol metabolism in cultured cells, detailed in the second section of this volume, have furthered our understanding of the molecular mechanisms by which ethanol disrupts cellular function.

Although there are common mechanisms of ethanol action on a variety of cell types, studies of the effects of ethanol on cellular function must also take into consideration the complex differentiated function of individual cells and tissues. Thus, expertise in the use of models of ethanol exposure, as well as in the design and analysis of experiments to ascertain the effects of ethanol on the highly regulated function of each differentiated cell and tissue type, must be combined to finely dissect the mechanisms of ethanol action. Therefore, an additional theme of this volume embraces the methodologies to investigate a variety of cells and tissues that are known to be disrupted by ethanol, from intestinal epithelial cells, to cells in the liver, including hepatocytes and Kupffer cells, to cells in the periphery, including skeletal muscle, adipose and bone. Specific methodologies to investigate the effects of ethanol on neuronal function, including the use of neuronal cell lines and organotypic cultures, are also presented.

It is likely that the effects of ethanol on cell, tissue, and organismal function are fundamentally based on the impact of ethanol on transcriptional and post-transcriptional regulation of gene expression. Novel methodologies to study the molecular mechanisms of ethanol action include the use of gene arrays, as well as proteomic analysis of the post-translational modifications of proteins in organelles and cells exposed to ethanol. Chapters providing the specific expertise required for the design and analysis of gene array and proteomic studies are included in this volume to enable investigators new to these data-rich approaches to successfully "mine" the vast amount of data that can be obtained by these approaches.

In the final analysis, studies into the molecular mechanisms for ethanol action not only result in a further understanding of the pathophysiology of ethanol-induced injury, but also contribute to our understanding of the fundamental mechanisms by which organisms have adapted to subtle changes in their environment. Although excessive alcohol consumption can result in profound impairments in the ability of the organism to develop and function, most organisms can readily handle the subtle insults associated with moderate alcohol consumption. Understanding the genetic, molecular, cellular, and physiological responses to ethanol that "tip the balance" from an adaptive response to a maladaptive/pathological response is critical to the development of therapeutic strategies for the intervention and/or prevention of the effects of ethanol on development and tissue injury. I hope that the very detailed and specific methods presented in this volume will further spur investigators to delve into the complex and fascinating story of the adaptive and maladaptive responses humans have developed to the consumption of alcohol.

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