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Nanomaterial carcinogenicity: Role of cancer stem cells and tumor microenvironment

Tumor Microenvironment (TME) has been recognized as a key determinant of tumorigenesis and metastasis, but how TME is affected by nanomaterials is largely unknown. We demonstrated that certain nanomaterials including Carbon Nanotubes (CNTs) can affect TME by activating Cancer-Associated Fibroblasts (CAFs) to promote tumor growth and metastasis of human lung cancer cells. This effect of CNTs is dependent on the physicochemical characteristics of CNTs such as tube wall number and surface reactivity and functionalization. Single-walled CNTs and to a lesser extent multi-walled CNTs and their COOH-functionalized forms strongly induce CAFs, which was shown to promote tumor formation of preexisting human lung cancer cells and CNT-transformed lung epithelial cells. The mechanism by which CNT-induced CAFs promote tumor growth involves acquisition of Cancer Stem Cells (CSCs) in the TME, which drives tumor growth and metastasis. Gene knockdown experiments showed that an expression of podoplanin on CAFs is essential for the tumor-promoting and CSC-inducing effects of CNTs. Together our findings indicate a novel role of TME in promoting CNT-induced carcinogenesis through the activation of podoplanin-associated CAFs that support CSC expansion and tumor growth. Our results also suggest the potential utility of podoplanin as a mechanism-based biomarker for CNT-induced malignancies.

Biography

Yon Rojanasakul is a Professor and Leader of the Sara and James Allen Comprehensive Lung Cancer Program at West Virginia University Cancer Institute, USA. He is also a Guest Scientist at the National Institute for Occupational Safety and Health. He has received his PhD in Pharmaceutical Sciences from the University of Wisconsin-Madison in 1989 and has since worked as a full-time Faculty Member at West Virginia University. His research is in the areas of environmental toxicology, nanotechnology and molecular carcinogenesis. His research focus is on cellular and molecular mechanisms of lung carcinogenesis induced by environmental agents including nanomaterials and heavy metals and on nanomedicine and anticancer drug discovery. He has published over 250 peer-reviewed original research articles in reputable journals and has served as a Grant Reviewer for the NIH and NSF and as an Editorial Board Member for many scientific journals.

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