In most cases, initial assessment of the impact on the immune function is done in the in vivo toxicity screening studies by hematological and histopathological examination. In case of concern because of the mode of action, additional parameters such as immunophenotyping of leukocytes or measurement of immunoglobulins may be included in such studies.

13 Omics Technologies

The neologism omics is a suffix for a series of technologies in life science, where pools of biological molecules are concomitantly analyzed by appropriate technologies. In the field of toxicology, toxicogenomics (i.e., the broad spectrum mostly array-based analysis of gene expression) and metabolomics (i.e., the analysis of metabolites in various body fluids by NMR and/or mass spectroscopy after adequate chromatographical separation) have found their entry. The development of toxicogenomics was largely triggered by the advent of the Human Genome Project (Burczynski et al. 2000). However, the big hope to resolve toxicological issues or even revolutionize toxicology by this technology has not been fulfilled. Despite large investments, predictive toxicology, which describes the identification of toxicities by gene expression analysis ideally in in vitro systems, plays no longer a significant role in early drug development. The main reason is the discrepancy between the in vitro test systems and the whole organism with regard to base-level gene expression and onset of gene expression upon a toxic insult (Pognan 2004). On the other hand, toxicogenomics, incorporated into an in vivo study, can provide valuable insights in the mechanisms of toxicity, particularly if the time course of the expression profile is investigated in such a study (Lühe et al. 2005).

Metabolomics can be regarded as an extension of single-analyte determination in conventional clinical chemistry (e.g., cholesterol, glucose, etc.) where the metabolite profile is broadened by using adequate technologies. The advantage of this technology in contrast to toxicogenomics is its low invasiveness, i.e., the body fluid can be collected over several time points in a study without killing the animal. As such the technology has the potential to identify new biomarkers (e.g., bile acids for cholestasis). Similar to toxicogenomics, the large data set resulting from such approaches prevent its use in early screens. However, inclusion into in vivo studies might provide valuable mechanistic insight. Key for the interpretation of metabolomics studies is the access to reference data sets. The sensitivity of metabolomics versus classical regulatory toxicology has been recently assessed for 500 compounds. Comparable sensitivity to classical toxicology assessment was noted in 75% of the cases, increased sensitivity of metabolomics in 8%, and decreased sensitivity in 18% of the cases, thus proving the potential of this technology (van Ravenzwaay et al. 2014).