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Species Differences in the Structure and Function of the Immune System (13-Nov-2004)

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For toxicologists and pathologists, questions of relevancy of laboratory animal-derived toxicology data for use in human risk assessment are frequently raised. This critical issue is particularly complex in immunotoxicology and it is unclear how species differences in the structure and function of the immune system impact the extrapolation of animal data to humans. In addition to recognition of species differences, it is important to identify which differences are biologically relevant for the endpoint being considered. It is the premise of this review that extrapolations from animals to man are necessary, but may not always be appropriate for a given species due to differences in the structure and function of the immune system.

The dramatic advancement in murine immunology over the last 40 years has led to the incorrect tendency to assume that all laboratory animals are immunologically similar to mice, and that mice are immunologically identical to humans. Unfortunately, studies that specifically attempt to identify and characterize species differences in immune structure and function, such as that by Lang et al (1993) and Smialowicz et al (1994), are few, and the characterization of most species differences are based on the comparison of data obtained from published results from many different laboratories collected under highly variable conditions.

Some examples of such species differences are as follows. Rats exposed to organotin develop thymic atrophy with concomitant deficits in cell-mediated immunity, whereas mice and guinea pigs do not (Seinen et al, 1979; Miller and Scott 1985; Vos et al, 1985). However, dioxin produces thymic atrophy and decreases in some humoral and cellular immune responses in all three species (Vos et al, 1980). Moreover, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) results in dose-related suppression of humoral immunity to sheep red blood cells (SRBC) in mice but an enhancement of this response in rats (Smialowicz et al, 1994). Thus, data obtained from the evaluation of a single compound in a single species may be insufficient to predict the response to the same compound in a different species.

Another example concerns laboratory animal models of chronic beryllium disease (CBD), an immune-mediated pulmonary granulomatous disease of humans that follows the inhalation of beryllium (Be) (Newman et al, 1989). In man, Be-specific cell-mediated immune responses within the lung result in an insidious and progressive granulomatous and fibrotic pulmonary disorder that may result in death. Rats exposed to Be by inhalation develop foreign-body granulomatous inflammation of the lung in the absence of Be-specific immune responses within the blood or lung (Haley et al, 1990). Alternatively, dogs and monkeys develop immune-mediated granulomatous inflammation within the lung accompanied by an increase in lung lymphocytes and Be-specific, cell-mediated immune responses within the blood and lung (Haley et al, 1989a; Haley et al, 1992; Haley et al, 1994). In this case, the dog and monkey respond to the inhalation of Be in a manner very similar to that of man and may therefore be more appropriate animal models as compared to rats for investigating the pathogenesis of CBD.

The following review is not meant to be exhaustive, and in some cases only a single example of a pertinent species difference will be highlighted. The intent of this review is to sensitize the investigator to potential species differences in the structure and function of the immune system, and the potential impact such differences may have on the extrapolation of data to man.

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