

Carcinogenesis Modeling: Results Reflect Representation

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The National Institute of Environmental Health Sciences (NIEHS) Predictive–Toxicology Evaluation (PTE) Project identifies standardized chemobioassays being performed by the National Toxicology Program (NTP), disseminates detailed information, and encourages researchers from a wide variety of disciplines to generate predictions using whatever approaches they find best and publish them in peer–reviewed journals. This effort has been augmented by Challenges sponsored by IJCAI–99 and ECML/PKDD–01. Overall, three PTE experiments focused on modeling chemocarcinogenesis in rodents have been conducted over the past decade. Each is a collaborative experiment that draws upon a broad range of cross–disciplinary resources, to develop and evaluate the performance of predictive models, objectively and rigorously. Both the design of each PTE experiment and the approaches used by model developers reflect a variety of hypotheses, i.e., perceptions or beliefs, about the nature of the problem. Analysis of results from the three PTE experiments leads to conclusions and insights that may help guide future research efforts. For example, the analysis of model performance across NIEHS PTE1 and PTC 2000–2001 shows how learning sets containing attributes that reflect possible interactions between chemical structure and biological system outperform those that contain attributes of chemical structure only. Alternative representations of the endpoint have hardly been explored, yet provide opportunities to discover features and relationships that may govern trans–species and gender effects. Examples taken from various models and PTE experiments are the basis for conclusions drawn.