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Mechanism based molecular design of chemicals with low carcinogenicity potential

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Chemical exposures represent one of the many environmental risk factors for cancer. Over a thousand new chemicals are introduced into the global stream of commerce annually. Most of these compounds have not been assessed in carcinogenicity studies in animals. Because of this, there is an urgent need to design safer chemicals with low carcinogenic potential to reduce the risk of human cancer. For many classes of carcinogenic compounds, the molecular basis of carcinogenic activity is known in considerable detail. The understanding of molecular mechanisms and structural features that affect carcinogenesis by various types of chemical carcinogens formed the basis for identifying suspect carcinogens by Structure-Activity Relationship (SAR) analysis. With the availability of carcinogenicity and mutagenicity data for a substantial number of chemical classes, SAR analysis has identified general as well as specific structural features that can either enhance or diminish the carcinogenesis and the relationship between molecular structure and carcinogenic activity not only can assist in identifying suspect carcinogens but also in designing chemicals of lower carcinogenic potential, since very minor structural changes can decrease or abolish the carcinogenicity of certain chemicals. This presentation will provide an overview of the use of mechanism-based SAR in the evaluation of several classes of electrophilic or potentially electrophilic chemicals and how to design compounds with lower carcinogenic potential.

Biography

David Y Lai completed his PhD in Biochemistry at the Medical College of Georgia and completed Postdoctoral research fellowships on chemical carcinogenesis at Tulane University Medical Center. He has worked at the US Environmental Protection Agency since 1987 and is currently a Senior Toxicologist in the Risk Assessment Division, Office of Chemical Safety and Pollution Prevention. He is an internationally recognized expert in Structure-Activity Relationships (SAR) and cancer risk assessment of chemical substances, including nanomaterials. He is the author/coauthor of 3 monographs, over 10 book chapters, and more than 50 publications in peer-reviewed scientific journals. He currently serves on the editorial board of the *Journal of Environmental Science & Health*.

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