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Proteomic biomarkers of cancer susceptibility from blood of girls exposed to Bisphenol A and Genistein

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Using blood and urine collected from prepubertal girls, we investigated proteomic biomarkers of cancer susceptibility. Proteomic analysis of blood serum utilized immunodepletion of the seven most abundant proteins using the Seppro IGY-R7 column system (Sigma). The flow-through fractions were digested, labelled, and combined with unique Isobaric Tandem Mass Tags (TMTs), and analyzed by an on-line automated 14 Fraction nano-LC-ESI-MS (SCX/ RP) MuDPIT (PQD-LTQXL ThermoFinnigan). From the serum of prepubertal girls containing high urine concentrations of BPA and genistein, we were able to identify 1992 and 1364 peptides of which 97 and 59 were unique, respectively. In blood of girls with high concentrations of BPA in the urine, the proteins KI-67 and Intersectin (ITSN1) were up-regulated, and Deleted in Liver Cancer (DLC1) was down-regulated. Ki-67 is a cancer antigen presently being used as a tumor marker. ITSN1 is a scaffolding protein that regulates phosphotidyl-inositol 3-kinase and proliferation. Gene expression of DLC1 has been reported to be lower in breast carcinomas. In blood of girls with high urinary concentrations of genistein, Ribosomal L29 (RPL29), Eukaryotic Initiation Factor 3a (eIF-3a) and Endothelium-Converting Enzyme (ECE-1) were down regulated. Up-regulated RPL29 has been associated with a poor outcome for carcinomas of the breast, colo-rectum and esophagus. Expression of eIF-3a was elevated in breast cancer tissues compared with paired normal mammary tissues. Over expression of ECE-1 is associated with unfavorable outcome for breast cancer treatment. These data demonstrate that TMT-MS technology can be used for the identification of biomarkers of cancer susceptibility in human serum.

Biography

Coral A Lamartiniere earned his PhD from Louisiana State University. He has trained at the University of Texas Southwestern Medical School, Der Georg-August Universitat Göttingen in Germany, Columbia University in New York, and worked at the National Institute of Environmental Health Sciences. He is Professor Emeritus at the University of Alabama at Birmingham. Dr. Lamartiniere's research interest lies in the potential of environmental chemicals to predispose for mammary cancer.

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