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X.1. Introduction

The primary function of the immune system is to destroy or neutralize pathogens and their toxic products and to protect the host from certain types of neoplastic cells. To successfully combat these challenges, all potential portals of entry, including the gastrointestinal, genitourinary and pulmonary systems and skin, are protected by specialized immune cells and tissues. The protective strategy is generally effective at preventing many types of acute infectious diseases, as demonstrated by a relatively low background rate of infection in spite of constant exposure to potentially pathogenic organisms. On the other hand, staging defenses to protect portals of entry

against outside threats increases the likelihood of defenders encountering chemical and physical agents that are able to modulate immune function, reducing resistance to infectious agents or increasing the risk allergic responses to otherwise innocuous plant, animal or chemical entities. Adverse exposure effects may be expressed locally (e.g., pulmonary and contact allergic hypersensitivity) and/or systemically (altered infection resistance, systemic allergic hypersensitivity, autoimmune disease[AID]), depending on absorption, distribution and (in some cases) site of metabolism to an active moiety. Although the clinical presentation of adverse effects (suppression, allergy, autoimmunity) are often unique, each type of immunotoxicity may be caused by disruption of the same immune homeostatic pathway(s), and immunotoxicity hazard identification testing strategies typically include assays of apical function that may be altered by multiple modes of xenobiotic action. The majority of immunotoxicity hazard identification data is generated in laboratory rodents; nevertheless, experimental data generated under laboratory conditions tends to reliably predict effects in exposed humans and to share modes of immunotoxicant action. This chapter will therefore focus on strategies used to identify immunotoxicants, immunotoxicity modes of action and utilization of experimental immunotoxicity data for human health risk assessment. A short overview of basic immunology concepts is presented to set the stage for subsequent sections.

X.2. Overview of the immune system

X.2.1 Organization

The immune system is comprised of primary (bone marrow and thymus) and secondary (spleen, lymph nodes and specialized collections of specialized lymphocytes) organs. The primary organs serve as sources of immune system cells. Hematopoietic stem cells in the bone marrow give rise to common myeloid and lymphoid progenitor subpopulations that differentiate